

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2021

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO

Commission File Number **001-38560**

AADI BIOSCIENCE, INC.

(Exact name of Registrant as specified in its Charter)

Delaware

EIN **61-1547850**

(State or other jurisdiction of incorporation or organization)

(I.R.S. Employer Identification No.)

17383 Sunset Boulevard Suite A250, Pacific Palisades, CA
(Address of principal executive offices)

90272

(Zip Code)

Registrant's telephone number, including area code: (424) 473-8055

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, \$0.0001 par value per share	AADI	The Nasdaq Stock Market LLC

Securities registered pursuant to section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES NO

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES NO

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES NO

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (\$232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES NO

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer

Non-accelerated filer Smaller reporting company

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market on June 30, 2021 was approximately \$60,377,007.

The number of shares of registrant's common stock outstanding as of March 11, 2022 was 20,929,715.

DOCUMENTS INCORPORATED BY REFERENCE

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Forward-Looking Statements

This Annual Report on Form 10-K (“Annual Report”) contains express or implied forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”) and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”) that are based on our management’s belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- our ability to maintain regulatory approval for FYARRO in advanced malignant perivascular epithelioid cell tumors (“PEComa”) or to obtain regulatory approval in additional indications, or any other product candidates we may develop in the future, and any related restrictions, limitations or warnings in the label of an approved product candidate;
- our plans and potential for success relating to commercializing FYARRO, or any other product candidate that we may develop, if approved;
- our plans related to the further development and manufacturing of FYARRO;
- the timing, scope or likelihood of regulatory filings and approvals for FYARRO for malignant PEComa in foreign jurisdictions and any additional indications we may pursue and any other product candidates we may develop in the future;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of FYARRO and any other product candidates we may develop in the future, if approved;
- the rate and degree of market acceptance of FYARRO and any other product candidates we may develop in the future, if approved;
- the timing, progress and results of preclinical studies and clinical trials for our programs and product candidates, including the anticipated impact of the COVID-19 pandemic, statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- our ability to recruit and enroll suitable patients in our clinical trials;
- the expectations regarding the beneficial characteristics, safety, efficacy and therapeutic effects of FYARRO and any other product candidates that we may develop in the future;
- our ability to develop and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and our strategic plans for our business, product candidates, technology and our discovery engine;
- our ability to establish or maintain collaborations or strategic relationships or obtain additional funding;
- our ability to contract with and rely on third parties to assist in conducting our clinical trials and manufacturing our product candidates;
- the size and growth potential of the markets for FYARRO and any other product candidates we may develop in the future, if approved, and our ability to serve those markets, either alone or in partnership with others;
- our ability to obtain funding for our operations, including funding necessary to commercialize FYARRO and to complete further development, approval and, if approved, commercialization of FYARRO in additional indications and any other product candidates we may develop in the future;

- the period over which we anticipate our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements;
- the potential for our business development efforts to maximize the potential value of our portfolio;
- our ability to compete with other companies currently marketing or engaged in the development of treatments for the indications that we are pursuing for FYARRO and any other product candidates we may develop in the future;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- our financial performance;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

Forward-looking statements are not historical facts, but rather are based on current expectations, estimates, assumptions, and projections about the business and future financial results of the pharmaceutical industry, and other legal, regulatory and economic developments. In some cases, you can identify forward-looking statements by terms such as "may," "will," "intend," "should," "could," "would," "expect," "plan," "anticipate," "believe," "estimate," "project," "predict," "potential," "continue," "likely," and similar expressions (including their use in the negative) intended to identify forward-looking statements although not all forward-looking statements contain these identifying words. Actual results could differ materially from the results contemplated by these forward-looking statements due to a number of factors, including, but not limited to, those described in Part I, Item 1A, Risk Factors of this Annual Report.

You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Annual Report and the documents that we reference in this Annual Report and have filed with or furnished to the U.S. Securities and Exchange Commission (the "SEC") completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company focused on developing and commercializing precision therapies for genetically defined cancers with alterations in mTOR pathway genes. Our lead drug product, FYARRO™, (*nab*-sirolimus) is a form of sirolimus bound to albumin. Sirolimus is a potent inhibitor of the mTOR biological pathway, the activation of which pathway can promote tumor growth, and inhibits downstream signaling from mTOR.

We have an exclusive license with Abraxis BioScience, LLC, a wholly owned subsidiary of Celgene Corporation, now Bristol Myers Squibb Company (“Celgene”), under which we obtained exclusive rights to develop, manufacture, and commercialize FYARRO, previously called ABI-009, *nab*-sirolimus, provided that we have granted to EOC Pharma (Hong Kong) Limited exclusive rights to develop and commercialize FYARRO for the Greater China region.

Throughout this document we refer to FYARRO, (*nab*-sirolimus, sirolimus protein-bound particles for injectable suspension (albumin-bound)) as FYARRO in the context of commercialization for the treatment of advanced malignant perivascular epithelioid cell tumors (“PEComa”), investigational use, our clinical trials and our license agreement with Celgene, all further discussed below and throughout this document.

In November 2019, we announced top-line results from the AMPECT study, including that the study achieved its primary endpoint of overall response rate (“ORR”), as determined by blinded independent central radiologic review using modified Response Evaluation Criteria in Solid Tumors, (“RECIST”) v1.1. In October 2021, the results of the AMPECT study with long-term follow up were published in the Journal of Clinical Oncology.

In May 2021, we completed the filing of a rolling new drug application (“NDA”) for FYARRO to the U.S. Food and Drug Administration (the “FDA”), for approval to treat patients with advanced malignant PEComa. The NDA was based on results from our Phase 2 registration-directed study, Advanced Malignant PEComa Trial, (“AMPECT”), in advanced malignant PEComa for which there were, prior to FYARRO, no approved therapies in the United States and for which there had never been a prior prospective clinical trial. The FDA accepted the NDA in July 2021, and we were granted approval for commercial sale on November 22, 2021.

During the first quarter of 2022, we launched FYARRO in the United States for treatment of advanced malignant PEComa and are evaluating in cancers with known mTOR pathway activation, including tumor agnostic indications targeting specific genomic alterations that activate the mTOR pathway.

In advanced malignant PEComa, other than FYARRO, there are no existing FDA approved therapies or drugs that have been studied in prospective clinical trials. Following FDA approval, the National Comprehensive Cancer Network (“NCCN”) Sarcoma panel included FYARRO as the only preferred regimen for treatment of malignant PEComa.

We have been actively engaged in commercial preparations to support the U.S. launch of FYARRO for the treatment of patients with advanced malignant PEComa. We have built a cross-functional commercial team consisting of marketing, market access, commercial operations, and sales. We have also built commercial infrastructure and capabilities designed to scale when necessary to support future commercial launches. The commercial team is hired and is educating the U.S. market.

In addition to advanced malignant PEComa, based on data from the completed AMPECT trial and our expanded access program, we have initiated a registration-directed tumor-agnostic Phase 2 study (“PRECISION 1”) of FYARRO in patients with Tuberous Sclerosis Complex 1 and 2 (“TSC1” & “TSC2”) alterations. We have completed a Type B meeting with the FDA in which we discussed the initial trial design and the PRECISION 1 trial is now open for enrollment in the United States.

We have built a management team with extensive experience in the discovery, development, and commercialization of cancer therapeutics, including in senior roles at leading oncology companies. We are supported by our board of directors and specialized scientific advisors, who contribute their deep understanding of drug discovery and development, as well as expertise in building public companies and business development. Furthermore, our investor base includes top life science investors. We believe that our team is well positioned to develop and commercialize FYARRO and future pipeline assets to ultimately bring significant benefit to cancer patients worldwide.

Our Strategy

Our objective is to develop and commercialize innovative drugs that address the serious unmet medical needs of cancer patients and patients with other diseases that are driven by alterations in the mTOR pathway. The principal components of our strategy include:

- ***Commercialize FYARRO in advanced malignant PEComa.***

For FYARRO, we are initially targeting advanced malignant PEComa, an ultra-rare sarcoma with no approved therapies. In May 2021, we completed the filing of a rolling NDA submission with the FDA for FYARRO for the treatment of advanced malignant PEComa based on the positive results from AMPECT, our pivotal Phase 2 study in this patient population, which met its primary endpoint. The FDA accepted the NDA in July 2021 and we were granted approval for commercial sale on November 22, 2021. We have built a cross functional commercial team and infrastructure and launched FYARRO for advanced malignant PEComa in the United States in the first quarter of 2022.

- ***Expand the market opportunity for FYARRO by pursuing development of a tumor-agnostic indication in cancer patients with alterations in the TSC1 or TSC2 genes.***

We have presented initial data for FYARRO in patients with different cancer types having alterations in the *TSC1* or *TSC2* genes as part of an expanded access program. Based on data in patients with *TSC1* or *TSC2* alterations from the completed AMPECT trial and the expanded access program, in the first quarter of 2022, we have initiated a registration-directed tumor-agnostic study called PRECISION 1 in patients with solid tumors driven by *TSC1* or *TSC2* alterations. We believe that this approach offers an opportunity to significantly expand the commercial potential of FYARRO over time.

- ***Expand the application of FYARRO as a monotherapy and combination therapy with other agents.***

We believe there is a significant opportunity to utilize FYARRO in other indications as a monotherapy as well as in combination with other targeted therapies, particularly in mTOR adjacent signaling pathways. These additional indications may be important drivers of commercial value and we believe that strategic partnerships, particularly in combination therapies, may be an effective means of developing and commercializing these opportunities. While we are primarily focused on cancer, the mTOR pathway is also relevant in other indications and we may opportunistically study these indications to broaden the application of FYARRO or satisfy unmet medical needs.

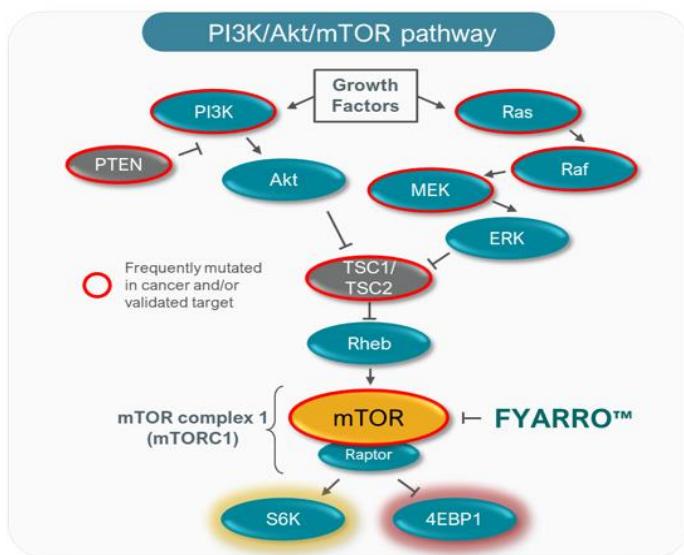
- ***Establish capabilities and partnerships to effectively commercialize and maximize the value of FYARRO.***

We have built capabilities in the United States to commercialize our products. We have partnered FYARRO with EOC Pharma Limited for commercialization in Greater China. Outside the United States and China, we intend to selectively evaluate strategic partnerships with partners whose development and commercial capabilities complement our own.

Importance of the mTOR Pathway in Cancer

mTOR is a serine–threonine kinase that is the key component of two multi-subunit complexes with non-overlapping downstream targets: mTOR Complex 1 (“mTORC1”) and mTOR Complex 2 (“mTORC2”). mTORC1 plays a vital role in the regulation of cell growth and division by controlling the balance between anabolic and catabolic cellular processes and facilitates the progression of cell-cycle from G1 to S phase. Due to its key role in anabolic processes needed for cell division, the majority of cancer cells have activation of mTORC1 through one mechanism or another. Thus, the effective inhibition of mTORC1 in cancer cells may inhibit their proliferation. Activation of mTORC1 may occur downstream of the PI3K/AKT or Ras/MEK/ERK pathways, or through inactivating alterations in negative regulators of the mTORC1 pathway, including *TSC1* or *TSC2*. Downstream signaling nodes of mTORC1, specifically S6K and 4EBP1, are key drivers of mTORC1 activity. Decreased phosphorylation of S6K leads to decreased activity, while decreased phosphorylation of 4EBP1 leads to increased activity. Sirolimus (also known as rapamycin) is an allosteric inhibitor of mTOR, which binds to the 12-kDa FK506-binding protein 12 (FKBP12), and the complex directly and strongly inhibits mTORC1.

Figure 1



Currently approved mTOR inhibitors are limited in their applicability due to poor and variable absorption of the oral drugs (sirolimus and everolimus) or variable conversion from prodrug to active drug (temsirolimus) and premedication requirements (temsirolimus). These drugs have a narrow therapeutic index and a reduction from the labelled dose can result in a decrease in efficacy. Preclinical study comparisons with FYARRO showed significantly higher tumor uptake, greater downstream mTOR target suppression and increased suppression of tumor growth for FYARRO compared to the oral mTOR inhibitors. A literature comparison of the clinical pharmacokinetic profiles of the drugs shows that FYARRO has a longer half-life, higher peak blood concentration and greater total exposure than the other approved mTOR inhibitors. FYARRO is administered in cycles that are given weekly for two weeks followed by a week off and does not require therapeutic monitoring to ensure adequate blood levels.

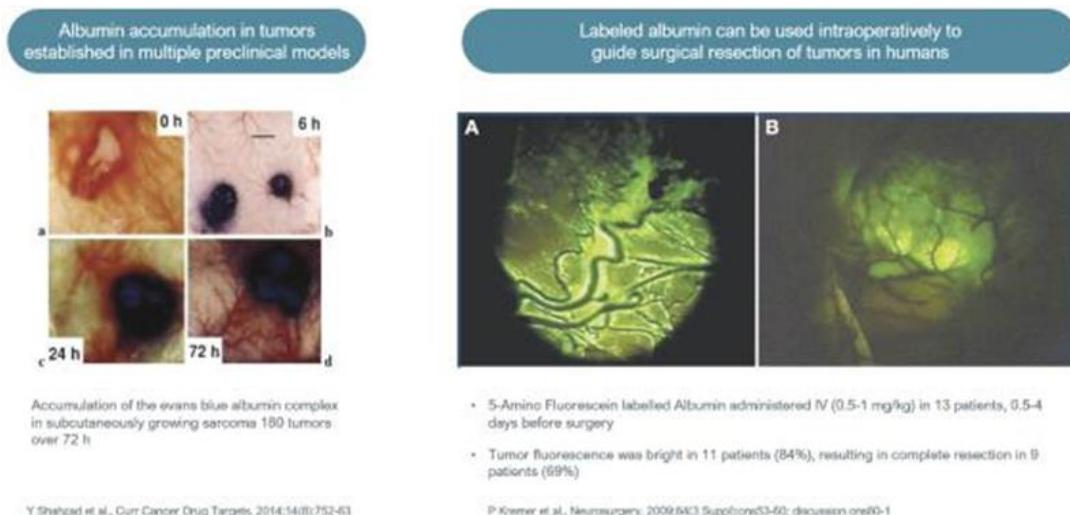
Our Approach: The Nanoparticle Albumin-Bound (nab) Technology

The nanoparticle albumin-bound, or nab, technology was created and developed by Neil Desai, our founder and CEO, and former colleagues while at Abraxis Bioscience. This technology takes advantage of the protein albumin, a natural carrier of water insoluble molecules (e.g., various nutrients, vitamins and hormones) found in humans. Due to various active and passive transport processes in the body, albumin can accumulate preferentially in different tissues including tumors, areas of inflammation, or areas of tissue remodeling, i.e., at sites of disease. The nab technology takes advantage of these transport properties of albumin and its affinity of binding to certain drug molecules to increase the efficiency with which these molecules may be brought to these sites of disease. The first clinical and commercial validation of this technology is the drug Abraxane®, which is approved in the U.S. and worldwide for the treatment of breast cancer, non-small cell lung cancer and pancreatic cancer. Abraxane has generated >\$1.0 billion of sales in the U.S. every year since 2018.

We are applying the nab technology to the molecule sirolimus, a potent inhibitor of the mTOR pathway that is hindered in large part by a poor pharmacologic profile (e.g., poor and variable absorption with incomplete target suppression). The relevance of albumin transport in cancer has been extensively studied and albumin is known to accumulate in tumor tissues due to the leaky capillary system within the tumor, defective lymphatic drainage of tumors, and active caveolae-mediated transport across tumor blood vessel endothelium. In addition, albumin can be taken up by proliferating tumor cells via endocytosis and macropinocytosis, then catabolized by lysosomal degradation to support de novo protein synthesis, energy, and tumor growth. Ultimately, nab technology allows FYARRO to take advantage of albumin transport pathways to accumulate at high levels in tumors and deliver sirolimus directly to cancer cells where it can effectively inhibit mTOR. The accumulation of albumin in tumors can be easily visualized by using the dye evans blue which has a high affinity for albumin. Intravenous injection of albumin-evans blue complex in animals bearing tumors resulted in rapid accumulation of the complex within the tumors which could be easily visualized in a few hours after injection. Similarly, a fluorescent labelled albumin when injected into human glioblastoma patients 24-48 hours before surgery resulted in excellent visualization of the

tumors during surgery under fluorescent light and allowed the complete resection of the tumor margins in the majority of the patients treated.

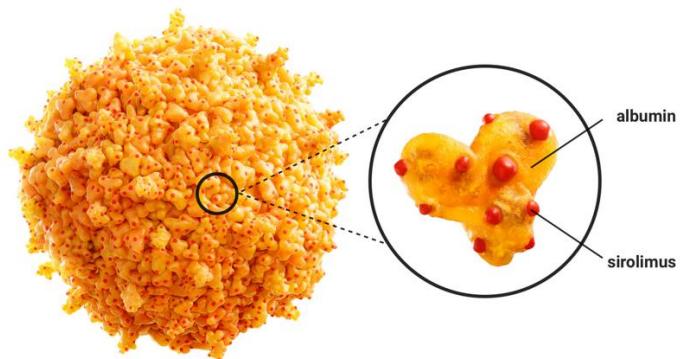
Figure 2 – Albumin Accumulation



FYARRO

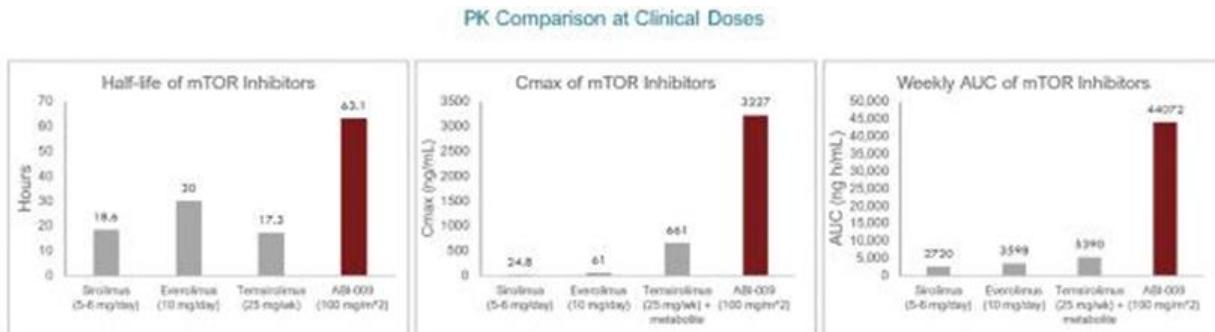
FYARRO (*nab*-sirolimus, sirolimus protein-bound particles for injectable suspension (albumin-bound)), is a form of sirolimus (rapamycin) bound to albumin. Sirolimus is a potent inhibitor of the mTOR biological pathway and inhibits downstream signaling from mTOR, which can promote tumor growth. FYARRO is in the form of nanoparticles of sirolimus bound to human albumin with average size less than 100 nanometers. An artist's impression of these nanoparticles is shown below.

Figure 3 – Nanoparticle artist impression



The orally available mTOR inhibitors have poor and variable absorption, often require therapeutic drug monitoring, and have incomplete target suppression. The combination of sirolimus with human albumin in FYARRO achieves higher AUC, Cmax and longer half-life in humans at its clinical dose when compared with published clinical data for other mTOR inhibitors, demonstrating FYARRO's differentiated clinical pharmacologic and pharmacokinetic profile.

Figure 4 – FYARRO PK Profile



These differences in pharmacology can result in advantageous differences in the clinical behavior of FYARRO when compared to the other mTOR inhibitors. This is effectively illustrated in comparative experiments in animals bearing bladder cancer tumors or liver cancer tumors. Data from these tumor-bearing animal models showed many-fold higher tumor drug levels for FYARRO at equal dose to the other mTOR inhibitors which was correlated with a greater degree of mTOR target suppression as indicated by inhibition of phosphorylation of S6 and 4EBP1 (downstream signaling nodes of mTORC1 that are known to play a role in downstream activity of mTOR as well as resistance to mTOR suppression), and a correspondingly higher suppression of tumor growth.

We believe that other mTOR inhibitors on the market or active in clinical development do not have the required favorable pharmacological profile to fully exploit the benefits of mTOR inhibition. We believe that FYARRO's differentiated *pharmacologic* profile, high tumor accumulation, and ability to effectively inhibit important targets in the mTOR pathway make it a well-positioned drug candidate to address resistance and suboptimal efficacy of existing mTOR inhibitors.

We are studying FYARRO in cancers with known mTOR pathway activation, including tumor agnostic indications targeting specific genomic alterations that activate the mTOR pathway. In addition, we have ongoing studies as well as studies in planning for testing the safety and efficacy of FYARRO in combination with other targeted agents. Our ongoing studies and studies in planning are summarized in the figure below.

Figure 5 – Pipeline



In November 2019, at the Connective Tissue Oncology Society (“CTOS”) Annual Meeting, we announced top-line results from the AMPECT study, including that the study achieved its primary endpoints of ORR, as determined by blinded independent central radiologic review using modified RECIST v1.1. In May 2021, we completed the filing of a rolling NDA for FYARRO to the FDA, for approval to treat patients with advanced malignant PEComa. The

NDA was based on results from the AMPECT study, in patients for whom there were no FDA approved therapies in the United States. The FDA accepted the NDA in July 2021, and we were granted approval for commercial sale on November 22, 2021.

PRECISION 1 is a tumor-agnostic registration-directed Phase 2 study of FYARRO in patients with *TSC1* and *TSC2* inactivating alterations that is based on evidence of activity seen in patients with *TSC1* and *TSC2* inactivating alterations from the completed AMPECT trial (presented at the CTOS Annual Meeting in 2020) and our Expanded Access Program (presented at the American Society of Clinical Oncology (“ASCO”) Annual Meeting in 2021). The PRECISION 1 study is now open for enrollment in the United States. We have completed a Type B meeting with the FDA in which we discussed the initial trial design with the FDA.

An Expanded Access Program (“EAP”) was opened to bridge access to FYARRO until market authorization and has been closed in the United States following the commercial availability of FYARRO. The EAP is available for advanced malignant PEComa patients in certain countries outside the United States.

In addition, we have other ongoing trials in early stages investigating the dose-finding of FYARRO in combination with various agents including tumor types such as colorectal cancer and sarcoma.

FYARRO for Advanced Malignant PEComa

PEComas are mesenchymal neoplasms, composed of histologically and immunohistochemically distinctive cells, perivascular epithelioid cells (“PEC”s). Most PEComas are clinically benign and do not metastasize, but malignant PEComas can demonstrate local invasion and aggressive metastatic spread. PEComas show a wide anatomical distribution, but most often arise in the retroperitoneum, abdominopelvic region, uterus and gastrointestinal tract, and have a 4:1 female predominance. Malignant PEComas are classified as one of the ultra-rare soft-tissue sarcomas with an estimated annual incidence of roughly 100-300 patients per year in the United States, although formal epidemiology studies have yet to be conducted.

FYARRO is the first FDA approved treatment specifically for malignant PEComa. The disease is often treated with the cytotoxic chemotherapy regimens used in soft tissue sarcomas, which have shown only modest benefit for malignant PEComa. PEComas commonly show evidence of mTORC1 activation at least in part due to loss-of-function mutations in or deletions of the *TSC1* or *TSC2* genes. In a retrospective analysis, patients with malignant PEComa treated with available mTOR inhibitors (mTORi, sirolimus, everolimus, and temsirolimus) benefited from treatment suggesting that mTORC1 inhibition may be a promising therapeutic approach for malignant PEComa. As a result, available mTOR inhibitors may also be used to treat malignant PEComa.

AMPECT, a pivotal phase 2 open-label clinical trial of FYARRO in advanced malignant PEComa

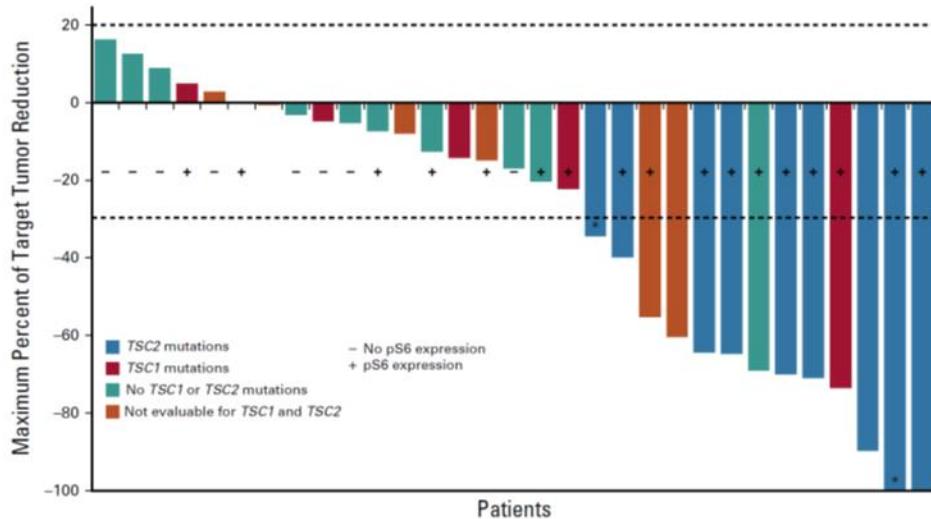
The AMPECT trial was the first prospective clinical trial in advanced malignant PEComa. Patients with metastatic or inoperable locally advanced disease were treated with FYARRO at 100 mg/m² administered as an intravenous (“IV”) infusion over 30 minutes on Days 1 and 8 of a 21-day cycle. The primary endpoint for the study was ORR evaluated by independent radiology review. Secondary efficacy endpoints included duration of response (“DOR”), progression free survival (“PFS”) and overall survival (“OS”). The sample size estimation assumed an observed ORR of 30% for a sample size of 30 patients, which would exclude values less than 14.7% for the lower bound of the 95% confidence interval.

This registrational trial met its primary endpoint demonstrating the efficacy of *nab*-sirolimus in this rare disease for which there was no FDA approved treatment, with an independently assessed ORR of 39% (95% CI: 22%, 58%). Disease control (defined as complete or partial response (“CR” or “PR”) + stable disease ≥12 weeks) was achieved in 71% of patients. FYARRO (*nab*-sirolimus) was subsequently approved by the FDA for the treatment of advanced malignant PEComa on November 22, 2021.

Sixty-seven percent (8 of 12) of responses were seen at the first scan after baseline at week six (median time to response 1.4 months, 95% CI: 1.3 to 2.8 months). At the time of the primary analysis (predefined as when all patients had an opportunity to be treated for 6 months), the median for the key secondary endpoint of DOR was not yet reached, with 9 of 12 responders still on treatment (DOR range 4.2+, 27.7+ months). At 1.5-years of follow-up after the primary analysis date (i.e., 2-years after the last patient-initiated treatment), 7 of 12 responders were still receiving treatment and the median DOR was still not reached, with 50% of patients exceeding 2.5 years (DOR range 5.6, 47.2+ months).

Figure 6 shows the target tumor responses (waterfall plot). One patient with a primary renal PEComa metastatic to the lungs and lymph nodes had a PR for 10 months that converted to a CR. Responses were independent of the primary site and were observed in tumors originating in the uterus (3), kidney (3), retroperitoneum (2), pelvis (2), liver (1), and small bowel (1). Notably, 43% (3/7) of patients with uterine PEComa had a partial response. Responses were also observed in 3/4 patients who had previously received chemotherapy

Figure 6 – Waterfall plot of Maximum Reduction in Target Lesions, Two-year Follow-up (Wagner et al., JCO 2021)



*A patient with unconfirmed PR is considered having SD as best response (trial required confirmation of responses per RECIST v1.1). Additionally, a patient with a complete response of target tumor reduction had a PR as best response because of unresolved nontarget lesions at the 2-year data cutoff (Wagner et al, JCO 2021); however, this patient later achieved a confirmed complete response (FYARRO Prescribing Information).

Treatment-related adverse events (“TRAE”) were consistent with those reported for other mTOR inhibitors. The most common hematologic events were anemia and thrombocytopenia, and the most common nonhematologic events were mucositis, rash and fatigue. The details are provided in Table 1 below. There were no grade 4 or 5 TRAEs. Noninfectious pneumonitis occurred in 6/34 (18%) patients and all were low grade (G1/G2). Patient discontinuation due to adverse events occurred on 2/34 (6%) patients (one grade 2 anemia and one grade 1 cystitis). Dose reductions occurred in 13/34 (38%) patients; 11 patients had a one dose reduction from 100 mg/m² to 75 mg/m² and 2 patients had two dose reductions to 56 mg/m².

Table 1

TRAE	Any Grade ≥ 25%, No. (%)	Grade 3, No. (%)
Patients with any TRAEs	34 (100)	
Hematologic TRAEs		
Anemia ^a	16 (47)	4 (12)
Thrombocytopenia ^a	11 (32)	1 (3)
Nonhematologic TRAEs		
Mucositis ^b	27 (79)	6 (18)
Rash ^a	19 (56)	—
Fatigue	20 (59)	1 (3)
Nausea	16 (47)	—
Diarrhea	13 (38)	—
Weight decreased	13 (38)	—
Hyperglycemia ^a	12 (35)	3 (9)
Hypertriglyceridemia ^a	11 (32)	1 (3)
Hypercholesterolemia ^a	11 (32)	—
Decreased appetite	11 (32)	—
Dermatitis ^a	10 (29)	—
Dysgeusia	10 (29)	—
Headache	10 (29)	—
Peripheral edema	9 (26)	—

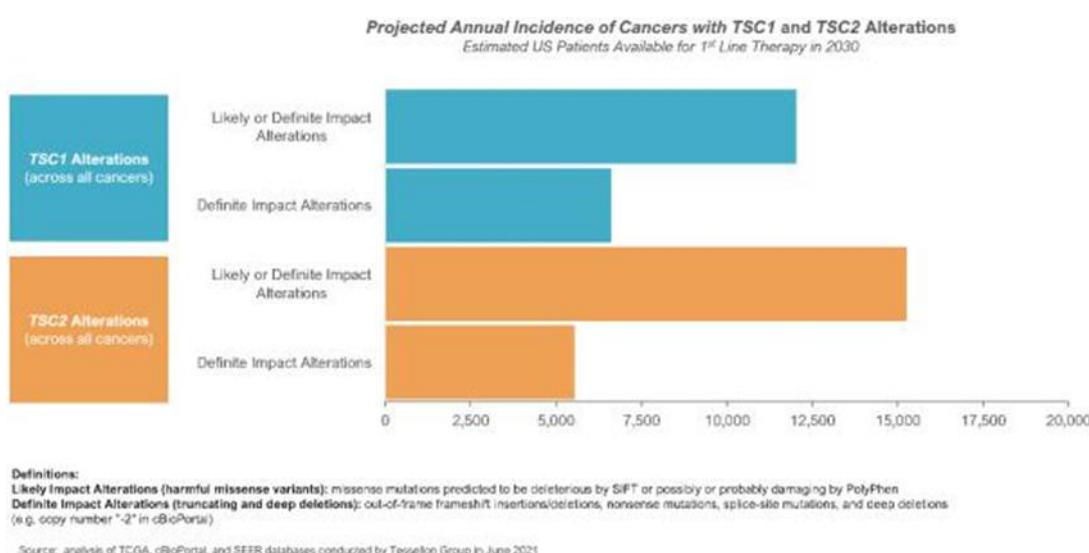
- “a” Indicates groupings of preferred terms defined by standardized queries in the Medical Dictionary for Regulatory Activities.
- Additional G3 TRAEs were 6% hypokalemia, and 3% each of AST/ALT, amylase, hypophosphatemia, insomnia, lipase, lymphocyte, skin infection, vomiting. No G4 TRAEs were reported

In December 2017, we received Orphan Drug Designation (“ODD”) for FYARRO for the treatment of patients with advanced malignant PEComa. In October 2018, the FDA granted Fast Track designation for FYARRO for the treatment of patients with advanced malignant PEComa. In December 2018, the FDA granted Breakthrough Therapy Designation (“BTD”) for FYARRO for the treatment of patients with advanced malignant PEComa. The FDA accepted the NDA in July 2021, and we were granted full approval on November 22, 2021.

FYARRO for TSC1 or TSC2 Alterations in Solid Tumors

The *TSC1* and *TSC2* genes encode for proteins that form a tumor suppressor complex that down regulates mTORC1 activity. Inactivating alterations in the *TSC1* or *TSC2* genes can result in activation of mTORC1. *TSC1* or *TSC2* alterations have been reported across a broad range of cancer types. Based on the SEER cancer statistics database and an analysis of mutation frequency by cancer type using the TCGA and cBioPortal databases, we believe there is a significant number of new patients with *TSC1* or *TSC2* inactivating alterations per year in the U.S (see chart titled “Projected Annual Incidence of Cancers with *TSC1* and *TSC2* Alterations” below). While there are no therapies approved specifically for *TSC1* or *TSC2* alterations, numerous case reports show durable responses to mTOR inhibition in patients with these alterations.

Figure 7

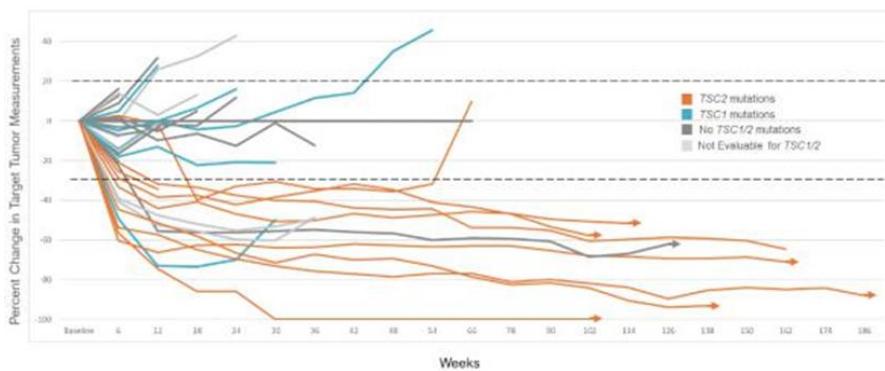


***TSC1* and *TSC2* Alterations in the AMPECT Study**

An exploratory mutational analysis was conducted on patients treated with FYARRO in the AMPECT study in advanced malignant PEComa. In 25 patients with available mutational analysis, *TSC1* or *TSC2* alterations were found in 14 patients (56%). In this subset of patients with *TSC1* or *TSC2* alterations, the response rate was 64% (9/14) (Figure 8). In particular, *TSC2* mutations were significantly associated with response (89% of patients) to FYARRO.

Figure 8 – Spider plot demonstrating change in the sum of target tumor measurements over time, based on mutation status.

Durability of Response in *TSC1* and *TSC2* altered PEComa



* Arrowheads indicate patients who were still on treatment

TSC1 and *TSC2* Alterations in the Expanded Access Program

An Expanded Access Program was opened to bridge access to FYARRO until market authorization for patients with advanced malignant PEComa; this program also included patients with various other malignancies having relevant genetic mutations in the mTOR pathway. Preliminary data was presented at ASCO Annual Meeting in 2021 showing the early results in tumors bearing *TSC1* or *TSC2* inactivating alterations in patients with histologies other than advanced malignant PEComa. Of the 8 patients treated with FYARRO, 7 patients were evaluable for response analysis and 1 patient progressed before the first scan. Five of 8 patients (63%, 95% CI: 25%-92%) achieved a confirmed PR. Amongst the patients who were mTOR inhibitor-naïve, 5 of 6 (83%, 95% CI: 36%-99+) achieved a confirmed PR. Duration of response at data cutoff ranged from 3.1 to 9.7+ months and 3 of 5 responders continue on treatment. A waterfall plot of tumor response is provided below Figure 9. Figure 10 shows the prior therapy and duration of treatment for each patient. Patients with inactivating alterations in either *TSC1* or *TSC2* achieved tumor shrinkage and clinical benefit.

Figure 9

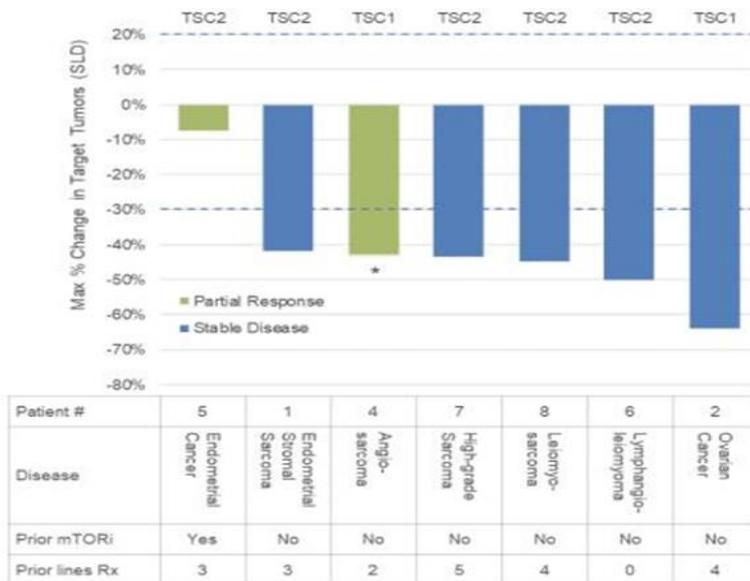


Figure 10



Treatment-emergent adverse events (“TEAE”) (30%) included edema, infections, mucositis, and pain (71% each), nail changes and vomiting (57% each), and hypertension and nausea (43% each). The majority of the events were G1/G2. Treatment-related serious adverse events (“TESAE”) were reported in 2 patients and included hyperglycemia and infection (patients #4 and #5) and acute kidney injury (patient #7) possibly also related to administration of contrast. Dose reductions occurred in 3/8 patients (38%) from 100 mg/m² to 75 mg/m².

A recent published case report summarized the results of a patient with malignant PEComa patient with a *TSC1* alteration who enrolled in the Expanded Access Program after having progressed through treatment with the mTOR inhibitor everolimus. The patient demonstrated a rapid and durable response to FYARRO.

FYARRO in patients with prior mTOR inhibitors

A post hoc electronic medical record review provided evidence of clinical benefit of *nab*-sirolimus in patients with malignant PEComa who had prior mTOR inhibitor exposure: 25% achieved a response (duration of response range: 1.3+–25.2+ months, 3 ongoing), and 50% had stable disease as best response as best response. Of patients with *TSC1* or *TSC2* inactivating alterations, 44% had a response.

FYARRO for other indications

FYARRO is currently being tested in early-stage, dose-finding studies to determine the appropriate dose of FYARRO in combination with various agents in tumor types including colorectal cancer, sarcoma and other indications. We expect to report data from one or more of these combination studies in the second half of 2022. We believe there is a significant opportunity to utilize FYARRO in other indications as a monotherapy, e.g., in other mTOR pathway mutations, as well as in combination with other targeted therapies, particularly in mTOR adjacent signaling pathways. These additional indications may be important drivers of commercial value and will be evaluated in the future.

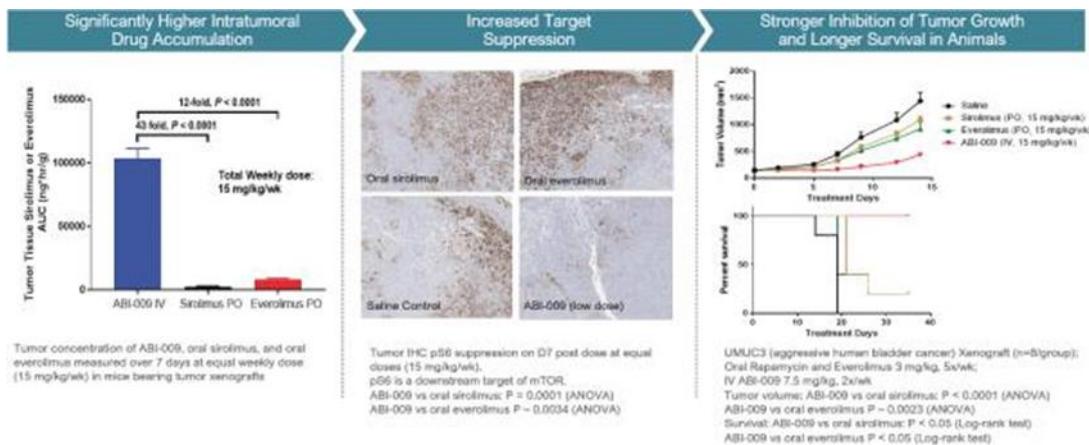
Preclinical profile FYARRO

We demonstrated the antitumor activity of FYARRO in a series of nonclinical pharmacology studies. FYARRO exhibited antitumor activity as a single agent and in combination with other therapeutic agents in a wide range of tumor types. As a single agent, FYARRO significantly inhibited tumor growth of multiple human and mouse tumor models with known mTOR pathway activation including colon, breast, ovarian, bladder, and liver human tumor xenograft models, and in a melanoma mouse tumor model. In addition, the antitumor activity of FYARRO was significantly increased in combination with an EGFR tyrosine kinase inhibitor, an AKT inhibitor, doxorubicin, a Hsp90 inhibitor, gemcitabine, and anti-PD1 (programmed cell death protein 1) antibody. In nonclinical PK studies, we have shown that FYARRO intravenous (“IV”) administration resulted in significant, rapid, and prolonged

sirolimus distribution to different organs and in tumors. As a single agent monotherapy and in combination with other therapies, FYARRO was well tolerated with limited body weight loss.

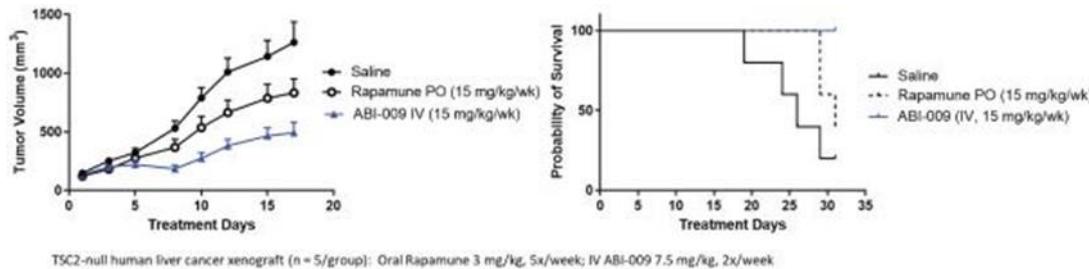
In March 2019, at the American Association for Cancer Research Annual Meeting, we presented preclinical data that describes the tumor accumulation, mTOR target inhibition, and antitumor activity of FYARRO IV in comparison to oral sirolimus and oral everolimus in athymic mice bearing UMUC3 human bladder tumor xenografts. At a clinically relevant dose of 15 mg/kg/week for all agents, FYARRO resulted in higher drug accumulation in tumors and stronger suppression of mTOR target pS6, which correlated with significantly greater tumor growth inhibition and prolonged survival compared with equal weekly dose of oral sirolimus and everolimus.

Figure 11



We also determined the antitumor activity of FYARRO in comparison to oral Rapamune against TSC2-null SNU-398 human liver tumor xenografts. At equal weekly dose of 15 mg/kg/week, FYARRO IV resulted in significantly greater tumor growth inhibition and longer animal survival, which correlated with stronger suppression of mTOR downstream targets pS6K, pS6, and p4EBP1 as measured by western blot.

Figure 12



Taken together, the nonclinical studies support the clinical development of FYARRO as an anticancer therapy.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including pursuing and maintaining patent protection intended to cover formulations of FYARRO, its methods of use, related technologies, and other inventions that are important to our business. In addition to patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, including our proprietary method of manufacturing FYARRO.

Our commercial success depends in part upon our ability to obtain and maintain patent and other proprietary protection for FYARRO and other commercially important technologies, inventions, and know-how related to our

business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets, and operate without infringing valid and enforceable intellectual property rights of others.

The patent positions for biotechnology and pharmaceutical companies like us are generally uncertain and can involve complex legal, scientific, and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that FYARRO will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented, or invalidated by third parties. For more information regarding the risks related to our intellectual property please see “Risk Factors—Risks Related to Our Intellectual Property”.

We exclusively license 10 patents from Celgene, by which Celgene granted us an exclusive, sublicensable license under Celgene’s rights to certain patents and patent applications relating to FYARRO. With regard to FYARRO, as of December 31, 2021, we licensed 4 issued U.S. patents with composition of matter and method of use claims covering this product. The first issued U.S. patent is expected to expire in 2029, and the other three are expected to expire in 2030, 2036, and 2036 respectively. In addition, we licensed related patents in Europe, Australia, North America, South America, and Asia that are expected to expire between 2022 and 2037. We also licensed 174 pending U.S. applications and related pending applications in Europe, Australia, North America, South America, Africa, and Asia. In addition, we also licensed two pending Patent Cooperation Treaty (“PCT”) patent applications directed to composition of matter and new uses related to this product, which if granted, are expected to expire in 2040.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the U.S., the term of a patent covering an FDA approved drug may, in certain cases, be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act, as compensation for the loss of patent term during FDA regulatory review process. The period of extension may be up to five years but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. In January 2022, we filed an application for patent term extension based on the approval of FYARRO. We also intend to seek patent term extensions in any jurisdictions where they are available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection, including, for example, certain aspects of our manufacturing processes for the nanoparticle compositions. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors, and potential collaborators, such individuals may breach such agreements and disclose our proprietary information including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. For more information regarding the risks related to our intellectual property please see “Risk Factors—Risks Related to Our Intellectual Property.”

Commercial Operations

We have built a cross-functional commercial organization and infrastructure to support the launch of FYARRO for advanced malignant PEComa in the United States and will continue to evaluate potential partners in markets outside the United States. In December 2020, we entered into a License Agreement with EOC Pharma Limited pursuant to which we granted EOC Pharma Limited exclusive rights to develop and commercialize FYARRO in

Greater China. We have hired an experienced oncology commercial team including marketing, market access, commercial operations and sales personnel to educate physicians who are prescribers of treatments for advanced malignant PEComa. Our sales team will be supported by marketing, commercial operations, and market access functions. We have assembled a network of specialty distributors and specialty pharmacies to distribute FYARRO across multiple sites of care in the United States. Additionally, the sales and marketing teams will manage relationships with key accounts such as managed care organizations, group purchasing organizations, hospital systems, physician group networks, and government accounts. To continue the development of commercial capabilities and infrastructure, we are investing significant amounts of financial and management resources.

For future approvals of FYARRO in other oncology indications, we intend to retain commercialization rights in the United States and leverage our commercial and marketing organization for FYARRO, with appropriate additions or modifications as necessitated by the specific indications pursued, assuming we obtain regulatory approval in the United States, and consider whether to build our own commercial and marketing organization in select markets outside the United States, or selectively establish partnerships. Accordingly, we will consider entering into relationships with strategic partners that enable the expansion of the ongoing clinical development and/or licenses for development and commercialization or distribution, while retaining significant value for our shareholders. These partnerships could focus on specific patient populations and their caregivers, on regional development, or on distribution and sales.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. While we believe that our technology, development experience, and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions. Any drug candidates that we successfully develop and commercialize will compete with existing drugs and new drugs that may become available in the future. We compete in the segments of the pharmaceutical, biotechnology, and other related markets that address inhibition of kinases in cancer and other rare genetic diseases. There are other companies working to develop therapies in the field of kinase inhibition for cancer and other diseases. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

Many of the companies against which we are competing against or which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination in our commercial opportunity if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any drugs that we or our collaborators may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of FYARRO are likely to be its efficacy, safety, convenience, price, the effectiveness of companion diagnostics, the level of generic competition, and the availability of reimbursement from government and other third-party payors.

Competition for FYARRO in Advanced Malignant PEComa

In advanced malignant PEComa, other than FYARRO, there are no existing FDA approved therapies or drugs that have been studied in prospective clinical trials. Following FDA approval, the National Comprehensive Cancer Network (“NCCN”) Sarcoma panel included FYARRO as the only preferred regimen for treatment of malignant PEComa. As of today, we are not aware of any other companies pursuing FDA approval for drugs to treat advanced malignant PEComa.

Competition for FYARRO in Tumor Agnostic TSC1 and TSC2 Inactivating Alterations

For tumor agnostic *TSC1* or *TSC2* inactivating alterations, there are no existing FDA approved drugs. If FYARRO receives marketing approval, it may face competition from available mTOR inhibitors including sirolimus, everolimus, and temsirolimus or other drug candidates in clinical trials that target the mTOR pathway, such as dual mTORC1/2 inhibitors or other next-generation mTOR inhibitors.

Manufacturing

We do not own or operate, and have no plans to establish, any manufacturing facilities. We currently rely on third parties to manufacture FYARRO for preclinical and clinical testing, as well as for our commercial supply of FYARRO.

The Amended and Restated License Agreement for FYARRO with Celgene dated November 2019, transferred the responsibility for manufacturing of FYARRO to us. FYARRO was previously manufactured for us by Celgene through their third-party manufacturer, Fresenius-Kabi, USA. As a result of the amendment to the License Agreement, we now obtain FYARRO directly from Fresenius-Kabi, USA.

To date, we have obtained drug substance and drug product from third-party manufacturers to support pre-clinical and clinical testing of FYARRO. On January 13, 2022, we entered into a Negotiated Purchase Order Terms and Conditions for Clinical and Commercial Product (the “Fresenius Agreement”) with Fresenius Kabi, LLC (“Fresenius Kabi”) pursuant to which Fresenius Kabi will manufacture FYARRO for us, and we will purchase FYARRO as a finished drug product from Fresenius Kabi, on a purchase-order basis. Under the Fresenius Agreement, which is effective through December 22, 2022 (or such later date as may be agreed between the parties in writing and currently being discussed), we may purchase FYARRO for either clinical or commercial purposes for use in the United States and Canada. In addition to manufacturing, Fresenius Kabi will perform specified labeling, packaging and serialization activities in respect of FYARRO for our benefit. The price of FYARRO will be fixed, subject to the ability of Fresenius Kabi to increase pricing under specified circumstances. We have an obligation to purchase certain minimum quantities of FYARRO. Failure to purchase those minimum quantities will result in an additional payment from us to Fresenius Kabi.

Future purchases of FYARRO for all purposes will utilize the Fresenius-Kabi Grand Island, New York clinical and commercial supply agreement effective through December 2022. We have a fully validated commercial manufacturing process in place for FYARRO at the Fresenius-Kabi Grand Island Manufacturing facility. We are evaluating options with Fresenius Kabi to create redundant supply of FYARRO beyond 2022. We have supply agreements in place for key raw materials used in the manufacture of FYARRO such as the drug substance sirolimus and for human albumin, which are key ingredients in the drug product. We do not currently have arrangements in place for redundant supply of the key raw materials used in the manufacture of FYARRO. We expect to continue to evaluate options to cost-effectively produce FYARRO at contract manufacturing facilities.

We generally expect to rely on third parties for the manufacture or development of any companion diagnostics if we are required to do so in the future for FYARRO.

Government Regulation

Government authorities in the United States, including federal, state, and local authorities, and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of pharmaceutical and biological products, such as those we are developing. In addition, some government authorities regulate the pricing of such products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

Government authorities in the United States, at the federal, state, and local level, and other countries extensively regulate, among other things, the research, development, nonclinical and clinical testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of products such as those we are developing.

Generally, before a new drug can be marketed, considerable data must be generated, which demonstrate the drug's quality, safety, and efficacy. Such data must then be organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

Drugs are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable regulatory requirements at any time during the product development process, approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the regulatory authority's refusal to approve pending applications, withdrawal of an approval, clinical holds, untitled or warning letters, voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, debarment, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

U.S. Drug Development

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. Drugs are also subject to other federal, state, and local statutes and regulations. Drugs must be approved by the FDA through the NDA process before they may be legally marketed in the U.S. The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- completion of extensive preclinical, sometimes referred to as nonclinical, laboratory tests, animal studies, and formulation studies all performed in accordance with applicable regulations, including the FDA's good laboratory practice ("GLP") regulations;
- submission to the FDA of an investigational new drug application ("IND"), which must become effective before human clinical trials may begin and must be updated annually and amended in accordance with the regulations;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as good clinical practices ("GCPs") to establish the safety and efficacy of the proposed drug for its proposed indication(s);
- submission to the FDA of an NDA for a new drug;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient ("API") and finished drug product are produced to assess compliance with the FDA's current good manufacturing practice requirements ("cGMP");
- potential FDA audit of the testing laboratories and clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the U.S.

Prior to beginning a clinical trial with a product candidate in the United States, companies must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols

detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A new IND, or a separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the clinical trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which may review data and endpoints at designated check points, make recommendations and/or halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages, and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can serve as the primary basis for approval of the drug. Generally, pivotal studies are also Phase 3 studies but may be Phase 2 studies if the trial design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need. Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse reactions, any finding from other clinical studies, tests in laboratory animals, or in vitro testing that suggests a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2, and Phase 3 trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop

additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, cGMPs impose extensive procedural, substantive, and recordkeeping requirements to ensure and preserve the long-term stability and quality of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

A manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy.

We may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus. For example, in March 2020, the FDA issued guidance, which has been subsequently updated, on conducting clinical trials during the COVID-19 pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical trial report contingency measures implemented to manage the clinical trial and any disruption of the clinical trial as a result of the COVID-19 pandemic, among other. Other COVID-19 related guidance documents issued by FDA include a guidance on good manufacturing practice considerations for responding to COVID-19 infection in employees in drug products manufacturing; manufacturing, supply chain, and drug and biological product inspections during COVID-19 public health emergency; and remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities during the COVID-19 public health emergency. Changes in FDA's operations and policies, including delays in providing regulatory review or feedback to sponsors or delays in pre-approval inspections, as a result of the COVID-19 public health emergency can materially impact our clinical development plans and regulatory approval.

NDA and the FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of preclinical studies and clinical trials are then submitted to the FDA as part of a NDA, along with proposed labeling for the drug and information about the manufacturing process and facilities that will be used to ensure drug quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain sufficient evidence of drug product quality, safety and efficacy, which is demonstrated by extensive analytical, preclinical and clinical testing. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a drug, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational drug product for a particular indication or indications to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be offered for sale in the United States.

The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality, and purity. Under the PDUFA guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes 12 months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification. In such event, the NDA must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed drug is safe and effective for its intended use, and whether the drug is being manufactured in accordance with cGMP to assure and preserve the drug's identity, strength, quality, and purity. The FDA may refer applications for novel drugs or drug candidates that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. In the course of its review, the FDA may re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving an NDA, the FDA typically conducts a pre-approval inspection of the manufacturing facilities for the new drug to determine whether they comply with cGMPs. The FDA will not approve the drug unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the drug within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process, and manufacturing facilities where the drug product and/or its API will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies, or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, challenge the determination set forth in the letter by requesting a hearing, or withdraw the application. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States and we may encounter significant difficulties or costs during the review process. If a drug receives marketing approval, the approval may be significantly limited to specific diseases, dosages, or patient subgroups, or the indications for use may otherwise be limited, which could restrict the commercial value of the drug. Further, the FDA may require that certain contraindications, warnings, precautions, or adverse events be included in the drug labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing or clinical trials, and surveillance to monitor the effects of approved drugs.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy ("REMS") to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use. It could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools.

Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription, or dispensing of drugs. Drug approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

In November 2021, we received approval for the commercial sale of FYARRO from the FDA to treat patients with advanced (metastatic or locally advanced) PEComas. The NDA submission was based on results from our Phase 2 registrational study AMPECT, in patients with advanced malignant PEComa, for whom there are currently no approved therapies in the U.S.

FDA Expedited Development and Review Programs

The FDA has various programs, including fast track designation, priority review, accelerated approval, and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. With regard to a fast track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis, or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality, or other clinical endpoint and to submit promotional materials for preapproval and pre-use review, which could adversely impact the timing of the commercial launch of the product. In addition, the drug may be subject to accelerated withdrawal procedures.

The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as “breakthrough therapies” that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a “breakthrough therapy” if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

In addition, the FDA may review new drug applications under the Oncology Center of Excellence Real-Time Oncology Review (“RTOR”), which, according to the FDA, aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality. Drugs considered for review under RTOR must be likely to demonstrate substantial improvements over available therapy, which may include drugs previously granted breakthrough therapy.

designation for the same or other indications, and must have straight-forward study designs and endpoints that can be easily interpreted. RTOR allows the FDA to review much of the data in an NDA earlier, before the applicant formally submits the complete application. This analysis of the pre-submission package gives the FDA and applicants an early opportunity to address data quality and potential review issues and allows the FDA to provide early feedback regarding the most effective way to analyze data to properly address key regulatory questions.

Fast track designation, priority review, accelerated approval, and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for FYARRO as appropriate.

Post-Marketing Requirements

Following approval of a new drug, a pharmaceutical company and the approved drug are subject to continuing regulation by the FDA, including, among other things, establishment registration and drug listing, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the drug, providing the regulatory authorities with updated safety and efficacy information, drug sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling, limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet.

In particular, the FDA closely regulates the marketing, labeling, advertising, and promotion of drug products. A company can make only those claims relating to safety and efficacy that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling. Modifications or enhancements to the drug or its labeling or changes of the site or process of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process.

Prescription drug advertising is subject to federal, state, and foreign regulations. In the U.S., the FDA regulates prescription drug promotion, including direct-to-consumer advertising. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Any distribution of prescription drugs and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act ("PDMA"), a part of the FDCA. The Drug Supply Chain Security Act ("DSCSA"), enacted in 2013, aims to build an electronic system to identify and trace certain prescription drugs distributed in the U.S. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. The law's requirements include the quarantine and prompt investigation of a suspect product to determine if it is illegitimate and notifying trading partners and the FDA of any illegitimate product. Drug manufacturers and their collaborators are also required to place a unique product identifier on prescription drug packages. This identifier consists of the National Drug Code, serial number, lot number, and expiration date, in the form of a 2-dimensional data matrix barcode that can be read by humans and machines.

In the U.S., once a drug is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. FDA regulations require that drugs be manufactured in specific facilities per the NDA approval and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of its drugs in accordance with cGMP regulations. cGMP regulations require among other

things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural, and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute drugs manufactured, processed, or tested by them. Discovery of problems with a drug after approval may result in restrictions on a drug, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the drug from the market, and may require substantial resources to correct.

The FDA also may require post-approval testing, sometimes referred to as Phase 4 testing, risk minimization action plans, and post-marketing surveillance to monitor the effects of an approved drug or place conditions on an approval that could restrict the distribution or use of the drug. Discovery of previously unknown problems with a drug or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial, or administrative enforcement actions. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on post-approval or Phase 4 clinical studies, if applicable;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases, and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Newly discovered or developed safety or effectiveness data may require changes to a drug's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures, including a REMS or the conduct of post-marketing studies to assess a newly discovered safety issue. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our drugs under development.

As a condition of the approval of the NDA for FYARRO, we are required to conduct certain post-marketing requirements ("PMR") and post-marketing commitments ("PMC"). If we fail to comply with the PMR and PMC, the FDA may take enforcement actions, which may include, among other things, the issuance of a Warning Letter and assessing civil monetary penalties. The product may also be deemed misbranded.

Orphan Drug Designation

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the drug for this type of disease or condition will be recovered from sales in the United States. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or

shorten the duration of, the regulatory review and approval process. After the grant of an orphan drug designation, FDA may revoke the designation if FDA finds that the request for designation contained an untrue statement of material fact, omitted required material information, or if FDA subsequently finds that the drug had not been eligible for the orphan drug designation at the time of the submission of the request.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

In the European Union, the European Commission, after receiving the opinion of the European Medicines Agency’s (“EMA”) Committee for Orphan Medicinal Products (“COMP”), grants Orphan Drug Designation to also promote the development of products. The relevant European legislation provides that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention, or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating, or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the product in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must also demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the product has to be of significant benefit compared to products available for the condition. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product.

In the European Union, Orphan Drug Designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following drug or biological product approval. During this market exclusivity period, neither the EMA nor the European Commission or the 27 member states that comprise the European Union can accept an application or grant a marketing authorization for the same therapeutic indication in respect of a “similar medicinal product.” A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. This period may be reduced to six years if, after five years, the Orphan Drug Designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration, and specifics of the FDA approval of our drug candidate, some of our United States patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product’s approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. The U.S. Patent and Trademark Office (“USPTO”), in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Marketing exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications for competing products. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (“ANDA”) or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication. However, an application may be

submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) applications for drugs containing the active agent for the original indication or condition of use.

These five-year and three-year exclusivities will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued “Written Request” for a pediatric trial.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion, and other activities following drug approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services (“CMS”), other divisions of the U.S. Department of Health and Human Services (“HHS”), the Drug Enforcement Administration for controlled substances, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, and state and local governments. In the United States, sales, marketing, and scientific/educational programs must also comply with state and federal fraud and abuse laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010 (the “ACA”). If drugs are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Drugs must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion, and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

We are subject to numerous foreign, federal, state, and local environmental, health, and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials and wastes. In addition, our leasing and operation of real property may subject us to liability pursuant to certain U.S. environmental laws and regulations, under which current or previous owners or operators of real property and entities that disposed or arranged for the disposal of hazardous substances may be held strictly, jointly, and severally liable for the cost of investigating or remediating contamination caused by hazardous substance releases, even if they did not know of and were not responsible for the releases.

The distribution of pharmaceutical drugs is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage, and security requirements intended to prevent the unauthorized sale of pharmaceutical drugs. The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines, or other penalties, injunctions, voluntary recall or seizure of drugs, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or efficacy of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes, or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product

labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Coverage and Reimbursement

Sales of our drugs will depend, in part, on the extent to which our drugs will be covered by third-party payors, such as government health programs, commercial insurers, and managed healthcare organizations, as well as the level of reimbursement such third-party payors provide for our products. Patients and providers are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products in which our products are used. These third-party payors are increasingly reducing reimbursements for medical drugs and services.

In the U.S., no uniform policy of coverage and reimbursement for drugs or biological products exists, and one payor's determination to provide coverage and adequate reimbursement for a product does not assure that other payors will make a similar determination. In the U.S., the principal decisions about reimbursement for new medicines are typically made by the CMS, an agency within the HHS, as the CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private third-party payors tend to follow Medicare coverage and reimbursement limitations to a substantial degree, but also have their own methods and approval process apart from Medicare determinations. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for FYARRO will be made on a payor-by-payor basis. As a result, the coverage determination process may be a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high.

Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic drugs. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for FYARRO or a decision by a third-party payor to not cover FYARRO could reduce physician usage of such drug and have a material adverse effect on our sales, results of operations and financial condition.

The Medicaid Drug Rebate Program (“MDRP”) requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the HHS as a condition for states to receive federal matching funds for the manufacturer’s outpatient drugs furnished to Medicaid patients. The ACA made several changes to the MDRP, including increasing pharmaceutical manufacturers’ rebate liability by raising the minimum basic Medicaid rebate percentage on most branded prescription drugs of average manufacturer price (“AMP”) and adding a new rebate calculation for “line extensions” (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, creating a new methodology by which rebates owed are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (“MMA”) established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, while all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not

required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. These Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for drugs for which we may obtain marketing approval. However, any negotiated prices for our drugs covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of FYARRO, if any such drug or the condition that they are intended to treat are the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our drug candidate. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

In recent years, additional laws have resulted in direct or indirect reimbursement reductions for certain Medicare providers. For example, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws, and future state and federal healthcare reform measures, as discussed further below, may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any indication of FYARRO for which it may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at increasing competition for prescription drugs. The HHS has released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and potential legislative policies that Congress could pursue to advance these principles. While no legislation or administrative actions have been finalized to implement these principles, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases and allowing Medicare to negotiate pricing for certain covered drug products. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The

implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize any of the product candidates for which we receive approval.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and other third-party payors fail to provide adequate coverage and reimbursement. We expect that an increasing emphasis on cost containment measures in the U.S. will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal drugs for which their national health insurance systems provide reimbursement and to control the prices of medicinal drugs for human use. A member state may approve a specific price for the medicinal drug or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal drug on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical drugs will allow favorable reimbursement and pricing arrangements for any of our drugs. Historically, drugs launched in the European Union do not follow price structures of the U.S. and generally tend to be significantly lower.

U.S. Healthcare Reform

The ACA has had a significant impact on the healthcare industry. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the ACA, among other things, addressed a new methodology by which rebates owed by manufacturers under the MDRP are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increased the minimum Medicaid rebates owed by manufacturers under the MDRP and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business.

The ACA requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Each such manufacturer is required to pay a prorated share of the branded prescription drug fee based on the dollar value of its branded prescription drug sales to certain federal programs identified in the law. The ACA also expanded the 340B program to include additional types of covered entities. Federal law requires that any company that participates in the Medicaid rebate program also participate in the 340B program in order for federal funds to be available for the manufacturer's drugs under Medicaid. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. In addition, in order to be eligible to have its products paid for with federal funds under the Medicaid programs and purchased by certain federal grantees and agencies, a manufacturer also must participate in the Department of Veterans Affairs Federal Supply Schedule ("FSS") pricing program, established by Section 603 of the Veterans Health Care Act of 1992. Under this program, the manufacturer is obligated to make products available for procurement on an FSS contract and charge a price to four federal agencies—the Department of Veterans Affairs, the Department of Defense, the Public Health Service, and the Coast Guard—that is at least 24% less than the Non-Federal Average Manufacturing Price for the prior fiscal year.

Since the enactment of the ACA, there have been judicial and Congressional challenges to certain aspects of the ACA. In June 2021, the Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, upholding the ACA. In January 2021, President Biden also issued an executive order to initiate a special enrollment period to allow people to obtain health insurance coverage through the ACA marketplace and instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to

healthcare, among others. We cannot predict how future litigation, healthcare reform measures of the Biden administration, or what other regulations will ultimately be implemented at the federal or state level, or the effect of any future legislation or regulation may have on our business.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. At the federal level, for example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. Additionally, CMS issued a final rule, effective on July 9, 2019, that requires direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product if it is equal to or greater than \$35 for a monthly supply or usual course of treatment. Prescription drugs and biological products that are in violation of these requirements will be included on a public list.

In 2020, at the federal level, under the Trump administration, HHS and CMS issued various rules that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, importation of prescription drugs from Canada and other countries, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of these new rules. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies. The impact of legislative, executive, and administrative actions of the current administration on us and the biopharmaceutical industry as a whole is unclear. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that additional federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare drugs and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability and may increase our regulatory burdens and operating costs.

Moreover, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Other Healthcare Laws

For our product and any product candidates that obtain regulatory approval and are marketed in the United States, our arrangements, directly or indirectly, with third-party payors, healthcare providers, and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we markets, sells, and distributes any products for which it obtains marketing approval. Our employees, consultants, and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements. Federal and state healthcare laws and regulations that may affect our ability to conduct business, include, without limitation:

- FDA, Department of Justice, and other government authority prohibitions against the advertisement, promotion and labeling of our products for off-label uses, or uses outside the specific indications approved by the FDA;
- the federal Anti-Kickback Statute, which broadly prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly,

in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs, such as Medicare or Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false claims, or knowingly using false statements, to obtain payment from the federal government. These laws have been interpreted to apply to arrangements between manufacturers, on the one hand, and prescribers, purchasers, and other healthcare-related professionals on the other. They can apply to manufacturers who provide inaccurate information on coverage, coding, and reimbursement of their products to persons who bill third-party payers. In addition, manufacturers have been prosecuted or faced civil and criminal liability under these laws for a variety of alleged promotional and marketing activities, including violations of the federal Anti-Kickback Statute and engaging in off-label promotion that caused claims to be submitted for non-covered off-label uses. Private individuals can bring False Claims Act “qui tam” actions, on behalf of the government and such individuals, commonly known as “whistleblowers,” may share in amounts paid by the entity to the government in fines or settlement;
- the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), as amended, which among other things, also created criminal liability for knowingly and willfully falsifying or concealing a material fact or making a materially false statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- Federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making, or causing to be made, false statements relating to healthcare matters;
- the federal Civil Monetary Penalties Law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary’s decision to order or receive items or services reimbursable by the government from a particular provider or supplier;
- the Foreign Corrupt Practices Act, the U.K. Bribery Act of 2010, and other local anti-corruption laws that apply to our international activities;
- the federal Physician Payment Sunshine Act (“Open Payments”), and implementing regulations, which require applicable group purchasing organizations and manufacturers of covered drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid, or the Children’s Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value made to covered recipients, including licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others), and teaching hospitals, and information regarding ownership and investment interests held by physicians and their immediate family members;
- analogous state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state laws that require pharmaceutical manufacturers to comply with the industry’s voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm customers, foreign and state laws, including the E.U. General Data Protection Regulation (“GDPR”), governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; and state laws related to insurance fraud in the case of claims involving private insurers.

The scope and enforcement of each of these laws are uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions, and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including those of our contractors or agents who conduct business for or on our behalf, are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight, and reporting obligations if we becomes subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties, and sanctions, which may also adversely affect our business. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

Privacy and Data Protection Laws

We are subject to laws and regulations covering data privacy and the protection of health-related and other personal information. Federal, state, and foreign laws also govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts in states or jurisdictions we conduct business. For example, California recently enacted the California Consumer Privacy Act (“CCPA”), which creates new individual privacy rights for California consumers, as defined in the law, and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020 and became enforceable by the California Attorney General on July 1, 2020. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. California also passed the California Privacy Rights Act, which imposes additional data protection obligations on companies doing business in California. These and other applicable state and foreign privacy laws, as well as uncertain changes in future regulation and legislation, could impact our business strategies, increase our potential liability, increase our compliance costs, and adversely affect our business.

The collection and use of personal health data in the European Union are governed by the provisions of the Data Protection Directive, and as of May 2018, the General Data Protection Regulation (“GDPR”). This directive imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities, and the security and confidentiality of the personal data. The Data Protection Directive and GDPR also impose strict rules on the transfer of personal data out of the European Union to the U.S. Failure to comply with the requirements of the Data Protection Directive, the GDPR, and the related national data protection laws of the European Union member states may result in fines and other administrative penalties. The GDPR introduces new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The GDPR regulations may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations, and prospects.

Foreign Regulatory Matters

European Drug Development

In Europe, any future drug products for which we receive marketing authorization will also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the United States, the various phases of preclinical and clinical research in Europe are subject to significant regulatory controls. Although the

European Union Clinical Trials Directive 2001/20/EC (“Clinical Trials Directive”) has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU member states have transposed and applied the provisions of the Clinical Trials Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated, it must be approved in each of the EU member states where the trial is to be conducted by two distinct bodies: the National Competent Authority (“NCA”) and one or more Ethics Committees (“ECs”). Under the current regime, all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the member state where they occurred.

In 2014, a new Clinical Trials Regulation 536/2014 (“Clinical Trials Regulation”), replacing the current Directive, was adopted. The Clinical Trials Regulation will become directly applicable in all EU member states (without national implementation) once the EU Portal and Database are fully functional. The implementation of the Clinical Trials Regulation depends on confirmation of full functionality of the Clinical Trials Information System through an independent audit, which commenced in September 2020. This system went into application in first quarter of 2022. The Clinical Trials Regulation seeks to simplify and streamline the approval of clinical trials in the European Union. For example, the sponsor can submit a single application for approval of a clinical trial via the EU Portal. As part of the application process, the sponsor will propose a reporting member state, which will coordinate the validation and evaluation of the application. The reporting member state shall consult and coordinate with the other member states in which the clinical trial will take place, also referred to as the Member States Concerned. If an application is rejected, it can be amended and resubmitted through the EU Portal. If an approval is issued, the sponsor can start the clinical trial in all Member States Concerned. However, a Member State Concerned can in limited circumstances declare an “opt-out” from an approval. In such a case, the clinical trial cannot be conducted in that member state. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database.

European Drug Review and Approval

In the European Economic Area (“EEA”), which is comprised of the 27 EU member states plus Norway, Iceland, and Liechtenstein, medicinal products can only be commercialized after obtaining approval of an EU marketing authorization application (“MAA”). There are two types of marketing authorizations. The first is the community or centralized EU MAA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use (“CHMP”) of the European Medicines Agency and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of drugs, such as biotechnology medicinal drugs, orphan medicinal drugs, and medicinal drugs containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune, and viral diseases. The Centralized Procedure is optional for drugs containing a new active substance not yet authorized in the EEA, or for drugs that constitute a significant therapeutic, scientific, or technical innovation or which are in the interest of public health in the EU.

National EU MAAs, which are issued by the competent authorities of the member states of the EEA and only cover their respective territory, are available for drugs not falling within the mandatory scope of the Centralized Procedure. Where a drug has already been authorized for marketing in a member state of the EEA, this National EU MAA can be recognized in another member states through the Mutual Recognition Procedure. If the drug has not received a National EU MAA in any member state at the time of application, it can be approved simultaneously in various member states through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the member states in which the EU MAA is sought, one of which is selected by the applicant as the Reference Member State (“RMS”). The competent authority of the RMS prepares a draft assessment report, a draft summary of the drug characteristics (“SPC”), and a draft of the labeling and package leaflet, which are sent to the other member states, or the Member States Concerned, for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the drug is subsequently granted a national EU MAA in all the member states, i.e., in the RMS and the Member States Concerned.

Under the above-described procedures, before granting the EU MAA, the EMA or the competent authorities of the member states of the EEA make an assessment of the risk-benefit balance of the drug on the basis of scientific criteria concerning its quality, safety, and efficacy.

European Chemical Entity Exclusivity

In Europe, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom ("UK") voted in favor of leaving the EU, commonly referred to as Brexit. Thereafter, on March 29, 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The UK formally left the EU on January 31, 2020. A transition period began on February 1, 2020, during which EU pharmaceutical law remains applicable to the UK and ends on December 31, 2020. Although the UK is no longer a member of the EU, EU law remains applicable in Northern Ireland. There are a number of new marketing authorization routes available in the UK, Great Britain (England, Scotland and Wales) or Northern Ireland, in addition to the national procedure. As with the EU position, a company can only start to market a medicine in the UK once it has received a marketing authorization. The main legislation that applies to clinical trials in the UK is the UK Medicines for Human Use (Clinical Trials) Regulations 2004, which transposes the Clinical Trials Directive into domestic law. Consequently, the requirements and obligations that relate to the conduct of clinical trials in the UK currently remain largely aligned with the EU position. It is unclear how future regulatory regime in the UK will impact regulations of products, manufacturers, and approval of product candidates in the UK.

Other Foreign Countries

For other countries outside of the United States and the European Union, the requirements governing the conduct of clinical trials, drug approval or marketing authorization, pricing, and reimbursement vary from country to country. In all cases, clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki, which is a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data, developed by the World Medical Association.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

Employees and Human Capital

We have operated by leveraging skilled experts, consultants, contract research organizations, and contractors to manage our clinical operations, manufacturing, research and development, and other functions under the leadership and direction of our management. We will continue to expand our infrastructure to manage our operations, including commercial with additional full-time employees.

As of December 31, 2021, we had 39 full-time or part-time employees. Of these employees, 22 employees are engaged in research and development activities and 17 employees are engaged in general and administrative activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider the relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees, advisors and consultants, while being committed to a diverse and dynamic workplace. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase shareholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Our Corporate Information

We (formerly known as "Aerpio Pharmaceuticals, Inc.") were originally incorporated in the State of Delaware in November 2007 under the name "Zeta Acquisition Corp. II." Prior to the merger with Aerpio Pharmaceuticals, Inc., Zeta Acquisition Corp. II was a "shell" company registered under the Exchange Act with no specific

business plan or purpose until it began operating the business of Aerpio Pharmaceuticals, Inc. through a merger in March 2017. In August 2021, we effected a reverse merger pursuant to which a wholly owned subsidiary of ours, merged with and into Aadi Subsidiary, Inc. (formerly Aadi Bioscience, Inc.) (“Private Aadi”), with Private Aadi surviving as a wholly owned subsidiary of ours. Upon the closing of the Merger, we changed our name from “Aerpio Pharmaceuticals, Inc.” to “Aadi Bioscience, Inc.” and the name of Private Aadi was changed from “Aadi Bioscience, Inc.” to “Aadi Subsidiary, Inc.”

Our principal executive offices are located at 17383 Sunset Boulevard, Suite A250, Pacific Palisades, California 90272. We maintain a website at www.aadibio.com, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the Securities and Exchange Commission (the “SEC”) will be available free of charge through the website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website does not constitute a part of this Annual Report on Form 10-K or any of our other filings with the SEC unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC’s Interactive Data Electronic Applications system at <http://www.sec.gov>. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors

Investing in our common stock involves significant risks, some of which are described below. In evaluating our business, investors should carefully consider the following risk factors. These risks and uncertainties summarized above and described below are not intended to be exhaustive and are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem immaterial may also impair our business operations. Please see page 2 of this Annual Report for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Summary of the Material and Other Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties that you should be aware of in evaluating our business, including those described in Part I, Item 1A. “Risk Factors” in this Annual Report. These risks include, but are not limited to, the following:

- We are an early commercial stage biopharmaceutical company, have a limited operating history, have not initiated or completed any large-scale clinical trials, and have a single product approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and viability.
- We have incurred significant net losses since our inception, and we expect to continue to incur significant net losses for the foreseeable future.
- Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates.
- Even following approval and commercialization of FYARRO for the PEComa indication, we will require additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.
- We are early in our development efforts and have only one product which has completed development and obtained regulatory approval by the FDA for a single indication, FYARRO. We are substantially dependent on the success of our lead product candidate, FYARRO. If we are unable to successfully commercialize FYARRO for the PEComa indication or complete development of, obtain approval for and commercialize FYARRO for one or more other indications in a timely manner, our business will be harmed.
- In addition to FYARRO, our prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.
- Results from early preclinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later preclinical studies and clinical trials of our product candidates. If we cannot replicate the results from our earlier preclinical studies and clinical trials of our product candidates in our later preclinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.
- If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our regulatory submissions or receipt of necessary regulatory approvals could be delayed or prevented.
- We have limited resources and are currently focusing our efforts on developing and commercializing FYARRO for particular indications. As a result, we may fail to capitalize on other indications or product candidates that may ultimately prove to be more profitable or to have a greater likelihood of success.
- We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or achieve regulatory approval before we do or that are more effective, safer or less expensive than the products we develop, our commercial opportunities will be negatively impacted.
- The market opportunities for FYARRO and any other product candidates we may develop in the future, if approved, may be limited to certain smaller patient subsets.
- The global COVID-19 pandemic has affected and is expected to continue to affect our business and operations.
- We may be unable to obtain United States approval for FYARRO for additional indications or our other product candidates that we may develop in the future or foreign regulatory approval for FYARRO or our

other product candidates that we may develop in the future and, as a result, may be unable to commercialize FYARRO or our product candidates and our business will be substantially harmed.

- FYARRO is, and any other product candidate we may develop in the future for which we obtain marketing approval for could be, subject to post-marketing restrictions or recall or withdrawal from the market, and we may be subject to penalties if we or our collaborators fail to comply with regulatory requirements or if we or our collaborators experience unanticipated problems with FYARRO, or any other product candidate we may develop in the future when and if any of them are approved.
- We may face difficulties from changes to current regulations and future legislation.
- Our success is highly dependent on our ability to attract and retain highly skilled executive officers, key scientific personnel and employees.
- If we are unable to establish sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to successfully sell or market our product candidates that obtain regulatory approval.
- Our success depends on our ability to protect our intellectual property and our proprietary technologies.
- Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.
- If we do not obtain patent term extension for our product candidates, our business may be materially harmed.
- The manufacture of drugs is complex, and our third-party manufacturers may encounter difficulties in production. If any of our third-party manufacturers encounter such difficulties, our ability to provide adequate supply of FYARRO for patients or for clinical trials or any other product candidate that we may develop in the future, if approved, could be delayed or prevented.
- We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.
- We contract with qualified third parties for the production of FYARRO for commercialization and expect to continue to do so for additional clinical trials. This reliance on third parties, some of which are sole source suppliers, increases the risk that we will not have sufficient quality and quantities of FYARRO or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- We are dependent on a single-source supplier for the drug product FYARRO, and the loss of such supplier could harm our business.
- We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.
- We entered into a collaboration agreement with EOC Pharma (“EOC”), and we may form or seek additional strategic alliances or collaborations in the future. Such alliances and collaborations may inhibit future opportunities, or we may not realize the benefits of such collaborations or alliances.
- We depend on EOC to develop and commercialize FYARRO within the EOC Territory, and we have limited control over how EOC will conduct development and commercialization activities for FYARRO.
- Our stock price is expected to be volatile.
- If we fail to attract and retain management and other key personnel, we may be unable to continue to successfully develop or commercialize our product candidates or otherwise implement our business plan.

Risks Related to Our Business, Financial Condition and Capital Requirements

We are an early commercial stage biopharmaceutical company, have a limited operating history, have not initiated or completed any large-scale clinical trials, and have a single product approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and viability.

We are an early commercial-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We have a single product, FYARRO, approved for commercial sale by the FDA in November 2021 and have not generated any revenue as of December 31, 2021, and we continue to

incur significant research and development and other expenses related to our ongoing operations. We have not yet demonstrated an ability to overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. Consequently, any predictions about our future performance may not be as accurate as they would be if we had a history of successfully developing and commercializing biopharmaceutical products.

To date, we have devoted substantially all of our resources to research and development activities, business planning, establishing and maintaining our intellectual property portfolio, preparing for commercialization of FYARRO, hiring personnel, raising capital and providing general and administrative support for these operations. Our Phase 2 registrational study of our drug FYARRO (*nab*-sirolimus) (the “AMPECT trial”) for advanced (metastatic or locally advanced) malignant perivascular epithelioid sarcoma (“PEComa”) has been completed. A rolling New Drug Application (an “NDA”) submission for our lead product candidate, FYARRO, was completed in May 2021, and the U.S. Food and Drug Administration (the “FDA”) accepted our NDA in July 2021 and approved FYARRO for the treatment of advanced malignant PEComa in November 2021. Based on the AMPECT trial and emerging data for FYARRO in other solid tumors with tumor-agnostic Tuberous Sclerosis Complex 1 and 2 (“TSC1 & TSC2”) alterations, and following discussions with the FDA, we opened enrollment for our tumor-agnostic registration-directed trial in cancers harboring TSC1 & TSC2 inactivating alterations in the first quarter of 2022. Our other programs are in early clinical research stages.

We have not yet demonstrated our ability to successfully manufacture a commercial-scale product, although we have arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for you to accurately predict our likelihood of success and viability than it could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by early commercial-stage biopharmaceutical companies in rapidly evolving fields. We also are transitioning to a company capable of supporting commercial activities. We have not yet demonstrated an ability to successfully overcome such risks and difficulties, or to make such a transition. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We have incurred significant net losses since our inception, and we expect to continue to incur significant net losses for the foreseeable future.

We have incurred significant net losses since our inception, have not generated any revenue from product sales to date and have financed our operations principally through private placements of our convertible preferred stock, federal grants and proceeds from licenses. Our net losses were \$110.1 million for the year ended December 31, 2021, and \$3.5 million for the year ended December 31, 2020. We had an accumulated deficit of \$142.7 million as of December 31, 2021, and \$32.6 million as of December 31, 2020. These losses have resulted primarily from a non-cash impairment charge of \$74.2 million related to an acquired contract intangible asset, costs incurred in connection with research and development activities, costs incurred in connection with commercializing FYARRO and general and administrative costs associated with our operations. We have only one product approved for commercial sale and have not generated any product revenue as of December 31, 2021, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we expect to continue to incur significant operating expenses for the foreseeable future due to the cost of commercializing FYARRO, research and development, including identifying and designing additional product candidates and conducting preclinical studies and clinical trials, and the regulatory approval process for our product candidates. We expect our expenses, and the potential for losses, to increase substantially as we commercialize FYARRO, continue to conduct clinical trials of our product candidates and seek to expand our pipeline. The amount of our future expenses and potential losses is uncertain.

Even if we succeed in commercializing FYARRO for its approved PEComa indication, and if we succeed in receiving regulatory approval for and commercializing one or more of our future product candidates, we expect to continue to incur significant expenses and increasing operating losses over the next several years and for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had, and will continue to have, an adverse effect on our

working capital, our ability to fund the commercialization of FYARRO, the development of our other product candidates, our ability to achieve and maintain profitability and the performance of our stock.

Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates.

We have one product approved for commercialization in the U.S., FYARRO, for the treatment of advanced malignant PEComa, which was approved by the FDA in November 2021 and launched commercially in the U.S. in February 2022. Our ability to generate substantial product revenue sufficient to achieve profitability depends on our ability, alone or with strategic collaboration partners, to obtain the regulatory and marketing approvals necessary to commercialize FYARRO in foreign jurisdictions and to successfully complete discovery, development and eventual commercialization of additional indications or one or more of our other current and future product candidates. We do not anticipate generating revenue from product sales significant enough to achieve profitability for the foreseeable future. Our ability to generate future revenue and achieve profitability depends significantly on our ability, or any current or future collaborator's ability, to achieve several objectives, including, but not limited to:

- demonstrating the safety and efficacy of FYARRO to the satisfaction of the FDA and obtaining regulatory approval for FYARRO for other indications and for other current and future product candidates, if any, for which there is a commercial market;
- launching and successfully commercializing FYARRO or any product candidates following any regulatory approval, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for FYARRO or any other product candidates we may develop, if approved;
- completing development activities, including planned clinical trials for FYARRO for *TSC1 & TSC2*, successfully and on a timely basis;
- obtaining additional regulatory and marketing approvals for FYARRO for additional indications;
- our ability to complete investigational new drug application (an "IND") enabling studies and successfully submit INDs or IND supplements or comparable applications, which become effective without any objections by the FDA or comparable regulatory authorities before commencing a clinical trial for any of our product candidates;
- establishing and maintaining relationships with contract research organizations ("CROs") and clinical sites for the clinical development of FYARRO in other indications and any other future product candidates that we may develop;
- timely receipt of regulatory approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development;
- developing or contracting for an efficient and scalable manufacturing process for our product candidates, including obtaining finished products that are appropriately packaged for sale;
- negotiating and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized;
- a continued acceptable safety profile following any regulatory approval of our product candidates;
- commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- satisfying any required post-regulatory approval commitments to applicable regulatory authorities;
- identifying, assessing and developing new product candidates;
- obtaining, maintaining and expanding patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protecting our rights in our intellectual property portfolio;
- defending against third-party interference or infringement claims, if any;

- entering into and maintaining, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining coverage and adequate reimbursement by third-party payors for our product candidates;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring and retaining qualified personnel.

We may never be successful in achieving our objectives and, even if we do, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business or continue our operations and could cause a decline in the value of our common stock.

We will require additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing and planned activities, particularly as we seek additional regulatory approval of FYARRO for additional indications, and the commercialization of FYARRO for its approved indications. Our expenses could increase beyond our current expectations if we are required by the FDA, the European Medicines Agency (the “EMA”) or other regulatory agencies to perform clinical trials or preclinical studies in addition to those that we currently anticipate, or if there are any delays in any of our clinical trials or the development of any of our product candidates. Other unanticipated costs may also arise. In addition, even if we obtain regulatory approval for any of our other product candidates, including additional indications for FYARRO, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution activities and ongoing compliance activities. We cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of FYARRO for the PEComa indication, or for any other additional indications, if approved, or any other product candidates or other indications we may develop. Upon receiving regulatory approval for FYARRO from the FDA in November 2021, we are only permitted to market or promote FYARRO for the PEComa indication, and not for any other indication, or any other product candidate, in the United States. In addition, we will incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

As of December 31, 2021, we had \$149.0 million in cash and cash equivalents. Based on our current operating plan, we believe that our cash and cash equivalents will enable us to fund our planned operating expenses and capital expenditures into 2024. Our estimate as to how long we expect our cash and cash equivalents to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

We plan to use our cash and cash equivalents to fund the commercialization of FYARRO for the PEComa indication, ongoing and planned clinical trials of FYARRO for other indications such as the *TSC1 & TSC2* indications, for manufacturing operations and to fund our other research for other product candidates and development activities, as well as for working capital and other general corporate purposes. Advancing the development of FYARRO and any other product candidate will require a significant amount of capital. Our existing cash and cash equivalents will not be sufficient to fund all of the activities that are necessary to complete the development of FYARRO.

We will be required to obtain further funding to support our continuing operations through public or private equity offerings, debt financings, third-party funding, marketing and distribution arrangements, collaborations with third parties and licensing arrangements or other sources or a combination of these approaches, which may dilute our stockholders or restrict our operating activities. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize FYARRO or

any other product candidates we may develop in the future, if approved. Adequate additional financing may not be available to us in sufficient amounts or on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder and the possibility of such issuance may cause the market price of our shares to decline. Debt financing may result in imposition of debt covenants, increased fixed payment obligations or other restrictions that may affect the conduct of our business. If we raise additional funds through up-front payments or milestone payments pursuant to strategic collaborations with third parties, we may have to relinquish valuable rights to certain of our technologies or our product candidates, or grant licenses on terms that are not favorable to us, which may have a material adverse effect on our business, operating results and prospects. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to significantly delay, reduce the scope of, suspend or eliminate one or more of our research or development programs, clinical trials or future commercialization efforts.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

We are early in our development efforts and have only one product which has completed development and obtained regulatory approval by the FDA for a single indication, FYARRO. We are substantially dependent on the success of FYARRO. If we are unable to commercialize FYARRO for the PEComa indication or complete development of, obtain approval for and commercialize FYARRO for one or more other indications in a timely manner, our business will be harmed.

We are early in our development efforts and have only one product that has completed development and been approved by the FDA, FYARRO, our lead product. Our future success is dependent on our ability to commercialize FYARRO, and to timely and successfully obtain regulatory approval for additional indications for FYARRO. We are investing the majority of our efforts and financial resources to commercialize FYARRO for the PEComa indication and in the research and development of FYARRO for multiple additional indications. FYARRO (sirolimus protein-bound particles for injectable suspension (albumin-bound)), a form of sirolimus bound to albumin, for the treatment of malignant PEComa, as well as other cancer types with mTOR pathway alterations in the *TSC1 & TSC2* genes that are most likely to respond to mTOR treatment.

In May 2021, we completed the filing of a rolling NDA for FYARRO to the FDA for approval to treat patients with advanced malignant PEComa, and the FDA accepted our NDA in July 2021 and approved FYARRO for advanced malignant PEComa in November 2021. Our NDA was based on results from our AMPECT trial, involving patients for whom there were no approved therapies in the United States. In November 2019, we announced top-line results from the AMPECT trial, including that the study achieved its primary endpoint of objective response rate (the “ORR”) as determined by blinded independent central radiologic review using modified Response Evaluation Criteria in Solid Tumors (“RECIST”). FYARRO will require additional clinical development, expansion of manufacturing capabilities, regulatory approval from foreign regulatory authorities in jurisdictions outside of the U.S. where we plan to market FYARRO for malignant PEComa and potentially in additional indications, if approved, substantial investment and significant marketing efforts before we can generate any revenues from product sales. We are not permitted to market or promote FYARRO for non-PEComa indications, before we receive regulatory approval from the FDA and comparable foreign regulatory authorities, and we may never receive such regulatory approvals.

The success of FYARRO will depend on several factors, including the following:

- the efficacy and safety of FYARRO in a larger number of patients in a non-clinical trial setting that those demonstrated in our clinical trials;
- the effectiveness of our sales, marketing and distribution efforts, particularly during the remote, COVID-19 environment;
- the maintenance of existing or the establishment of new supply arrangements with third-party drug product suppliers and manufacturers for sufficient commercial supplies and additional clinical development of FYARRO;

- the successful launch of commercial sales, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- the timely receipt of regulatory approval for FYARRO from applicable foreign regulatory authorities for advanced malignant PEComa;
- the successful completion of any clinical trials, regulatory approval and commercialization of FYARRO for one or more label expansion indications;
- the extent of any required post-regulatory approval commitments to applicable regulatory authorities;
- the willingness of medical professionals to prescribe and patients to use FYARRO and continue to use FYARRO;
- the prevalence and severity of adverse side effects;
- the convenience of prescribing, administrating and initiating patients on FYARRO;
- the potential and perceived value and relative cost of FYARRO;
- the availability of coverage and adequate reimbursement and pricing by private and government payors;
- the successful and timely completion of the required preclinical studies and clinical trials of FYARRO for current and future indications;
- INDs going into effect with the FDA for our planned and future clinical trials;
- the initiation and successful patient enrollment and completion of additional clinical trials of FYARRO on a timely basis, including the planned registration-directed Phase 2 study (“PRECISION 1”) of FYARRO in patients with tumor-agnostic *TSC1* & *TSC2* alterations;
- maintaining and establishing relationships with CROs and clinical sites for the development of FYARRO both in the United States and internationally;
- the type, frequency and severity of adverse events in clinical trials;
- demonstrating efficacy and safety profiles that are satisfactory to the FDA and any comparable foreign regulatory authority for regulatory approval obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- the protection of our rights in our intellectual property portfolio;
- a continued acceptable safety profile following our current and future regulatory approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

In addition to advanced malignant PEComa, based on data from the completed AMPECT trial and our ongoing expanded access program, we have initiated a registration-directed tumor-agnostic Phase 2 study, PRECISION 1, of FYARRO in patients with *TSC1* & *TSC2* alterations. We completed a Type B meeting with the FDA in which we discussed the initial trial design. The PRECISION 1 trial is now open for enrollment in the United States. Our product development costs could increase if we experience delays. Significant trial delays also could shorten any periods during which we may have the exclusive right to commercialize FYARRO or allow our competitors to bring products to market before we do, which would impair our ability to successfully capitalize on FYARRO and may harm our business, results of operations and prospects. Events that may result in a delay or unsuccessful completion of additional clinical development of FYARRO include, among other things:

- unexpectedly high rate of patients withdrawing consent or being lost to follow-up;
- feedback from the FDA and foreign regulatory authorities, institutional review boards (“IRBs”), or a data safety monitoring board, or results from clinical trials that might require modification to a clinical trial protocol;
- imposition of a clinical hold by the FDA or other regulatory authorities, a decision by the FDA, other regulatory authorities, IRBs or us, or a recommendation by a data safety monitoring board to suspend or terminate trials at any time for safety issues or for any other reason;
- deviations from the trial protocol by clinical trial sites and investigators or failure to conduct the trial in accordance with regulatory requirements;
- failure of third parties, such as CROs, to satisfy their contractual duties or meet expected deadlines;

- delays in the testing, validation, manufacturing and delivery of FYARRO to customers or the clinical trial sites;
- delays caused by patients dropping out of a trial due to side effects, disease progression or other reasons;
- unacceptable risk-benefit profile or unforeseen safety issues or adverse drug reactions;
- failure to demonstrate the efficacy of FYARRO in this clinical trial;
- changes in government regulations or administrative actions or lack of adequate funding to continue the trials; or
- business interruptions resulting from geo-political actions, including war and terrorism, such as the Russia-Ukraine conflict, or natural disasters and public health epidemics, such as the COVID-19 pandemic.

An inability by us to timely complete clinical development could result in additional costs to us or impair our ability to generate substantial product revenues or development, regulatory, commercialization and sales milestone payments and royalties on product sales.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of our current or any future collaborators. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize FYARRO for multiple indications, which would materially harm our business. If we do not receive regulatory approvals for FYARRO in additional indications or for other product candidates, we may not be able to continue our operations.

In addition to FYARRO, our prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.

Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates other than FYARRO. All of our current product candidates other than FYARRO are in research or preclinical development. Prior to initiating clinical trials with our other product candidates, we will need to file an IND or similar application to the FDA or regulatory authorities in other jurisdictions. We may not be able to file future INDs for our product candidates on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing further clinical trials to begin, or that, once begun, issues will not arise that result in the suspension or termination of clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND. Any failure to file INDs on the timelines we expect or to obtain regulatory clearance for our trials may prevent us from developing our product candidates on a timely basis, if at all. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical studies or early clinical trials of a product candidate may not be predictive of the results that will be obtained in later stage clinical trials of the product candidate.

The success of other product candidates we may develop will depend on many factors, including the following:

- generating sufficient preclinical data to support the initiation of clinical trials;
- obtaining regulatory permission to initiate clinical trials;
- contracting with the necessary parties to conduct preclinical studies and clinical trials;
- successful enrollment of patients in, and the completion of, clinical trials on a timely basis;
- the timely manufacture of sufficient quantities of a product candidate for use in clinical trials; and

- generating sufficient safety and efficacy data to warrant continued development and which are satisfactory to the FDA or any other regulatory authority for marketing approval.

Even if we successfully advance any other product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this “Risk Factors” section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from any additional product candidates beyond FYARRO for advanced malignant PEComa.

FYARRO or any other product candidates we may develop in the future may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success, which would limit the revenue that we generate from our sales.

Even though FYARRO has been approved for advanced malignant PEComa, and even if any other product candidates that we may develop in the future receive regulatory approval, such approved product candidates may not gain adequate market acceptance among physicians, patients, third-party payors and others in the medical community. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including, among others:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which a product candidate is approved;
- restrictions on the use of product candidates in the labeling approved by regulatory authorities, such as boxed warnings or contraindications in labeling, or a risk evaluation and mitigation strategy, if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement by third-party payors, including government authorities or the willingness of patients to pay out-of-pocket in the absence of third-party payor coverage;
- the availability of an approved product candidate for use as a combination therapy;
- the prevalence and severity of any adverse effects associated with any approved product candidate;
- any restrictions on the use of our product candidates together with other medications;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and undergo required diagnostic screening to determine treatment eligibility and of physicians to prescribe these therapies and diagnostic tests;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to our product candidates; and
- the approval of other new therapies for the same indications.

Even though FYARRO is approved for advanced malignant PEComa, it may never achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, and we may not generate or derive sufficient revenue from that product and our financial results could be negatively impacted. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful.

The market opportunities for FYARRO and any other product candidates we may develop in the future, if approved, may be limited to certain smaller patient subsets.

Cancer therapies are sometimes characterized by line of therapy (first-line, second-line, third-line, etc.) and the FDA often approves new therapies initially only for a particular line or lines of use. When cancer is detected early enough, first-line therapy, such as chemotherapy, hormone therapy, surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. FYARRO for malignant PEComa

has been approved as a first-line therapy. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. Our completed and planned clinical trials for FYARRO are with patients who may have received one or more prior treatments. There is no guarantee that product candidates that we develop, even if approved, would be approved for first-line or second-line therapy and, prior to any such approvals, we may have to conduct additional clinical trials that may be costly, time-consuming and subject to risk.

The number of patients who have the cancers we are targeting may turn out to be lower than expected. Our projections of addressable patient populations that may benefit from treatment with our product candidates are based on our estimates, which may prove to be incorrect. Additionally, the potentially addressable patient population for FYARRO and other product candidates may be limited or may not be amenable to treatment with our product candidates. Regulatory approval may limit the market of a product candidate to target patient populations when such biomarker-driven identification and/or highly specific criteria related to the stage of disease progression are utilized. If any of our estimates prove to be inaccurate, the market opportunity for any product candidate that we or our strategic partners develop could be significantly diminished and have an adverse material impact on our business.

Even if we obtain significant market share for any approved product, if the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications.

Any product candidates we develop may become subject to unfavorable third-party coverage and reimbursement practices, as well as pricing regulations.

The availability and extent of coverage and adequate reimbursement by third-party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. Sales of FYARRO or any other product candidate we may develop in the future that receives regulatory approval will depend substantially, both in the United States and internationally, on the extent to which the costs of such product candidate will be covered and reimbursed by third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize FYARRO or any other product candidates that we may develop in the future. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, FYARRO or any other product candidate that we may develop in the future for which we obtain regulatory approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize FYARRO or any other product candidate that we may develop in the future for which we obtain regulatory approval.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products, which would include FYARRO and any other product candidate we may develop in the future for which we may obtain regulatory approval. Market acceptance and sales of FYARRO or any other product candidates we may develop in the future for which we obtain regulatory approval will depend on reimbursement policies and may be affected by healthcare reform measures. Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payors are critical to new product acceptance. Third-party payors decide which drugs they will pay for and establish reimbursement levels. In the United States, for example, principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services (“CMS”), an agency within the U.S. Department of Health and Human Services (“HHS”). CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS’s decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor’s determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. As a result, the coverage determination process is often time-consuming and costly. Factors that payors consider in determining reimbursement are based on whether the product is: (i) a covered benefit under the health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational. This process will require us to provide scientific and clinical support for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs such as FYARRO. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price (an “ASP”) and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, FYARRO or any other product candidate we may develop in the future may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for FYARRO or any other product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

There has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to prescription drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, under the American Rescue Plan Act of 2021, effective January 1, 2024 (the “American Rescue Plan”), the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at increasing competition for prescription drugs. In response to this executive order, the HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and potential legislative policies that Congress could pursue to advance these principles. In addition, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such laws once we begin commercialization for FYARRO or, after obtaining regulatory approval, any of our other product candidates that we may develop in the future. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize FYARRO or any other product candidates that we may develop in the future if approved. Complying with any new legislation and regulatory changes could be time-intensive and expensive, resulting in a material adverse effect on our business.

Outside the United States, the commercialization of therapeutics is generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as FYARRO or any other product candidates that we may develop in the future if approved. In many countries, particularly the countries of the European Union, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives regulatory approval. To obtain favorable reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of FYARRO or any other product candidate that we may develop in the future if approved to other available therapies. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for FYARRO or any other product candidates that we may develop in the future if approved. Accordingly, in markets outside the United States, the reimbursement for FYARRO or any other products that we may develop in the future and receive regulatory approval for may be unavailable or reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits. If reimbursement is conditioned upon our completion of additional clinical trials, or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

If we are unable to establish or sustain coverage and adequate reimbursement for FYARRO or any other product candidates that we may develop in the future if approved from third-party payors, the adoption of FYARRO or those other products if approved, the prices of FYARRO or those other products if approved and sales revenue from FYARRO or those other products if approved will be adversely affected, which, in turn, could adversely affect the ability to market or sell FYARRO or any other product candidates that we may develop in the future, if approved. Coverage policies and third-party payor reimbursement rates may change at any time. Further, due to the COVID-19 pandemic, millions of individuals have lost/will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize FYARRO or any other products candidates that we may develop in the future if approved. It is unclear what effect, if any, the American Rescue Plan will have on the number of covered individuals. Even if favorable coverage and reimbursement status is attained for FYARRO or one or more product candidates that we may develop in the future for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

We may not be able to obtain FDA approval of any future NDA for FYARRO or any other product candidates we may develop in the future.

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, import, marketing and distribution and other possible activities relating to FYARRO and any other product candidate that we may develop in the future are subject to extensive regulation in the United States. Prior to the recent approval of our NDA for FYARRO for advanced malignant PEComa, we had not submitted an application for approval or obtained FDA approval for any product.

Approval of an NDA is not guaranteed, and the approval process is an expensive and uncertain process that may take several years. The FDA and foreign regulatory entities also have substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to target and the regulations applicable to any particular product candidate. Data are subject to varying interpretation and the FDA may not agree that our clinical data support that any of our product candidates are safe and effective for the proposed therapeutic use. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage, and we could encounter problems that require us to repeat or perform additional preclinical studies or clinical trials or generate additional chemistry, manufacturing and controls data, including drug product stability data. The FDA and similar foreign authorities could delay, limit or deny approval of a product candidate, and may ultimately approve the product for narrower indications or with unfavorable labeling that would impede our commercialization of the drug.

Approval procedures vary among countries and can involve additional product testing and additional administrative review periods, including obtaining reimbursement and pricing approval in select markets. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks associated with FDA approval as well as additional, presently unanticipated, risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others, including the risk that our product candidates may not be approved for all indications requested and that such approval may be subject to limitations on the indicated uses for which the product may be marketed.

Failure to obtain marketing approval in international jurisdictions would prevent FYARRO and any other product candidates we may develop in the future from being marketed abroad.

In order to market and sell our products in the European Union and any other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, failure to obtain approval in one jurisdiction may impact our ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

A variety of risks associated with marketing FYARRO and any other product candidates we may develop in the future internationally could affect our business.

We may seek regulatory approval for FYARRO and our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market with low or lower prices rather than buying them locally;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

In addition, the conflict between Russia and Ukraine could lead to disruption, instability and volatility in global markets and industries that could negatively impact our operations. The U.S. government and other governments in jurisdictions in which we may operate in the future have imposed severe sanctions and export controls against Russia and Russian interests and threatened additional sanctions and controls. The impact of these measures, as well as potential responses to them by Russia, is currently unknown and they could adversely affect our business, supply chain, business partners or customers.

These and other risks associated with our international operations may compromise our ability to achieve or maintain profitability

The preclinical studies and clinical trials for FYARRO or any other of our product candidates that we may develop in the future may not demonstrate safety and efficacy to the satisfaction of the FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results, which would prevent, delay, or limit the scope of development, regulatory approval and commercialization.

Before obtaining regulatory approval from the EMA or other foreign regulatory authorities for the sale of FYARRO for malignant PEComa or any additional indications that we may seek approval for, or other product candidates when approved, we, among other requirements, must complete preclinical development and extensive clinical trials to demonstrate with substantial evidence the safety and efficacy of such product or other product candidates. Each product or product candidate must demonstrate an adequate risk versus benefit profile in our intended patient population and for our intended use. Drug product must also be manufactured and tested in accordance with regional regulatory requirements which may differ from region to region. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its ultimate outcome is inherently uncertain. A failure of one or more preclinical studies or clinical trials can occur at any stage of the process. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies in the biopharmaceutical industry that have believed their product candidates performed satisfactorily in preclinical

studies and clinical trials have nonetheless failed to obtain regulatory approval of their products. Our current or future clinical trials may not ultimately be successful or support further clinical development of FYARRO or any other product candidates we may develop in the future.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive regulatory approval or our ability to commercialize FYARRO for additional indications or for any other product candidates we may develop in the future, including:

- receipt of feedback from regulatory authorities that require us to modify the design of our clinical trials;
- negative or inconclusive clinical trial results that may require us to conduct additional clinical trials or abandon certain drug development programs;
- the number of patients required for clinical trials being larger than anticipated, enrollment in these clinical trials being slower than anticipated or participants dropping out of these clinical trials at a higher rate than anticipated;
- clinical trial sites or our CRO failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the suspension or termination of our clinical trials for various reasons, including non-compliance with regulatory requirements or a finding that our product candidates have undesirable side effects or other unexpected characteristics or risks;
- the cost of clinical trials of our product candidates being greater than anticipated;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates being insufficient or inadequate; and
- delays due to the recent COVID-19 pandemic, including starting any clinical trials for other indications or programs.

For instance, we do not know whether FYARRO will perform in current or future clinical trials for additional indications as it has performed in preclinical studies or prior clinical trials. Product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA, EMA, and other comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Additionally, while we are aware of several other approved and clinical-stage mTOR inhibitors being developed by multiple other companies, to our knowledge, there are no mTOR inhibitors approved specifically for the treatment of advanced malignant PEComa other than FYARRO. As such, the development of FYARRO and our stock price may be impacted by inferences, whether correct or not, that are drawn between the success of our product and those of other companies' mTOR inhibitors. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety and efficacy results, which could delay regulatory approval, limit the size of the patient population to which we may market our product candidates, or prevent regulatory approval.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our products may also be undergoing surgical, radiation and chemotherapy treatments and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our products. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes.

We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain approval to market FYARRO for additional indications or for any other product candidates we may develop in the future. If we are required to conduct additional clinical trials or other testing of our product beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product or other testing in a timely manner, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may (i) incur unplanned costs, (ii) be delayed in seeking and obtaining regulatory approval for respective indications, if we receive such approval at all, (iii) receive more limited or restrictive regulatory approval for respective indications, (iv) be subject to additional post-marketing testing requirements or (v) have the drug removed from the market after obtaining regulatory approval. Even if

regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidates, which may also limit their commercial potential.

Our product candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that could delay or prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

If our product candidates are associated with serious adverse events or other undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs, we may need to conduct additional studies to further evaluate the product candidates' safety, interrupt, delay or abandon their development or halt clinical trials or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial or result in a more restrictive label, delay or denial of regulatory approval or potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate, could substantially increase the costs of commercializing our product candidates and significantly impact our ability to successfully commercialize our product candidates and generate revenues, and may harm our business, financial condition and prospects significantly. For example, in our AMPECT trial of FYARRO, most treatment-related adverse events were mild or moderate, with the most commonly reported adverse events being anemia, edema, infections, mucositis, pain, nail changes, vomiting, thrombocytopenia, hypertension and nausea. Treatment-related adverse events in our other oncology and PAH trials of FYARRO included thrombocytopenia, diarrhea, fatigue, mucosal inflammation, nausea, anemia, and rash. Additionally, in our first-in-human study of FYARRO in solid tumors, one patient died of dyspnea which was deemed possibly related to FYARRO.

Patients in our completed and planned clinical trials may in the future suffer other significant adverse events or other side effects not observed or anticipated based on our preclinical studies or previous clinical trials. FYARRO or other product candidates may be used in populations for which safety concerns may be particularly scrutinized by regulatory agencies. In addition, FYARRO is being studied in combination with other therapies, which may exacerbate adverse events associated with the therapy. Patients treated with FYARRO or our other product candidates that we may develop in the future may also be undergoing surgical, radiation and/or chemotherapy treatments, which can cause side effects or adverse events that are unrelated to our product candidate but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. For example, it is expected that some of the patients enrolled in our FYARRO clinical trials will die or experience major adverse clinical events either during the course of our clinical trials or after such trials, which has occurred in the past.

If further significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, EMA, other comparable regulatory authorities or an institutional review board may suspend or terminate clinical research at any time for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development.

Even if the side effects do not preclude the product candidate from obtaining or maintaining regulatory approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects.

Further, for FYARRO for advanced malignant PEComa, or if FYARRO receives regulatory approval for any other indication, or if any other product candidate that we may develop in the future if any of our product candidates obtains regulatory approval, toxicities associated with such product candidates and not seen during clinical testing may also develop after such approval and lead to a requirement to (i) conduct additional clinical safety trials, (ii) add additional contraindications, warnings and precautions to the drug label, (iii) significantly restrict the use of the product, (iv) change the way the product is distributed or administered, (v) implement a risk evaluation and mitigation strategy, or create a medication guide outlining the risks of such side effects for distribution to patients,

or (vi) suspend or withdraw the product from the market. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early-stage clinical trials.

Results from early preclinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later preclinical studies and clinical trials of our product candidates. If we cannot replicate the results from our earlier preclinical studies and clinical trials of our product candidates in our later preclinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Any results from early preclinical studies and clinical trials of our product candidates may not necessarily be predictive of the results from later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies and clinical trials of our product candidates according to our current development timeline, the results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval.

Additionally, some of our ongoing, planned and future clinical trials may utilize an open-label study design and may be conducted at a limited number of clinical sites on a limited number of patients. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates when studied in a controlled environment with a placebo or active control.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim or topline data from our clinical trials, such as the preliminary data from our completed AMPECT trial of FYARRO in patients with malignant PEComas. The preliminary data is based on a preliminary analysis of then available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. For example, we may report tumor responses in certain patients that are unconfirmed at the time and which do not ultimately result in confirmed responses to treatment after follow-up evaluations. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially

change as patient enrollment continues and more patient data become available. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

In addition, the information we choose to publicly disclose regarding a particular clinical trial is typically selected from a more extensive amount of available information. You or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, FYARRO in other indications or any other product candidates that we may develop in the future may be harmed, which could harm our business, financial condition, results of operations and prospects.

Adverse results of clinical trials conducted by third parties investigating the same product candidates as us in different territories could adversely affect our development of such product candidate.

Lack of efficacy, adverse events, undesirable side effects or other adverse results may emerge in clinical trials conducted by third parties investigating our approved product or the same product candidates as us in different territories for the same or different indications. For example, pursuant to the exclusive license agreement (the “EOC License Agreement”) with EOC Pharma (Hong Kong) Limited (“EOC”) for the development and commercialization of FYARRO in Greater China, including the Republic of China, Hong Kong, Macau and Taiwan (collectively, the “EOC Territory”), EOC has been granted the right to develop and commercialize the same compounds licensed to us, as specified in the EOC License Agreement, including FYARRO, in the EOC Territory and, subject to certain restrictions, to collaborate with others for such development and commercialization. We do not have control over EOC’s clinical trials or development program, and adverse findings from or EOC’s conduct of clinical trials could adversely affect our development and commercialization of FYARRO or the viability of FYARRO as a product candidate. We may be required to report EOC’s adverse events or unexpected side effects to the FDA or comparable foreign regulatory authorities, which could, among other things, order us to cease further development of FYARRO.

If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our regulatory submissions or receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to such trial’s conclusion as required by the FDA, EMA or other comparable foreign regulatory authorities. Orphan indications, in particular, have small populations, and it may be difficult for us to locate and enroll sufficient patients in trials for orphan-designated indications. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to identify and enroll eligible patients for clinical trials may be limited or may result in slower enrollment than we anticipate. For instance, patients for our trials for the TSC1 & TSC2 study are screened using genomic information to identify alterations in the TSC1 & TSC2 genes and utilizing such criteria and/or certain highly specific criteria related to the cancer sub-types may limit patient populations eligible for our clinical trials. In particular, because we are focused on patients with specific genetic mutations for certain of our development programs, our ability to enroll eligible patients may be limited or may result in slower enrollment than anticipated. For example, with respect to FYARRO, we cannot be certain how many patients will harbor the TSC1 & TSC2 mutations that FYARRO is designed to target or that the number of patients enrolled for each mutation will suffice for regulatory approval and inclusion of each such mutation in the approved label. We may also engage third parties to develop companion diagnostics for use in our clinical trials, but such third parties may not be successful in developing such companion diagnostics, furthering the difficulty in identifying patients with the targeted genetic mutations for our clinical trials. If our strategies for patient identification prove unsuccessful, we may have difficulty enrolling or maintaining patients appropriate for FYARRO.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors’ product candidates.

Also, marketing authorization of competitors in this same class of drugs may impair our ability to enroll patients into our clinical trials, delaying or potentially preventing us from completing recruitment for one or more of our

trials. Patient enrollment and retention for our current or any future clinical trials may be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol or as mandated by regulatory agencies;
- perceived risks and benefits of the product candidate under study;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates, including any new products that may be approved or other product candidates being investigated for the indications we are investigating;
- the ability to recruit clinical study investigators with the appropriate competencies and experience;
- clinicians' willingness to screen their patients for biomarkers to indicate which patients may be eligible for enrollment in our clinical trials;
- patient referral practices of physicians;
- the ability to obtain and maintain patient consents;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- factors we may not be able to control, such as current or potential pandemics that may limit patients, principal investigators or staff or clinical site availability (e.g., the COVID-19 pandemic).

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Furthermore, any negative results we may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in other clinical trials we are conducting. Similarly, negative results reported by our competitors about their drug candidates may negatively affect patient recruitment in our clinical trials. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain regulatory approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, there is a risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they may be late-stage cancer patients, will not survive the full terms of the clinical trials. As a result, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods. In addition, we rely on clinical trial sites to ensure timely conduct of our clinical trials and, while we have entered into agreements governing their services, we are limited in our ability to compel their actual performance.

We expect to develop FYARRO and potentially other product candidates in combination with other therapies, which exposes us to additional risks.

We intend to develop FYARRO and potentially other product candidates, in combination with one or more currently approved or unapproved therapies to treat cancer or other diseases. Patients may not be able to tolerate FYARRO or any of our other product candidates in combination with other therapies or dosing of FYARRO in combination with other therapies may have unexpected consequences. Even though FYARRO has received FDA approval for advanced malignant PEComa, and even if FYARRO receives regulatory approval for additional indications, if any of our product candidates were to receive regulatory approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, EMA or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates, the FDA, EMA or comparable foreign regulatory authorities in other jurisdictions requiring additional clinical trials, or our own products being removed from the market or being less successful commercially.

We may also evaluate our product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA, EMA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate in combination with any such unapproved cancer therapies that do not ultimately obtain regulatory approval.

If the FDA, EMA or other comparable foreign regulatory authorities do not approve or revoke their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with FYARRO or any other product candidate, we may be unable to obtain approval of or successfully market any one or all of the product candidates we develop. These unapproved therapies face the same risks described with respect to our product candidates currently in development, including serious adverse effects and delays in their clinical trials. In addition, other companies may also develop their products or product candidates in combination with the unapproved therapies with which we are developing our product candidates for use in combination. Any setbacks in these companies' clinical trials, including the emergence of serious adverse effects, may delay or prevent the development and approval of our product candidates.

Additionally, if the third-party providers of therapies or therapies in development used in combination with our product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We have limited resources and are currently focusing our efforts on developing and commercializing FYARRO for particular indications. As a result, we may fail to capitalize on other indications or product candidates that may ultimately prove to be more profitable or to have a greater likelihood of success.

We are currently focusing our resources and efforts on developing and commercializing FYARRO for particular indications and advancing our preclinical programs for certain other product candidates. As a result, because we have limited financial and managerial resources, we may forgo or delay pursuit of opportunities for other indications or with other product candidates that may later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Failure to properly assess potential product candidates could result in our focus on product candidates with low market potential, which would harm our business, financial condition, results of operations and prospects. Our spending on current and future research and development activities for FYARRO and other programs may not yield any commercially viable drugs. If we do not accurately evaluate the completed clinical trial data, likelihood of future clinical trial success, commercial potential or target markets for FYARRO or any of our other product candidates that we may develop in the future, we may relinquish valuable rights to that product candidate or program through collaboration, licensing or other strategic or royalty arrangements in cases in which we would have been more advantageous for us to retain sole development and commercialization rights to such product candidate or program.

We face significant competition, and if our competitors develop and market technologies or products more rapidly than we do or achieve regulatory approval before we do or that are more effective, safer or less expensive than the products we develop, our commercial opportunities will be negatively impacted.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with FYARRO for advanced malignant PEComa or for any additional indications we may seek approval for, and for any other product candidates that we may develop in the future, if approved. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates. In addition, our products may need to compete with drugs that physicians currently use to treat the indications for which we seek approval. This may make it difficult for us to replace existing therapies with our products.

In particular, there is intense competition in the field of oncology. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology

companies, specialty pharmaceutical companies, emerging and start-up companies, government agencies, universities and other research institutions. We also compete with these organizations to recruit and retain management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in-licensing new product candidates.

Other than FYARRO, we are not aware of any FDA or EMA approved products indicated specifically for the treatment of advanced malignant PEComa. Patients with malignant PEComa commonly receive chemotherapy regimens and currently mTOR inhibitors including sirolimus, everolimus, and temsirolimus are recommended in the National Comprehensive Cancer Network (the “NCCN”) guidelines for treatment of advanced malignant PEComa based on published retrospective data. Following FDA approval, FYARRO was added to the NCCN guidelines as the only preferred regimen for treatment of malignant PEComa. For tumor agnostic *TSC1* & *TSC2* inactivating alterations, there are no existing FDA or EMA approved products indicated for such use. If FYARRO receives additional regulatory approval for these *TSC1* & *TSC2* indications, it may face competition from other drug candidates in clinical trials that target the mTOR pathway. These may include dual mTORC1/2 inhibitors in clinical trials or next generation mTOR inhibitors in development. Any potential competitors may have significantly greater financial, manufacturing, marketing, drug development, technical and human resources, and commercial expertise than us. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical and biotechnology companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result of all of these factors, our competitors may succeed in obtaining approval from the FDA, EMA or other comparable foreign regulatory authorities or in discovering, developing and commercializing products in the field before us.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, have a broader label, are marketed more effectively, are more widely reimbursed or are less expensive than any products that we may develop and commercialize. Our competitors also may obtain regulatory approval from the FDA, EMA or other comparable foreign regulatory authorities for their products more rapidly than we may obtain approval for our products, which could result in our competitors establishing a strong market position before we are able to enter the market. Our approved product, or product candidates we may develop in the future which achieve regulatory approval, may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of FYARRO or any other products we may develop in the future, if approved, could be adversely affected.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates progress through preclinical studies and clinical trials to regulatory approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. For example, we may introduce alternative formulations or dosage forms of FYARRO in additional clinical trials for other indications. Such material changes will require regulatory approval before implementation and carry the risk that they will not achieve these intended objectives. Any of these changes could cause FYARRO and any other product candidate that we may develop in the future to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval

of our product candidates and jeopardize our ability to commercialize FYARRO or any other product candidates that we may develop in the future, if approved, and generate revenue.

We may not be successful in growing our product pipeline through acquisitions and in-licenses.

We believe that accessing external innovation and expertise is important to our success; and while we plan to leverage our leadership team's prior business development experience as we evaluate potential in-licensing and acquisition opportunities to further expand our portfolio, we may not be able to identify suitable licensing or acquisition opportunities, and even if we do, we may not be able to successfully secure such licensing and acquisition opportunities. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We may also be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully license or acquire additional product candidates to expand our portfolio, our pipeline, competitive position, business, financial condition, results of operations, and prospects may be materially harmed.

Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage such inability could have a material adverse effect on our business and financial condition.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims might be brought against us by patients, healthcare providers, or others selling or otherwise coming into contact with FYARRO or any other product candidates that we may develop in the future. For example, we may be sued if FYARRO or any other product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we become subject to product liability claims and cannot successfully defend against them, we could incur substantial liabilities. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an FDA, EMA or other regulatory authority investigation of the safety and effectiveness of our products, our (or third-party) manufacturing processes and facilities or our marketing programs. FDA, EMA or other regulatory authority investigations could potentially lead to a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources and substantial monetary awards to trial participants or patients. Although we have obtained product liability insurance coverage, our insurance coverage may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain or maintain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could also cause our stock price to decline.

The recent global COVID-19 outbreak has affected and is expected to continue to affect our business and operations.

Broad-based business or economic disruptions could adversely affect our ongoing or planned research and development activities. To date, the COVID-19 pandemic has caused significant disruptions to the United States and global economy. Further, infections and deaths related to COVID-19 are disrupting certain healthcare and healthcare regulatory systems globally. Such disruptions could divert healthcare resources away from, or materially delay review by, the FDA and comparable foreign regulatory agencies. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially adversely affect the development and study of our product candidates. The COVID-19 pandemic caused us to modify business practices (including but not

limited to curtailing or modifying employee travel, curtailing or modifying our clinical trials, moving to full remote work, and cancelling physical participation in meetings, events, and conferences). For example, we have experienced, and continue to experience, some clinical development disruptions due to the pandemic, including closures at certain lab facilities, which have led, and continue to lead, to longer than anticipated clinical development times. In addition, our clinical trials have been, and may continue to be, affected by the closure of offices, or country borders, among other measures being put in place around the world. The inability to travel and conduct face-to-face meetings can also make it more difficult to enroll new patients in ongoing or planned clinical trials.

As a result of the evolving COVID-19 pandemic, we have experienced and expect to continue to experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- continued delays or difficulties in enrolling and retaining and adequate number of patients in our clinical trials;
- continued delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays in receiving authorizations from regulatory authorities to initiate our planned clinical trials;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations (“CMOs”) due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems, including as a result of the COVID-19 pandemic;
- interruptions in preclinical studies due to restricted or limited operations at our laboratory facility;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require changes in the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- interruption or delays to our sourced discovery and clinical activities; and
- refusal of the FDA to accept data from clinical trials in affected geographies outside the United States.

The extent of the impact of the COVID-19 pandemic on our future liquidity and operational performance will depend on certain developments, including the duration and spread of the outbreak, the availability and effectiveness of vaccines, the impact on our clinical trials, patients, and collaboration partners, and the effect on our suppliers.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

If the FDA does not conclude that our product candidates and/or new indications satisfy the requirements under the 505(b)(2) regulatory pathway, or if the requirements for such product candidates and/or new indications under Section 505(b)(2) are not as we expect, the approval pathway for our product candidates and/or new indications may take longer, cost more or entail greater complications and risks than anticipated, which may delay or prevent the approval of our product candidates and/or new indications for commercial use.

We submitted a Section 505(b)(2) NDA to the FDA in May 2021 for FYARRO for the treatment of advanced malignant PEComa, and the FDA approved the NDA in November 2021. We may not be successful in obtaining FDA approval under 505(b)(2) regulatory pathway for other indications or product candidates that we develop.

Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (the “FDCA”) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984 (the “Hatch-Waxman Amendments”) and permits the submission of an NDA where at least some of the information required for approval comes from preclinical studies or clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The FDA interprets Section 505(b)(2) of the FDCA to permit the applicant to rely upon the FDA’s previous findings of safety and efficacy for an approved product. The FDA requires submission of information needed to support any changes to a previously approved drug, such as published data or new studies conducted by the applicant or clinical trials demonstrating safety and efficacy. The FDA is not required to meet the PDUFA goal date, and the FDA could require additional information to sufficiently demonstrate safety and efficacy to support approval. Moreover, even if any new indication or product candidate is approved under the Section 505(b)(2) regulatory pathway, the approval may be subject to limitations on the indicated uses for which we may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product.

We may be unable to obtain United States approval for FYARRO for additional indications or our other product candidates that we may develop in the future or foreign regulatory approval for FYARRO or our other product candidates that we may develop in the future and, as a result, may be unable to commercialize FYARRO or our product candidates and our business will be substantially harmed.

Our product candidates are and will continue to be subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the United States and in many foreign jurisdictions before a new drug can be approved for marketing. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. we cannot provide any assurance that any product candidate we may develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them.

We submitted an NDA under Section 505(b)(2) to the FDA in May 2021 for FYARRO for the treatment of advanced malignant PEComa, and the FDA approved the NDA in November 2021. The time required to obtain approvals from the FDA and other regulatory authorities is unpredictable and requires successful completion of extensive clinical trials which typically takes many years, depending upon numerous factors, including the type, complexity and novelty of the product candidate. The standards that the FDA and our foreign counterparts use when evaluating clinical trial data can, and often does, change during drug development, which makes it difficult to predict with any certainty how they will be applied. We may also encounter unexpected delays or increased costs due to new government regulations, including future legislation or administrative action, or changes in FDA policy during the period of drug development, clinical trials and FDA regulatory review. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. It is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Additionally, as of March 18, 2021, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the COVID-19 pandemic and travel restrictions the FDA is unable to complete such required inspections during the review period. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA’s inability to complete required inspections for their applications.

Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from any particular product candidates we are developing and for which we are seeking approval. Furthermore, any regulatory approval to market a drug may be subject to significant limitations on the

approved uses or indications for which we may market, promote and advertise the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy (“REMS”) plan as part of approving an NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. These requirements or restrictions might include limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may significantly limit the size of the market for the drug and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries, and generally includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval.

The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue, and our business will be substantially harmed.

Obtaining approval by the FDA, EMA and other comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Even though FYARRO has been approved by the FDA, and even if we eventually complete clinical testing and receive approval for FYARRO in additional indications or for any other product candidates that we may develop in the future, the FDA, EMA and other comparable foreign regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested or may impose other prescribing limitations or warnings that limit the product’s commercial potential. We have not obtained regulatory approval for any product candidate, and it is possible that none of our product candidates will ever obtain regulatory approval.

Further, regulatory approval may be delayed for reasons beyond our control. For example, a United States federal government shutdown or budget sequestration, such as ones that occurred during 2013, 2018 and 2019, or the current diversion of resources to handle the COVID-19 public health emergency and pandemic may result in significant reductions to the FDA’s budget, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to obtain regulatory approval for our product candidates. In addition, the impact of COVID-19 may cause the FDA to allocate additional resources to product candidates focused on treating related illnesses, which could lead to longer approval processes for our product candidates. Finally, our competitors may file citizens’ petitions with the FDA in an attempt to persuade the FDA that our product candidates, or the clinical trials that support their approval, contain deficiencies. Such actions by our competitors could delay or even prevent the FDA from approving any of our NDAs.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe or effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude us from obtaining regulatory approval or prevent or limit commercial use;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

- We may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that our product candidate's risk-benefit ratio for our proposed indication is acceptable;
- the FDA, EMA or other comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- the FDA, EMA or other comparable regulatory authorities may fail to approve companion diagnostic tests for our product candidates, if required; and
- the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in us failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects.

The FDA, EMA and other comparable foreign regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.

Our clinical trials have been and may in the future be undertaken in the United States. We may choose to conduct additional clinical trials internationally as well. For example, we may conduct our PRECISION 1 trial of FYARRO in the United States, Europe and other countries. The acceptance of study data by the FDA, EMA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from United States clinical trials are intended to serve as the basis for regulatory approval in foreign countries outside the United States, the standards for clinical trials and approval may be different. There can be no assurance that any United States or foreign regulatory authority would accept data from trials conducted outside of its applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Brexit and uncertainty in the regulatory framework as well as future legislation in the United Kingdom (the "UK"), European Union, and other jurisdictions can lead to disruption in the execution of international multi-center clinical trials, the monitoring of adverse events through pharmacovigilance programs, the evaluation of the benefit-risk profiles of new medicinal products, and determination of marketing authorization across different jurisdictions. Uncertainty in the regulatory framework could also result in disruption to the supply and distribution as well as the import/export both of active pharmaceutical ingredients and finished product. Such a disruption could create supply difficulties for ongoing clinical trials. The cumulative effects of the disruption to the regulatory framework, uncertainty in future regulation, and changes to existing regulations may increase our development lead time to marketing authorization and commercialization of products in the European Union and/or the UK and increase our costs. We cannot predict the impact of such changes and future regulation on our business or the results of our operations.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA or EMA grants regulatory approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. The regulatory approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States, as well as other risks. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it

can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable regulatory approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Following Brexit, to the extent we conduct any operations in the UK, we will be subject to applicable regulatory requirements in the UK. Although the UK is no longer a member of the European Union, European Union law remains applicable in Northern Ireland. There are a number of new marketing authorization routes available in the UK, Great Britain (England, Scotland and Wales) or Northern Ireland, in addition to the national procedure. As with the European Union position, a company can only start to market a medicine in the UK once it has received a marketing authorization. The main legislation that applies to clinical trials in the UK is the UK Medicines for Human Use (Clinical Trials) Regulations 2004, which transposes the Clinical Trials Directive into domestic law. Consequently, the requirements and obligations that relate to the conduct of clinical trials in the UK currently remain largely aligned with the European Union position. It is unclear how future regulatory regime in the UK will impact regulations of products, manufacturers, and approval of product candidates in the UK. In the immediately foreseeable future, the UK regulatory approval process is likely to remain similar to that applicable in the European Union, albeit that the processes for applications will be separate. Longer term, the UK is likely to develop its own legislation that diverges from that in the European Union.

FYARRO is, and any other product candidate we may develop in the future for which we obtain marketing approval for could be, subject to post-marketing restrictions or recall or withdrawal from the market, and we may be subject to penalties if we or our collaborators fail to comply with regulatory requirements or if we or our collaborators experience unanticipated problems with FYARRO, or any other product candidate we may develop in the future when and if any of them are approved.

FYARRO is, and any other product candidate we may develop in the future for which we obtain marketing approval could be, subject to a comprehensive regulatory scheme, which includes the regulation of manufacturing processes, post-approval clinical data, labeling, advertising, marketing, distribution and promotional activities for such product, by the FDA and other regulatory authorities. The FDA has significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical trials to evaluate serious safety risks related to the use of a drug. For example, the FDA may require the submission of a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any REMS required by the FDA may lead to increased costs to assure compliance with new post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. In addition, if the FDA or foreign regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with current good manufacturing practices (“cGMPs”), good laboratory practices (“GLPs”) and good clinical practices (“GCPs”) for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

FYARRO is, and if marketing approval of any other product candidate we may develop in the future is granted may be, subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS, which could involve requirements for, among other things, a medication guide, special training for prescribers and dispensers, and patient registries. As a condition of the approval of the NDA for FYARRO, we are required to conduct certain post-marketing requirements (“PMR”) and/or post-marketing commitments (“PMC”). If we fail to comply with the PMR and/or PMC, the FDA may take

enforcement actions, which may include, among other things, the issuance of a Warning Letter and assessing civil monetary penalties. The product may also be deemed misbranded.

FYARRO does, and if any other product candidate that we may develop in the future receives marketing approval they may, have a label that limits their approved uses, including more limited subject populations, than we request, and regulatory authorities may require that contraindications, warnings or precautions be included in the product labeling, including a boxed warning, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of products to ensure products are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our prodrug products, if any, for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug and Cosmetic Act relating to the promotion of prescription drugs may lead to a number of actions and penalties, including warning letters, cyber letters, or untitled letters, adverse publicity, the requirement for dear-health-care-provider letters or other corrective information, fines and other monetary penalties, civil or criminal prosecution, including False Claims Act liability, restrictions on our operations and other operating requirements through consent decrees or corporate integrity agreements, debarment, exclusion from participation in federal health care programs and refusal of government contracts or future orders under existing contracts, among other consequences.

We will be required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. In addition, failure to comply with FDA, EMA and other comparable foreign regulatory requirements may have negative consequences, including:

- adverse inspection findings;
- additional warnings or otherwise restrict the product's indicated use, label, or marketing;
- restrictions on our FYARRO products, distribution, manufacturers or manufacturing processes;
- issuance of warning letters, safety alerts, dear-healthcare-provider letters, press releases or other communications containing warnings regarding the product that would result in adverse publicity;
- voluntary or mandatory product recalls and publicity requirements or withdrawal of FYARRO from the market;
- suspension or withdrawal of marketing or regulatory approvals or other permits or voluntary;
- product seizures, detentions or import bans;
- total or partial suspension of production;
- imposition of restrictions on operations, including costly new manufacturing requirements;
- requirement to establish or modify a REMS;
- requirement to conduct post-marketing studies or surveillance;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- refusal to approve pending applications or supplements to approved applications that we submit and other delays;
- delays in or the rejection of approvals of additional indications for FYARRO;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on, or the suspension or termination of, ongoing or planned trials;
- fines, restitution or disgorgement of profits or revenue;
- reputational harm;

- refusal of government contracts or future orders under existing contracts, exclusion from participation in federal health care programs; or
- injunctions or the imposition of civil or criminal penalties, including False Claims Act liability.

The holder of an approved NDA or comparable regulatory approval must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process and the FDA or comparable foreign regulatory authority may refuse to approve pending applications or supplements to approved applications filed by us.

The occurrence of any event or penalty described above may inhibit our ability to commercialize FYARRO and any other product candidates that we may develop in the future, if approved, and generate revenue. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of the company and our operating results will be adversely affected.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies, including the U.S. Department of Justice, strictly regulate the post-approval marketing and promotional claims that may be made about prescription products, such as for FYARRO. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties. As such, we may not promote our products for indications or uses for which they do not have approval. For example, physicians may, in their practice of medicine, use drug products for their patients in a manner that is inconsistent with the approved label. If we, or any of our contractors or agents acting on behalf of us, are found to have promoted such off-label uses, we may become subject to significant liability. The United States federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of FYARRO and any other product candidate that we may develop in the future, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

If we are required by the FDA to obtain approval of a companion diagnostic product in connection with approval of any future product in candidates or new indication that we may develop, and if we fail to obtain or face delays in obtaining FDA approval of such companion diagnostic product, we will not be able to commercialize such product candidate intended for use with such companion diagnostic product and our ability to generate revenue from such product candidate will be materially impaired.

In connection with the development of any future product candidates or new indication we may develop or work with collaborators to develop or obtain access to companion diagnostic tests to identify patient subsets within a disease category who may derive selective and meaningful benefit from our programs. Such companion diagnostics would be used during our clinical trials as well as in connection with the commercialization of any future product candidates or new indication we may develop. To be successful in developing and commercializing such product candidate in combination with these companion diagnostics, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared at the same time the product candidate is approved. To date, the FDA has required marketing approval of all companion diagnostic tests for cancer therapies. Various foreign regulatory authorities also regulate in vitro companion diagnostics as medical devices and, under those regulatory frameworks, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of our current diagnostics and any future diagnostics we may develop, which we expect will require separate regulatory clearance or approval prior to commercialization.

The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express certain biomarkers or the specific genetic alteration that the

companion diagnostic was developed to detect. If the FDA, EMA or a comparable regulatory authority requires approval of a companion diagnostic for any future product candidate or new indication that we may develop, whether before or concurrently with approval of such product candidate, we, and/or future collaborators, may encounter difficulties in developing and obtaining approval for these companion diagnostics. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval or continued marketing of such product candidate. Further, in April 2020, the FDA issued new guidance on developing and labeling companion diagnostics for a specific group of oncology therapeutic products, including recommendations to support a broader labeling claim rather than individual therapeutic products. We will continue to evaluate the impact of this guidance on our companion diagnostic development and strategy. This guidance and future issuances from the FDA and other regulatory authorities may impact our development of a companion diagnostic for our product candidates and result in delays in regulatory approval. We may be required to conduct additional studies to support a broader claim. Also, to the extent other approved diagnostics are able to broaden their labeling claims to include our approved drug products, we may be forced to abandon our companion diagnostic development plans or we may not be able to compete effectively upon approval, which could adversely impact our ability to generate revenue from the sale of our approved products and our business operations.

Additionally, we may rely on third parties for the design, development and manufacture of companion diagnostic tests for our product candidates that may require such tests. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our product candidates, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop companion diagnostics for any future product candidate or new indication, or experience delays in doing so, the development of such product candidate may be adversely affected, the product candidate may not obtain marketing approval, and we may not realize the full commercial potential of such product candidate after obtaining marketing approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic test that we anticipate using in connection with development and commercialization of any such future product candidate or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of any such future product or new indication, or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of any such future product candidate we may develop.

A Fast Track or Breakthrough Therapy designation for FYARRO may not lead to a faster development or review process, or we may be unable to maintain or effectively utilize such a designation. We may also seek additional Fast Track designations from the FDA for FYARRO or any of our other product candidates. Even if one or more of our product candidates receive Fast Track designation, we may be unable to obtain or maintain the benefits associated with the Fast Track designation.

In October 2018, we announced that the FDA granted Fast Track designation for FYARRO for the investigation of the treatment of patients with advanced malignant PEComa. This Fast Track designation does not guarantee that we will qualify for or be able to take advantage of the expedited review procedures or that we will ultimately obtain regulatory approval of FYARRO in other indications. Even though we received this Fast Track designation in the past, we may not experience a faster development process, review or approval compared to conventional FDA procedures for other indications for FYARRO. We may also seek Fast Track designation for additional cancer indications or other diseases, and we may not be successful in securing such additional designation or in expediting development if such designations were received. Even if we receive Fast Track designation for additional cancer indications, the FDA may withdraw such Fast Track designation if it believes that the Fast Track designation is no longer supported by data from our clinical development program.

Fast Track designation is designed to facilitate the development and expedite the review of therapies intended for the treatment of a serious or life-threatening condition which demonstrate the potential to address unmet medical

needs for the condition. Programs with Fast Track designation may benefit from early and frequent communications with the FDA, potential priority review and the ability to submit a rolling application for regulatory review. Fast Track designation applies to both the product candidate and the specific indication for which it is being studied. If FYARRO for any other indication or any other product candidates that we may develop in the future receive Fast Track designation but do not continue to meet the criteria for Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program. The FDA may withdraw any Fast Track Designation at any time. Furthermore, Fast Track designation does not change the standards for approval. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures and we may not experience a faster development process, review or approval compared to conventional FDA procedures.

In December 2018, we announced that the FDA granted Breakthrough Therapy designation for FYARRO for the treatment of patients with advanced malignant PEComa. We may also seek a Breakthrough Therapy designation for FYARRO for various cancer indications or other diseases. Breakthrough Therapy designation is for a product candidate that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A sponsor may request the FDA to designate our product candidate as a Breakthrough Therapy at the time of, or any time after, the submission of an IND for the product candidate. For product candidates that have been designated as a Breakthrough Therapy, the FDA may take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the product candidate; providing timely advice to, and interactive communication with, the sponsor regarding the development of the product candidate to ensure that the development program to gather the nonclinical and clinical data necessary for approval is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients exposed to a potentially less efficacious treatment.

The FDA has broad discretion in determining whether to grant a Fast Track or Breakthrough Therapy designation for a drug. Obtaining a Fast Track or Breakthrough Therapy designation does not change the standards for product approval but may expedite the development or approval process. There is no assurance that the FDA will grant either such designation for any other indication or product candidate that we may pursue. Even if the FDA does grant either such designation, it may not actually result in faster clinical development or regulatory review or approval. Furthermore, such a designation does not increase the likelihood that FYARRO will receive regulatory approval in the United States in other indications.

We may not be able to obtain or maintain orphan drug designation or obtain or maintain orphan drug exclusivity for our product candidates and, even if we do, such exclusivity may not prevent the FDA, EMA or other comparable foreign regulatory authorities, from approving competing products.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Our target indications may include diseases with large patient populations or may include orphan indications. However, there can be no assurances that we will be able to obtain orphan designations for our product candidates.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years,

except in limited circumstances. The applicable exclusivity period is ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if orphan drug designation is granted for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain regulatory approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, that the orphan drug exclusivity may not effectively protect an approved product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to priority review.

We received orphan drug designation from the FDA for FYARRO for the treatment of advanced malignant PEComa. We may be unable to obtain orphan drug designation for any other indication or regulatory approval for FYARRO for any other orphan population, or we may be unable to successfully commercialize FYARRO for such orphan population due to risks that include:

- the orphan patient populations may change in size;
- there may be changes in the treatment options for patients that may provide alternative treatments to FYARRO;
- the development costs may be greater than projected revenue of drug sales for the orphan indications;
- the regulatory agencies may disagree with the design or implementation of our clinical trials;
- there may be difficulties in enrolling patients for clinical trials;
- FYARRO may not prove to be efficacious in the respective orphan patient populations;
- clinical trial results may not meet the level of statistical significance required by the regulatory agencies; and
- FYARRO may not have a favorable risk/benefit assessment in the respective orphan indication.

If we are unable to obtain regulatory approval for FYARRO in any other orphan population for which we obtain orphan drug designation or we are unable to successfully commercialize FYARRO for such orphan population, it could harm our business prospects, financial condition and results of operations.

We may not be able to obtain orphan drug exclusivity for FYARRO in additional indications or for one or more of our product candidates that we may develop in the future, and even if we do, that exclusivity may not prevent the FDA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan product candidates by the EMA in the European Union. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for another similar product candidate for the same orphan therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our product candidates, the agency must find that the product candidate is indicated for the treatment of a condition or disease that affects fewer than 200,000 individuals in the United States or that affects 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product candidate available for the disease or condition will be recovered from sales of the product in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different product candidates can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product candidate for the same condition if the FDA concludes that the later product candidate is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care compared with the product that has orphan exclusivity. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

Where appropriate, we plan to secure approval from the FDA or comparable foreign regulatory authorities through the use of accelerated registration pathways. If we are unable to obtain such approval, we may be required to conduct additional preclinical studies or clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary regulatory approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous PMRs, the FDA may seek to withdraw accelerated approval.

Where possible, we plan to pursue accelerated development strategies in areas of high unmet need. We may seek an accelerated approval pathway for one or more of our product candidates. Under the accelerated approval provisions in the FDA, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that generally provides a meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Prior to seeking such accelerated approval, we will seek feedback from the FDA and will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation (e.g., breakthrough therapy designation), there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidate would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

We may face difficulties from changes to current regulations and future legislation.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained, and we may not achieve or sustain profitability.

For example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (the “ACA”), was passed, which substantially changes the way healthcare is financed by both the government and private insurers, and significantly impacts the United States pharmaceutical industry. In December 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of the federal district court litigation regarding the method CMS uses to determine this risk adjustment. Since then, the ACA risk adjustment program payment parameters have been updated annually. Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the former Trump administration to repeal or replace certain aspects of the ACA. In June 2021, the Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case without specifically ruling on the constitutionality of the ACA. Accordingly, the ACA remains in effect in its current form. It is unclear how this decision and other healthcare reforms will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2030, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. In January 2013, former President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for FYARRO or any other product candidates that we may develop if the future, if approved, and accordingly, our financial operations.

Moreover, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, at the federal level, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019. Additionally, CMS issued a final rule, effective on July 9, 2019, that requires direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product if it is equal to or greater than \$35 for a monthly supply or usual course of treatment. Prescription drugs and biological products that are in violation of these requirements will be included on a public list. In 2020, at the federal level, under the former Trump administration, HHS and CMS issued various rules that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, importation of prescription drugs from Canada and other countries, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of these new rules. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies.

Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of

products, which could have a material impact on our business. Further, in July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at increasing competition for prescription drugs. In response to this executive order, the HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and potential legislative policies that Congress could pursue to advance these principles. In addition, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved. Complying with any new legislation and regulatory changes could be time-intensive and expensive, resulting in a material adverse effect on our business.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. Implementation of cost containment measures or other healthcare reforms that affect the pricing and/or availability of drug products may impact our ability to generate revenue, attain or maintain profitability, or commercialize products for which we may receive regulatory approval in the future.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (Right to Try Act), was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new product candidates that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its products available to eligible patients as a result of the Right to Try Act.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA’s approval process may significantly delay or prevent regulatory approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or in other jurisdictions. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our product candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Additionally, the collection and use of health data in the European Union is governed by the General Data Protection Regulation (the “GDPR”), which extends the geographical scope of European Union data protection law to non-European Union entities under certain conditions and imposes substantial obligations upon companies and new rights for individuals. Failure to comply with the GDPR and the applicable national data protection laws of the European Union Member States may result in fines up to €20.0 million or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties. The

GDPR may increase our responsibility and liability in relation to personal data that we may process, and we may be required to put in place additional mechanisms in an effort to comply with the GDPR. This may be onerous and if our efforts to comply with GDPR or other applicable European Union laws and regulations are not successful, it could adversely affect our business in the European Union.

Finally, state and foreign laws may apply generally to the privacy and security of information we maintain, and may differ from each other in significant ways, thus complicating compliance efforts. For example, the California Consumer Privacy Act of 2018 (the “CCPA”), which took effect on January 1, 2020, gives California residents expanded rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. In addition, the CCPA (a) allows enforcement by the California Attorney General, with fines set at \$2,500 per violation (i.e., per person) or \$7,500 per intentional violation and (b) authorizes private lawsuits to recover statutory damages for certain data breaches. While it exempts some data regulated by the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) and certain clinical trials data, the CCPA, to the extent applicable to our business and operations, may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. Some observers note that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the United States, which could increase our potential liability and adversely affect our business.

Inadequate funding for the FDA, the Securities and Exchange Commission and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the Securities and Exchange Commission (the “SEC”) and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the United States government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities and products as well as routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials. In April 2021, the FDA issued guidance for industry formally announcing plans to employ remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates and based on updated guidance issued in May 2021, FDA continues to conduct mission-critical inspections on a case-by-case basis, or, where possible to do so safely, has, since July 2020, resumed prioritized domestic inspections, which generally include pre-approval, pre-license, surveillance, and for-cause inspections. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue a complete response letter or defer action on the application until an inspection can be completed. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA’s inability to complete required inspections for their applications. While the FDA indicated that it will consider alternative methods for inspections and exercise discretion on a case-by-case basis to approve products based on a desk review, if a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities on a timely basis, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. Further, in our operations as a public company, future government shutdowns could

impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

If we fail to comply with other United States healthcare laws and compliance requirements, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business. Further, our relationships with healthcare professionals, clinical investigators, CROs and third-party payors in connection with our current and future business activities may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws, which could expose us to significant losses, including, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain regulatory approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain regulatory approval. Restrictions under applicable federal and state healthcare laws and regulations may include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti- Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties;
- the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery;
- Federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making, or causing to be made, false statements relating to healthcare matters;
- the federal Civil Monetary Penalties Law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary’s decision to order or receive items or services reimbursable by the government from a particular provider or supplier;
- the FCPA, the U.K. Bribery Act of 2010, and other local anti-corruption laws that apply to our international activities;
- the federal HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare

matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (“HITECH”) and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance effort;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program, with specific exceptions, to annually report to CMS information regarding certain payments and other transfers of value made to covered recipients in the previously year, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members; our failure to submit required information timely, accurately, and completely may result in significant civil monetary penalties and may increase our liability under other federal laws or regulations; and
- additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America’s Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. State and foreign laws, including for example the European Union General Data Protection Regulation, which became effective May 2018 also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement, we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance effort.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exceptions or safe harbors, it is possible that some of our activities, including those of our contractors or agents who conduct business for or on behalf of us, could be subject to challenge under one or more of such laws. Any action brought against us for violations of these laws or regulations, even successfully defended, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business. We may be subject to private “qui tam” actions brought by individual whistleblowers on behalf of the federal or state governments.

If we were to grow our business and expand our sales organization or rely on distributors outside of the United States, we would be at increased risk of violating these laws or our internal policies and procedures. The risk of us being found in violation of these or other laws and regulations is further increased by the fact that many have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of

interpretations. Any action brought against us for violation of these or other laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare and data privacy laws and regulations will involve on-going substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. Any of the foregoing consequences could seriously harm our business and our financial results. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in fraud, misconduct or other improper activities. Misconduct by these parties could include intentional, reckless, and negligent conduct that fails to: comply with the regulations of the FDA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA and other comparable foreign regulatory authorities; comply with manufacturing standards we have established; comply with federal and state health care fraud and abuse laws and regulations and similar foreign fraudulent misconduct laws; accurately report financial information or data or disclose unauthorized activities to us. In particular, research, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, certain customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending our self or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

If we or any contract manufacturers and suppliers we engage fails to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures, the generation, handling, use, storage, treatment and disposal of hazardous and regulated materials and wastes, the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. The operations of our contractors may involve the use of hazardous and flammable materials, including chemicals and biological materials, and accordingly may produce hazardous waste products. Our contract manufacturers and suppliers generally contract with third parties for the disposal of these materials

and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, including any contamination at our current or past facilities and at third-party facilities, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of hazardous and flammable materials, including chemicals and biological materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our business activities may be subject to the United States Foreign Corrupt Practices Act ("FCPA") and similar anti-bribery and anti-corruption laws of other countries in which we operate, as well as United States and certain foreign export controls, trade sanctions, and import laws and regulations. Compliance with these legal requirements could limit our ability to compete in foreign markets and subject us to liability if we violate them.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the UK Bribery Act. The FCPA generally prohibits companies and their employees and third-party intermediaries from offering, promising, giving or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, hospitals are owned and operated by the government, and doctors and other hospital employees are employed by the government and would be considered foreign officials under the FCPA, and often the purchasers of pharmaceuticals are government entities; therefore, our dealings with these doctors, hospital employees and purchasers are subject to regulation under the FCPA. Recently, the SEC and DOJ have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, collaborators, or contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers or our employees, disgorgement, and other sanctions and remedial measures, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international activities, our ability to attract and retain employees and our business, prospects, operating results and financial condition.

In addition, our products may be subject to U.S. and foreign export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, United States export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by United States sanctions. For example, the U.S. government and other governments in jurisdictions in which we may operate in the future have imposed severe sanctions and export controls against Russia and Russian interests and threatened additional sanctions and controls in connection with the conflict between Russia and Ukraine. The impact of these measures, as well as potential responses to them by Russia, is currently unknown and they could adversely affect our business, supply chain, business partners or customers.

If we fail to comply with export and import regulations, and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or products targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to, existing or potential customers with international operations. Any decreased use of our products or limitation on our ability to export or sell our products would likely adversely affect our business.

Further, with rising international trade tensions or sanctions, our business may be adversely affected following new or increased tariffs that result in increased global clinical trial costs as a result of international transportation of clinical drug supplies, as well as the costs of materials and products imported into the U.S. Tariffs, trade restrictions or sanctions imposed by the U.S. or other countries, including as a result geopolitical tension, such as a deterioration in the relationship between the United States and China or escalation in conflict between Russia and Ukraine, including any additional sanctions, export controls or other restrictive actions that may be imposed by the United States and/or other countries against governmental or other entities in Russia, could increase the prices of our and our collaboration partners' drug products, affect our and our collaboration partners' ability to commercialize such drug products, or create adverse tax consequences in the U.S. or other countries. As a result, changes in international trade policy, changes in trade agreements and the imposition of tariffs or sanctions by the U.S. or other countries could materially adversely affect our results of operations and financial condition.

Risks Related to Employee Matters, Managing Our Growth and Other Risks Related to our Business

Our success is highly dependent on our ability to attract and retain highly skilled executive officers, key scientific personnel and employees.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers or key scientific personnel could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We will need to hire additional personnel as we expand our clinical development and commercial activities. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than us. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed.

Additionally, we rely on our scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting relationships with these advisors or they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be significantly harmed.

If we are unable to establish sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to successfully sell or market our product candidates that obtain regulatory approval.

In order to commercialize FYARRO or any other product candidate that we may develop in the future, if approved, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make

arrangements with third parties to perform these services for each of the territories in which we may have approval to sell or market our product candidates. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services and we may not be successful in accomplishing these required tasks, which may negatively impact the successful commercialization of FYARRO for advanced malignant PEComa.

Establishing an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates will be expensive and time-consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any of our product candidates that we obtain approval to market, if we do not have arrangements in place with third parties to provide such services on our behalf. If the commercial launch of a product candidate for which we recruit a sales team and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel. Alternatively, if we choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration and such arrangements may prove to be less profitable than commercializing the product on its own. If we are unable to enter into such arrangements when needed, on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are unable to successfully commercialize our approved product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of March 1, 2022, we had 51 full-time employees, including 32 employees engaged in research and development. In order to successfully implement our development and commercialization plans and strategies, and as we continue operating as a public company, we expect to need additional managerial, operational, development, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA, EMA and other comparable foreign regulatory agencies' review process for FYARRO and any other product candidates, while complying with any contractual obligations to contractors and other third parties we may have; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and commercialize FYARRO and any other product candidates we may develop in the future, if approved, will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of our attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third-party service providers is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval of FYARRO and any other product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third-party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize FYARRO and other product candidates and, accordingly, may not achieve our research, development and commercialization goals.

Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems, and those of our third-party CROs, other contractors (including sites performing our clinical trials) and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. As the cyber-threat landscape evolves, these attacks are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect. To the extent that any disruption or security breach were to result in a loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. We cannot assure you that our data protection efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties, will prevent significant breakdowns or breaches in systems or other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage to, our data that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, data (including trade secrets or other confidential information, intellectual property, proprietary business information, and personal information or individually identifiable health information), which could result in financial, legal, business, and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Some of the federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors or organizations with which it has formed strategic relationships. Notifications and follow-up actions related to a security incident could impact our reputation and cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security incident were to result in a loss, destruction or alteration of, or damage to, our data, or inappropriate disclosure of confidential or proprietary

information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and/ or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption, failure or security breach of our systems or third-party systems where information important to our business operations or commercial development is stored. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

We, or the third parties upon whom we depend, may be adversely affected by earthquakes, wildfires and other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, such as the COVID-19 pandemic, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party CMOs, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidate or interruption of our business operations. Earthquakes, wildfires or other natural disasters could further disrupt our operations, including at our California headquarters, and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party CMOs, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our ability to utilize our NOL carryforwards and certain other tax attributes to offset future taxable income may be limited.

Our NOL carryforwards may be unavailable to offset future taxable income because of restrictions under United States tax law. Our NOLs generated in tax years beginning before January 1, 2018 are only permitted to be carried forward for 20 taxable years under applicable United States federal tax law, and therefore could expire unused. Under the Tax Cuts and Jobs Act of 2017 (the “Tax Act”), as modified by the Coronavirus Aid, Relief, and Economic Security Act (the “CARES Act”), our federal NOLs generated in tax years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of federal NOLs in tax years beginning after December 31, 2020 is limited to 80% of our current year taxable income. NOLs generated in tax years beginning before January 1, 2018 will not be subject to the taxable income limitation and will continue to have a two-year carryback and twenty-year carryforward period. California recently enacted legislation limiting our ability to use our state NOLs for taxable years 2020, 2021, and 2022. It is uncertain if and to what extent various states will conform to the Tax Act. As of December 31, 2021, after consideration of the NOLs that have been estimated to expire unused under Section 382, we had federal NOL carryforwards of approximately \$150.9 million, \$44.3 million of which will begin to expire in 2030, the remaining \$106.6 million of federal NOL carryforwards do not expire. We also have available California NOL carryforwards of approximately \$44.4 million as of December 31, 2021, which begin to expire in 2037.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the “Code”), if a corporation undergoes an “ownership change” (generally defined as a cumulative change in the corporation’s ownership by “5-

percent stockholders” that exceeds 50 percentage points over a rolling three-year period), the corporation’s ability to use its pre-change NOLs and certain other pre-change tax attributes to offset its post-change taxable income may be limited. Similar rules may apply under state tax laws. We have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of the Merger or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2021, we have completed an IRC Section 382 analysis through the date of the Merger. Ownership changes were identified that will result in annual limitations on future utilization of NOL and research and development credit carryforwards. To the extent such limitations will cause NOL and research and development credit carryforwards to expire unused, these tax attributes have been removed from our deferred tax asset. Our ability to utilize our NOLs and certain other tax attributes could be limited by an “ownership change” as described above and consequently, we may not be able to utilize a material portion of our NOLs and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations.

United States federal income tax reform could materially adversely affect our financial condition.

Legislation or other changes in United States and international tax laws could increase our tax liability and adversely affect after-tax profitability. For example, the Biden administration has proposed to increase the United States corporate income tax rate, increase the United States taxation of international business operations and impose a global minimum tax on corporate income. Such proposed changes, as well as regulations and legal decisions interpreting and applying these changes, may have significant impacts on our effective tax rate, cash tax expenses and net deferred tax assets in future periods.

A variety of risks associated with marketing our products or any product candidates that we may develop in the future, if approved, internationally could materially adversely affect our business.

We may seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements and reimbursement regimes in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

Risks Related to Our Intellectual Property

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection in the United States and other countries for our product and product candidates, proprietary technologies and their uses, and know-how related to our business, as well as our ability to operate without infringing upon the valid and enforceable patents and proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product and product candidates, proprietary technologies and their uses that are important to our business. We also seek to protect our proprietary position by acquiring or in-licensing relevant issued patents or pending applications from third parties. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or the patent applications of our licensors will result in additional patents being issued in any particular jurisdiction or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties.

Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for us and our licensors' proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties and/or limitations in our ability to properly protect the intellectual property rights relating to our product or product candidates could have a material adverse effect on our financial condition and results of operations.

Although we own or license ten (10) issued patents in the United States, four (4) of which have composition of matter and method of use claims covering FYARRO, we cannot be certain that the claims in our other United States pending patent applications, corresponding international patent applications and patent applications in certain foreign territories, or those of our licensors, will be considered patentable by the United States Patent and Trademark Office (the "USPTO"), courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued patent will not be found invalid or unenforceable if challenged.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our current or potential future collaborators will be successful in protecting our product or product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- if clinical trials encounter delays, the period of time during which we could market our current or future product candidates under patent protection would be reduced;
- patents may be challenged, invalidated, modified, narrowed, revoked, circumvented, found to be unenforceable, found to be not infringed or otherwise may not provide any competitive advantage;
- Our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that could limit, interfere with or eliminate our ability to make, use and sell our product or potential product candidates or design around any of our owned, co-owned, or licensed patents;
- since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either (i) file any patent application related to our product; or (ii) invent any of the inventions claimed in our patents or patent applications;

- even when laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. Moreover, any actions we may bring to enforce our intellectual property against our competitors could provoke them to bring counterclaims against us;
- there may be significant pressure on the United States government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing products or product candidates.

The patent prosecution process is also expensive, complex, and time-consuming, and we and our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we and our licensors will fail to identify patentable aspects of our (or such licensor's) research and development output before it is too late to obtain patent protection. If we are unable to obtain or maintain patent protection with respect to any of our proprietary products and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to our products.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical products or product candidates would be adversely affected.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. Our pending and future patent applications and those of our licensors may not result in patents being issued that protect our product or product candidates or effectively prevent others from commercializing competitive products or product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and our scope can be reinterpreted after issuance. Even if patent applications we own or in-licenses currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-licenses may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product or product candidates will be protectable or remain protected by valid and enforceable patents.

Our competitors or other third parties may be able to circumvent our patents or the patents of our licensors by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents or the patents of our licensors may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review (“PGR”) and *inter partes* review (“IPR”), or other similar proceedings challenging our owned patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights or put its patent applications at risk of not issuing, allow third parties to commercialize our product or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, our patents or the patents of our licensors may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, which challenge our priority of invention or other features of patentability with respect to our patents and patent applications and those of our licensors. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product or product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of our licensors is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products or product candidates. If any of our patents, if and when issued, covering our product candidates are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. We may not prevail in any lawsuits that we or any third-party initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to develop products that are similar to FYARRO or our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors or collaborators might not have been the first to make the inventions covered by the issued patents or patent application that we own or license;
- We or our licensors or collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that the pending patent applications we own or license will not lead to issued patents;
- issued patents that we own or license may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- We may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- We may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, it could significantly harm our business, financial condition, results of operations and prospects.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

Our commercial success depends in part on avoiding infringement or misappropriation of the patents, intellectual property and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our products or products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party United States and foreign issued patents and pending patent applications exist in the fields in which we are developing products or product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product or product candidates.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our product or product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third-party patents that may be infringed by commercialization of our product or any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product or technology. Moreover, because patent applications can take many years to issue, and because patent claims can be revised before issuance, there may be currently pending patent applications that may later result in issued patents that our product or product candidates may infringe or which such third parties claim are infringed by our technologies. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If a patent holder believes one or more of our products or product candidates infringes such holder's patent rights, the patent holder may sue us even if we have received patent protection. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this Annual Report, others may hold proprietary rights that could prevent FYARRO or our product candidates from being marketed. For example, various patent offices periodically grant mode of action patents and a third party may have or obtain a patent with claims covering modes of action relevant to our product or product candidates. While these mode of action patents may be difficult to enforce, the third party may assert a claim of patent infringement directed at one of our products or product candidates. Any patent-related legal action or any claim relating to intellectual property

infringement that is successfully asserted against us claiming damages and seeking to enjoin commercial activities relating to our products or processes could subject us to significant liability for damages, including treble damages and attorney's fees if it was determined that we willfully infringed, and require us to obtain a license to manufacture or market our product or product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our current or future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product or product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent or delay us from developing and commercializing our product or product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of our outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product or product candidates and technology.

In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Our rights to develop and commercialize our technology, product and product candidates may be subject, in part, to the terms and conditions of licenses granted to us by others.

We have entered into license agreements with third parties and we may enter into additional license agreements in the future with others to advance our research or allow commercialization of our product or product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. In such an event, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we had licensed may be reduced or eliminated, and our rights to develop and commercialize any of our products that are subject of such licensed rights could be adversely affected.

Our licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, product, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product or product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture, sales or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experiences disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- our right to transfer or assign the license;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by us and our licensors and partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product or product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

The patent protection and patent prosecution for our product and for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product or product candidates, there may be times when the filing and prosecution activities for patents relating to our product or product candidates are controlled by our licensors or collaboration partners, including those licensed to us under our license agreements. If any of our licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product or product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize our product or those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. We collaborate with other companies and institutions with respect to research and development matters. Also, we rely on numerous third parties to provide us with materials that we use to develop our technology. If we cannot successfully negotiate sufficient ownership, licensing, and/or commercial rights to any invention that result from our use of any third-party collaborator's materials, or if disputes arise with respect to the intellectual property developed with the use of a collaborator's materials, or data developed in a collaborator's study, our ability to capitalize on the market potential of these inventions or developments may be limited or precluded altogether. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

We may not be successful in obtaining or maintaining necessary rights to our product or product candidates through acquisitions and in-licenses.

Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product or product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we choose to enter into such arrangements. We may also be unable to license or acquire third-party intellectual property rights on terms that would be favorable to us or allow us to make an appropriate return on our investment or at all. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may be involved in lawsuits or other proceedings to protect or enforce our patents or intellectual property or our licensors' patents or intellectual property, which could be expensive, time consuming and unsuccessful. Further, our issued patents or our licensors' patents could be found invalid or unenforceable if challenged in court.

Competitors and other third parties may infringe, misappropriate, or otherwise violate our patents and other intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the attention of our management and key personnel from our business operations. In addition, in a patent infringement proceeding, a court may decide that a patent we own or in-license is not valid, is unenforceable and/or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our products or product candidates, the defendant could counterclaim that our patent or the patent of our licensors is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, non-enablement, or obviousness-type double patenting. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution of the patent application.

Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re-examination, PGR, IPR, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of or amendment to our patents or our licensors' patents in such a way that such patents no longer cover our technology or platform, product or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, product or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

The outcome following legal assertions of invalidity and/or unenforceability is unpredictable, and prior art could render our patents or our licensors' patents invalid. There is no assurance that all potentially relevant prior art relating to our patents and patent applications, or the patents and patent applications of our licensors has been found. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications or the patents and patent applications of our licensors, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim.

If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we may lose at least part, and perhaps all, of the patent protection on such product or product candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or the patents and patent applications of our licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future products or product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings.

In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings or developments in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our product or product candidates, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to us from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product or product candidates to market.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of our licensors and the enforcement or defense of our issued patents or those of our licensors.

On September 16, 2011, the Leahy-Smith America Invents Act (the “Leahy-Smith Act”), was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a “first inventor to file” system in which,

assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we may not be certain that we or our licensors are the first to either (1) file any patent application related to our product or product candidates or (2) invent any of the inventions claimed in the patents or patent applications.

The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications or those of our licensors and the enforcement or defense of our issued patents or those of our licensors, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in United States patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product or product candidates.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing pharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

For example, the United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the United States federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and the patents we might obtain or license in the future.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that our former employees or our licensors or other third parties have an ownership interest in our patents or other intellectual property. Confidentiality and intellectual property assignment agreements may not be honored and may not effectively assign intellectual property rights to us. The assignment of intellectual property rights under these agreements may not be automatic upon the creation of the intellectual property or the assignment agreements may be breached, and we may be forced to bring claims against third

parties, or defend claims that they may bring against it, to determine the ownership of what we regard as our intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our product or product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest United States non-provisional effective filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product or product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to us.

If we do not obtain patent term extension for our product or product candidates, our business may be materially harmed.

In January 2022, we filed an application for patent term extension based on the approval of FYARRO. Depending upon the timing, duration and specifics of FDA regulatory approval of our product candidates, one or more of our United States patents or those of our licensors may also be eligible for limited patent term restoration under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request or require. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request or require, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may not be able to protect our intellectual property rights throughout the world.

Although we own, co-own, or have licensed issued patents in the United States and pending patent applications in the United States and other countries, filing, prosecuting and defending patents on our product or product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. In addition, the statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications and we may not timely file foreign patent applications.

Competitors may use our technologies in jurisdictions where we do not pursue or have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product or product candidates, and our patents, the patents of our licensors, or other intellectual

property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or our licensors' patents or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents or the patents of our licensors at risk of being invalidated or interpreted narrowly and our patent applications or the patent applications of our licensors at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on our owned and in-licensed patents and/or applications will be due to be paid to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications and those of our licensors and any patent rights we may own or license in the future. We have systems in place to remind us to pay these fees, and, in certain instances, we rely on our licensor partners to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and over the lifetime of our owned patents and applications. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, competitors or other third parties might be able to enter the market earlier than would otherwise have been the case and it could have a material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. In addition, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. However, trade secrets are difficult to protect. For example, we may be required to share our trade secrets with third-party licensees, collaborators, consultants, contractors, or other advisors and we have limited control over the protection of trade secrets used by such third parties. Although we have taken steps to protect our trade secrets and unpatented know-how, including by entering into confidentiality agreements with third parties and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed or that they have been obtained in all circumstances, and it is possible that any of these parties may breach the agreements and may unintentionally or willfully disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. Enforcing a claim that a party illegally obtained, disclosed, used or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or proceedings. If any of these events occurs or if we otherwise lose protection for our trade secrets or confidential or proprietary information, the value of this information may be greatly reduced, and our competitive position in the marketplace, business, financial condition, results of operations and prospects may be materially adversely affected. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we or our employees, consultants or advisors have wrongfully used or disclosed alleged confidential information or trade secrets.

We have entered into and may enter in the future into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, and other third parties. We may become subject to litigation where a third party asserts that we or our employees, consultants or advisors inadvertently or otherwise breached the agreements and used or disclosed trade secrets or other information proprietary to the third parties. Defense of such matters, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product or product candidates and technology. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product or product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including competitors or our potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade

secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Intellectual property discovered through government funded programs may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a preference for United States-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-United States manufacturers.

Our licensed patent applications may have been or may be in the future supported through the use of United States government funding awarded by the National Institute of Health or the FDA Office of Orphan Products Development and the Army Medical Research and Development Command. Although we do not currently own issued patents or pending patent applications that have been generated through the use of United States government funding, we have licensed, or may acquire or license in the future, intellectual property rights that have been generated through the use of United States government funding or grant. Pursuant to the Bayh- Dole Act of 1980, the United States government has certain rights in inventions developed with government funding. These United States government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the United States government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (“march-in rights”). The United States government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the United States government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for United States industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for United States industry may limit our ability to contract with non-United States product manufacturers for products covered by such intellectual property.

Risks Related to Our Reliance on Third Parties

We contract with qualified third parties for the production of FYARRO for commercialization and expect to continue to do so for additional clinical trials. This reliance on third parties, some of which are sole source suppliers, increases the risk that we will not have sufficient quality and quantities of FYARRO to meet demand or otherwise or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have, nor do we plan to acquire, the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We rely, and expect to continue to rely, on third-party manufacturers for the production of our products and product candidates for preclinical studies and clinical trials under the guidance of members of our organization. In the case of FYARRO, we rely on a single third-party manufacturer, Fresenius-Kabi, LLC (“Fresenius-Kabi”), and currently have no alternative manufacturer in place. On January 13, 2022, we entered into a Negotiated Purchase Order Terms and Conditions for Clinical and Commercial Product (the “Fresenius Agreement”) with Fresenius-Kabi pursuant to which Fresenius-Kabi will manufacture FYARRO for intravenous use for us, and we will purchase FYARRO as a finished drug product from Fresenius-Kabi, on a purchase-order basis. The Fresenius Agreement shall be effective through December 22, 2022 (or such later date as may be agreed between the parties in writing), and we may purchase FYARRO for either clinical or commercial purposes for use in the United States and Canada. The price of FYARRO will be fixed, subject to the ability of Fresenius-Kabi to increase pricing under specified circumstances. We also have an obligation to purchase certain minimum

quantities of FYARRO and any failure to purchase those minimum quantities will result in an additional payment from us to Fresenius-Kabi. We have other supply agreements in place for key raw materials used in the manufacture of FYARRO such as for the drug substance sirolimus and for human albumin, which are key ingredients in the drug product. If we were to engage another third-party manufacturer, we will be required to verify that the new third-party manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a bridging study, that any new manufacturing process will produce FYARRO or any other product candidate we may develop in the future, if approved, according to the specifications previously submitted to the FDA or another regulatory authority. If we were to experience an unexpected loss of supply of FYARRO or any other product candidate that we may develop in the future for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations in commercializing FYARRO for advanced malignant PEComa, or be required to restart or repeat, any pending or ongoing clinical trials for FYARRO in other indications or for any other product candidates we may develop in the future, in a timely manner or on budget. Moreover, if we are unable to keep up with demand for FYARRO, our revenue could be impaired, market acceptance for FYARRO could be adversely affected.

We expect to rely on third-party manufacturers for the commercial supply of FYARRO, and the continued development of FYARRO in other indications or any other product candidates we may develop in the future for which we obtain regulatory approval. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Further, any delay in identifying and qualifying a manufacturer for commercial production could delay the potential commercialization of FYARRO, and, in the event that we do not have sufficient product to complete our planned clinical trials, it could delay such trials. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture FYARRO or any of our other product candidates that we may develop in the future according to our schedule and specifications, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates, are constrained by the recent COVID-19 pandemic or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements, including manufacturing drug supply pursuant to strictly-enforced cGMPs;
- the failure of the third-party contractor to manufacture FYARRO or any of our other product candidates that we may develop in the future according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of our contract manufacturing partners and are dependent on these contract manufacturing partners for compliance with cGMP regulations for manufacturing both active pharmaceutical ingredients (“API”) and finished drug products. To date, we have obtained drug substance and drug product from third-party manufacturers to support preclinical and clinical testing of FYARRO. For example, we have obtained our supplies of FYARRO from a single source supplier, Fresenius-Kabi. We have supply agreements in place for key raw materials used in the manufacture of FYARRO such as for the drug substance sirolimus and for human albumin, which are key ingredients in the drug product. We are in the process of developing our supply chain for FYARRO, including through the Fresenius Agreement. As we commercialize FYARRO and advance FYARRO for additional indications or any other product candidates we may develop in the future through development, we will consider redundant supply for the API and drug product for FYARRO and each of our product candidates that we may develop in the future to protect against any potential

supply disruptions. However, we may be unsuccessful in putting in place such framework agreements or protecting against potential supply disruptions.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or others, they will not be able to pass a pre-approval inspection or secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we do not have control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, many of our CMOs are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our CMOs facilities generally. If the FDA, EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of FYARRO or any of our other product candidates that we may develop in the future or if we withdraws any such approval in the future, we will need to find alternative manufacturing facilities, and those new facilities would need to be inspected and approved by FDA, EMA or comparable regulatory authority prior to commencing manufacturing, which would significantly impact our ability to commercialize FYARRO for advanced malignant PEComa and develop, obtain regulatory approval for or market FYARRO for other indications or any of our other product candidates that we may develop in the future, if approved. Our reliance on CMOs also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on the parties, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of FYARRO or any of our other product candidates or drugs that we may develop in the future and harm our business and results of operations.

In addition, the manufacture of pharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production and absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if contaminants are discovered in our supply of FYARRO or in our third-party manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any stability or other issues relating to the manufacture of our product candidates may occur in the future. Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause FYARRO or any of our other product candidates that we may develop in the future to perform differently and affect commercialization or the results of planned clinical trials or other future clinical trials. In addition, quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at our third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for FYARRO or any of our product candidates that we may develop in the future. Further, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our product candidate to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical study costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial

condition, results of operations, and growth prospects. Our current and anticipated future dependence upon others for the manufacture of FYARRO and any of our other product candidates that we may develop in the future may adversely affect our future profit margins and our ability to commercialize FYARRO or any other product candidates that we may develop in the future that receives regulatory approval on a timely and competitive basis.

We are dependent on a single-source supplier for the drug product FYARRO, and the loss of such supplier could harm our business.

We rely on a single-source supplier, Fresenius-Kabi for our drug product FYARRO. In January 2022, we entered into the Fresenius Agreement, but will continue to place purchase orders from Fresenius-Kabi on an as-needed basis, subject to certain minimum quantities as agreed to under the Fresenius Agreement. The Fresenius Agreement is effective through December 22, 2022 (or such later date as may be agreed between the parties). We also have supply agreements in place for key raw materials used in the manufacture of FYARRO such as for the drug substance sirolimus and for human albumin, which are key ingredients in the drug product. Our suppliers could discontinue the manufacturing or supply of FYARRO at any time. We do not carry a significant inventory of FYARRO or our key raw materials used in the manufacture of FYARRO. Our suppliers may not be able to meet our demand for their products, either because of acts of nature, the nature of our agreements with those manufacturers or our relative importance to them as a customer, and our manufacturers may decide in the future to discontinue or reduce the level of business they conduct with us either entirely or for a particular territory. The loss of any of the foregoing would require significant time and effort to locate and qualify an alternative source of supply. We currently rely on a single company for such manufacturing for FYARRO. Any contractual disputes between us and such manufacturer, the termination of the Fresenius Agreement or loss of manufacturing ability by such manufacturer could similarly require significant time, effort and expense to locate and qualify an alternative source of manufacturing, which could materially harm our business.

In addition, we might not be able to identify and qualify additional or replacement suppliers for the drug product FYARRO or for the key raw materials used in the manufacture of FYARRO quickly or at all or without incurring significant additional costs. We cannot guarantee that we will be able to establish alternative relationships on similar terms, without delay or at all. We may also face regulatory delays or be required to seek additional regulatory clearances or approvals if we experience any delay or deficiency in the quality of products obtained from suppliers or if we have to replace our suppliers. In addition, we do not currently have arrangements in place for redundant supply of the drug product FYARRO or for the key raw materials used in the manufacture of FYARRO.

Establishing additional or replacement suppliers for the drug product FYARRO or for the key raw materials used in the manufacture of FYARRO, if required, or any supply interruption from our suppliers, could limit our ability to manufacture our products, result in production delays and increased costs and adversely affect our ability to deliver products to our customers on a timely basis. Our inability to obtain sufficient quantities of the drug product FYARRO or for the key raw materials used in the manufacture of FYARRO also could adversely affect clinical development of FYARRO in other indications. If we are not able to identify alternate sources of supply for the drug product FYARRO or for the key raw materials used in the manufacture of FYARRO, we will not be able to, or may be delayed in our efforts to, successfully commercialize FYARRO or any other product candidate that we may develop in the future or we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for FYARRO in other indications or for any other product candidates that we may develop in the future.

The manufacture of drugs is complex, and our third-party manufacturers may encounter difficulties in production. If any of our third-party manufacturers encounter such difficulties, our ability to provide adequate supply of FYARRO for patients or for clinical trials or any other product candidate that we may develop in the future, if approved, could be delayed or prevented.

Manufacturing drugs, especially in large quantities, is complex and highly regulated and may require the use of innovative technologies. Each lot of an approved drug product must undergo thorough testing for identity, strength, quality, purity and efficacy. Manufacturing drugs requires facilities specifically designed for and validated for this purpose, as well as sophisticated quality assurance and quality control procedures. Manufacturing drugs is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and

clinical data showing the comparable identity, strength, quality, purity or efficacy of the products before and after such changes. If microbial, viral or other contaminations or impurities are discovered at the facilities of our manufacturer, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination or impurity, which could delay clinical trials and adversely harm our business. If our third-party manufacturers are unable to produce sufficient quantities of consistent quality for clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. We entered into a license agreement with Abraxis BioScience, LLC, a wholly owned subsidiary of Celgene Corporation, now Bristol Myers Squibb Company (“Celgene”) pursuant to which we have licensed exclusive global rights to intellectual property and know-how related to FYARRO (the “Celgene License”). We are required to use commercially reasonable efforts or diligent efforts to commercialize products based on the licensed rights and to pay certain royalties based off our net sales, certain sublicense fees (such as with respect to our license agreement with EOC) and certain other fees. We may not meet these requirements, which could result in a loss or termination of any rights under such agreements. Any termination of these licenses will result in the loss of significant rights and will restrict our ability to commercialize our product candidates.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described above under “Risks Related to Our Intellectual Property.” If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.

We do not have the ability to independently conduct all of our preclinical studies and clinical trials. We currently rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct, supervise and monitor our current or planned preclinical studies and clinical trials of FYARRO for additional indications, and we expect to continue to rely upon third parties to conduct additional preclinical studies and clinical trials of FYARRO for additional indications and other product candidates we may develop in the future. We enter into agreements with third parties that have a significant role in the conduct of our preclinical studies and clinical trials and the subsequent collection and analysis of data. These third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we have limited ability to control the conduct of such third party, the amount or timing of resources that any such third party will devote to our preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. The third parties we rely on for these services may also (i) have staffing difficulties, (ii) fail to comply with contractual obligations, (iii) experience regulatory compliance issues, (iv) undergo changes in priorities or become financially distressed, or (v) have relationships with other entities, some of which may be our competitors, which may draw time and resources from our development programs. The third parties with whom we may contract might not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies and clinical trials being delayed or unsuccessful. Some of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements with a third party, we would delay our drug development activities.

Our reliance on these third parties for such drug development activities will reduce our control over these activities but will not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and legal, regulatory, and scientific requirements and standards. Moreover, the FDA requires us and our third parties to comply with applicable GLP and GCP standards, regulations for conducting, monitoring, recording and reporting the results of preclinical studies and clinical trials to assure that the data and reported results are reliable and accurate and for clinical trials that the rights, integrity and confidentiality of trial participants are protected and that they are adequately informed of the potential risks of

participating in clinical trials. The EMA also requires us to comply with similar standards. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our preclinical studies and clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our preclinical studies and clinical trials substantially comply with GCP regulations. In addition, our clinical trials must be conducted with product candidates produced under current cGMP regulations and will require a large number of test patients. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties. We are also required to register certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not successfully carry out their contractual duties or perform preclinical studies and clinical trials in a satisfactory manner, meet expected deadlines or conduct our preclinical studies and clinical trials in accordance with legal and regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We entered into a collaboration agreement with EOC Pharma, and we may form or seek additional strategic alliances or collaborations in the future. Such alliances and collaborations may inhibit future opportunities, or we may not realize the benefits of such collaborations or alliances.

In December 2020, we granted to EOC exclusive rights to develop and commercialize FYARRO in the EOC Licensed Territory, pursuant to the EOC License, and we may form or seek strategic alliances, joint ventures or collaborations or enter into licensing arrangements with other third parties that we believe will complement or augment our development and commercialization efforts with respect to FYARRO or any future product candidates that we may develop. Under the EOC License Agreement, we received an upfront payment and are eligible to receive regulatory and sales-based milestone payments upon the occurrence of certain milestone events totaling \$257 million. We are also eligible to earn tiered royalties based on annual net sales of FYARRO based upon the royalties we are obligated to pay Celgene for sales of products in the EOC Territory pursuant to the Celgene License, plus an additional single-digit percentage that is variable based on the level of annual net sales. EOC will be responsible for development, regulatory submissions, and commercialization in the EOC Territory. We retain our rights outside of the EOC Territory.

Future efforts for additional alliances or collaborations may also require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process is time-consuming and complex. Furthermore, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction.

We depend on EOC to develop and commercialize FYARRO within the EOC Territory, and we have limited control over how EOC will conduct development and commercialization activities for FYARRO.

Under the EOC License Agreement, we rely on EOC for a substantial portion of the financial resources and for the development, regulatory, and commercialization activities for FYARRO in the EOC Territory, and we have limited control over the amount and timing of resources that EOC devotes to FYARRO. In addition, payments associated with development, regulatory and commercial milestones that we may be eligible to receive, as well as royalties, will be dependent upon further advancement of the FYARRO by EOC. If these milestones are not met and if FYARRO is not commercialized in the EOC Territory, we will not receive future revenues from the collaboration. EOC may fail to develop or effectively commercialize FYARRO for a variety of reasons and the EOC License Agreement subjects us to a number of risks, including:

- EOC may not commit sufficient resources to the development, regulatory approval, marketing, or distribution of FYARRO;

- EOC may be unable to successfully complete the clinical development of FYARRO or obtain all necessary approvals from foreign regulatory agencies in the EOC Territory required to market FYARRO;
- EOC may terminate their agreement with us prior to completing development or commercialization of the FYARRO under the collaboration, in whole or in part, adversely impacting the potential approval and our revenue from the licensed product;
- our third-party manufacturer may be unable or unwilling to manufacture FYARRO in compliance with requirements of Chinese regulatory agencies, which would impact clinical development of FYARRO, and in commercial quantities sufficient to meet market demand;
- there may be disputes between us and EOC, including disagreements regarding the EOC License Agreement with us, that may result in (1) the delay of (or prevent entirely) the achievement of development, regulatory and commercial objectives that would result in milestone payments, (2) the delay or termination of the development or commercialization of FYARRO in the EOC Territory, costly litigation or arbitration that diverts our management's attention and resources; and/or
- termination of the underlying license agreement;
- EOC may not comply with applicable regulatory guidelines with respect to developing or commercializing FYARRO, which could adversely impact the development of or sales of FYARRO and could result in administrative or judicially imposed sanctions, including warning letters, civil and criminal penalties, injunctions, product seizures or detention, product recalls, total or partial suspension of production and refusal to approve any new drug applications;
- EOC may experience financial difficulties;
- business combinations or significant changes in either the business strategy of EOC may also adversely affect EOC's ability to perform its obligations under its license agreement with us;
- EOC may not properly maintain our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- EOC may develop or commercialize FYARRO in a manner that may adversely impact our development or commercialization of FYARRO and/or future product candidates outside of such collaboration; and
- Although EOC is subject to a limited non-compete obligation, EOC could independently move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors.

If EOC does not perform in the manner we expect or fulfill our responsibilities in a timely manner, or at all, the development, regulatory approval, and commercialization efforts related to FYARRO could be delayed. It may be necessary for us to assume the responsibility at our own expense for the development of FYARRO in the EOC Territory. In that event, we would likely need to seek additional funding and our potential to generate future revenues from FYARRO could be significantly reduced and our business could be materially and adversely harmed.

We have entered into collaborations with third parties in connection with the development of FYARRO. Even if we believe that the development of such product candidate is promising, our partners may choose not to proceed with such development.

Our existing agreement with EOC, and any future collaboration agreements we may enter into, are generally subject to termination by the counterparty on short notice upon the occurrence of certain circumstances, including, in the case of EOC, without cause subject to a specified notice period. Accordingly, even if we believe that the development of product candidates is worth pursuing, our partners may choose not to continue with such development. If any of our collaborations are terminated, we may not receive additional milestones or royalties under those collaborations. In addition, we may be required to devote additional resources to the development of our product candidates or seek a new collaboration partner on short notice, and the terms of any additional collaboration or other arrangements that we establish may not be favorable to us.

We are also at risk that our current and any potential collaborations or other arrangements may not be successful. Factors that may affect the success of our collaborations include the following:

- Our collaboration partners may incur financial and cash flow difficulties that force them to limit or reduce their efforts under their collaboration agreement with us;
- Our collaboration partners may be pursuing alternative technologies or developing alternative products that are competitive to our technology and products, either on their own or in partnership with others;
- Our collaboration partners may terminate their collaboration with us, which could make it difficult for us to attract new partners or adversely affect perception of us in the business and financial communities; and
- Our collaboration partners may pursue higher priority programs or change the focus of their development programs, which could affect their commitment to us.

If we cannot maintain successful collaborations, our business, financial condition, and operating results may be adversely affected.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property, and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- Our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

If we decide to establish additional collaborations but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We may seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties. Any of these relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We would face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed

collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Even if we are successful in entering into a collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements on certain terms with potential collaborators.

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay our development program or one or more of our other development programs, delay our potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We may enter into collaborations with third parties for the development and commercialization of product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

If we enter into any collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates would pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a business combination or sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than us;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of FYARRO or any other product candidate that we may develop in the future, if approved, relative to other products;
- We may grant exclusive rights to our collaborators that would prevent us from collaborating with others;

- collaborators may not properly obtain, maintain, defend or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all;
- collaborators may not provide us with timely and accurate information regarding development progress and activities under the collaboration or may limit our ability to share such information, which could adversely impact our ability to report progress to our investors and otherwise plan our own development of our product candidates;
- collaborators may own or co-own intellectual property covering our products that results from us collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws, resulting in civil or criminal proceedings.

General Risks

Our stock price is volatile.

The market price of our common stock could be subject to significant fluctuations. From the completion of the Merger through December 31, 2021, the market price for our common stock ranged from a low of \$18.75 to a high of \$32.99. Market prices for securities of early-stage pharmaceutical, biotechnology, and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- Our ability to obtain regulatory approvals for FYARRO in other indications or for any other product candidates that we may develop in the future, and delays or failures to obtain such approvals;
- the failure of FYARRO or any other product candidates that we may develop in the future, if approved for marketing and commercialization, to achieve commercial success;
- any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices;
- the entry into, or termination of, key agreements, including key licensing, supply or collaboration agreements;
- adverse regulatory authority decisions;
- the initiation of material developments in, or conclusion of, disputes or litigation to enforce or defend any of our intellectual property rights or defend against the intellectual property rights of others;
- changes in laws or regulations applicable to our product candidates;
- the results of current, and any future, nonclinical or clinical trials of our product candidates;
- announcements by commercial partners or competitors of new commercial products, clinical progress (or the lack thereof), significant contracts, commercial relationships, or capital commitments;
- failure to meet or exceed financial and development projections we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

- general market conditions and other factors unrelated to our operating performance or the operating performance of our competitors, including deteriorating market conditions due to investor concerns regarding inflation and hostilities between Russia and Ukraine;
- adverse publicity relating to our markets, including with respect to other products and potential products in such markets;
- the introduction of technological innovations or new therapies competing with our potential products;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- the loss of key employees;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business and stock;
- changes in the market valuations of similar companies;
- general and industry-specific economic conditions potentially affecting our research and development expenditures;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in the structure of health care payment systems;
- adverse regulatory decisions;
- trading volume of our common stock; and
- period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies or the biotechnology sector. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Regardless of the merits or the ultimate results of such litigation, if instituted, such litigation could result in substantial costs and diversion of management's attention and resources, which could significantly harm our profitability and reputation.

Additionally, a decrease in our stock price may cause our common stock to no longer satisfy the continued listing standards of Nasdaq. If we are not able to maintain the requirements for listing on Nasdaq, we could be delisted, which could have a materially adverse effect on our ability to raise additional funds as well as the price and liquidity of our common stock.

We must maintain effective internal controls over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could have a material adverse effect on our business and stock price.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, and therefore will be able to take advantage of certain exemptions from various reporting requirements that are applicable to other companies that are not "emerging growth companies" including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act.

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a public company, the Sarbanes-Oxley Act requires, among other things, that we assess the effectiveness of our disclosure controls and procedures quarterly and the effectiveness of our internal control over financial reporting at the end of each fiscal year. We rely heavily on direct management oversight of transactions, along with the use of legal and outsourced accounting professionals. As we grow, we plan to hire additional personnel and engage external temporary resources and may implement, document, and modify policies and procedures to maintain effective internal controls. However, we may identify deficiencies and weaknesses or fail to remediate previously identified deficiencies in our internal controls.

The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These stringent standards require that our audit committee be advised and regularly updated on management's review of internal control over financial reporting. Our management may not be able to effectively and timely implement controls and procedures that adequately respond to the increased regulatory compliance and reporting requirements that are applicable to us as a public company. If we fail to staff our accounting, finance and information technology functions adequately or maintain internal control over financial reporting adequate to meet the demands that are placed upon us as a public company, including the requirements of the Sarbanes-Oxley Act, our business and reputation may be harmed and our stock price may decline. Furthermore, investor perceptions of us may be adversely affected, which could cause a decline in the market price of our common stock.

Financial reporting obligations of being a public company in the United States are expensive and time-consuming, and our management will be required to devote substantial time to compliance matters.

Following the recently completed Merger, we have incurred and expect to continue to incur significant additional legal, accounting and other expenses as a publicly traded company that we did not incur as a privately-held company, including costs associated with public company reporting requirements. The obligations of being a public company in the United States require significant expenditures and place significant demands on our management and other personnel, including costs resulting from public company reporting obligations under the Exchange Act and the rules and regulations regarding corporate governance practices, including those under the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"), the Dodd-Frank Wall Street Reform and Consumer Protection Act (the "Dodd-Frank Act") and the Nasdaq listing requirements. These rules require the establishment and maintenance of effective disclosure and financial controls and procedures, internal control over financial reporting and changes in corporate governance practices, among many other complex rules that are often difficult to implement, monitor and maintain compliance with. For example, our management team consists of executive officers and other personnel of the operating company that survived the Merger prior to the Merger, some of whom have not previously managed and operated a public company. Thus, our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements and to keep pace with new regulations, otherwise we may fall out of compliance and risk becoming subject to litigation or being delisted, among other potential problems. In addition, these rules and regulations may also make it difficult and expensive for us to obtain and maintain director's and officer's liability insurance. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers, which may adversely affect investor confidence in and could cause our business or stock price to suffer.

There can be no assurance that we will be able to comply with the continued listing standards of Nasdaq.

If Nasdaq delists our shares of common stock from trading on its exchange for failure to meet Nasdaq's listing standards, we and our stockholders could face significant material adverse consequences including:

- a limited availability of market quotations for our securities;
- reduced liquidity for our securities;
- a determination that our common stock is a "penny stock" which will require brokers trading in our common stock to adhere to more stringent rules and possibly result in a reduced level of trading activity in the secondary trading market for our securities;
- a limited amount of new and analyst coverage; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

Our principal stockholders and management own a significant percentage of our common stock and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned a significant portion of our outstanding voting stock.

These stockholders, acting together, may be able to impact matters requiring stockholder approval. For example, they may be able to impact the elections of directors, amendments to our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the

interests of other stockholder and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by war, terrorism, geopolitical uncertainties, other business interruptions, and by general conditions in the global economy and in the global financial markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. In the event of prolonged business interruptions due to geopolitical events, we could incur significant losses, require substantial recovery time and experience significant expenditures in order to resume our business or clinical operations. We have no operations in Russia or the Ukraine, but we do not and cannot know if the current uncertainties in these geopolitical areas, which are unfolding in real-time, may escalate and result in broad economic and security conditions or rationing of medical supplies, which could limit our ability to conduct clinical trials outside the U.S. or result in material implications for our business. In addition, our insurance policies typically contain a war exclusion of some description and we do not know how our insurers are likely to respond in the event of a loss alleged to have been caused by geopolitical uncertainties. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

In addition, our operations and performance may be affected by political or civil unrest or military action, including the current conflict between Russia and Ukraine, terrorist activity, unstable governments and legal systems. As a result of global economic conditions, some third-party payers may delay or be unable to satisfy their reimbursement obligations. Job losses or other economic hardships may also affect patients' ability to afford healthcare as a result of increased co-pay or deductible obligations, greater cost sensitivity to existing co-pay or deductible obligations, lost healthcare insurance coverage or for other reasons. Our ability to conduct clinical trials in regions experiencing political or civil unrest could negatively affect clinical trial enrollment or the timely completion of a clinical trial. We believe the aforementioned economic conditions could lead to reduced demand for our drug products, which could have a material adverse effect on our revenues, business and results of operations.

We are a smaller reporting company. We cannot be certain whether the reduced disclosure requirements applicable to smaller reporting companies will make our common stock less attractive to investors or otherwise limit our ability to raise additional funds.

We are a "smaller reporting company" under applicable securities regulations. A smaller reporting company is a company that, as of the last business day of its most recently completed second fiscal quarter, has an aggregate market value of the company's voting stock held by non-affiliates, or public float, of less than \$250 million, or has at least \$100 million in revenue and at least \$700 million in public float. SEC rules provide that companies with a non-affiliate public float of less than \$75 million may only sell shares under a Form S-3 shelf registration statement, during any 12-month period, in an amount less than or equal to one-third of the public float. If we do not meet this public float requirement, any offering by us under a Form S-3 will be limited to raising an aggregate of one-third of our public float in any 12-month period. In addition, a smaller reporting company is able to provide simplified executive compensation disclosures in its filings, is exempt from the provisions of Section 404(b) of the Sarbanes-Oxley Act requiring that an independent registered public accounting firm provide an attestation report on the effectiveness of internal control over financial reporting if its public float is less than \$75 million, and has certain other reduced disclosure obligations in our SEC filings, including, among other things, only being required to provide two years of audited financial statements in annual reports. Reduced disclosure in our SEC filings due to our status as a smaller reporting company may make it harder for investors to analyze our results of operations and financial prospects.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

The current expectation is that we will retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be stockholders' sole source of gain, if any, for the foreseeable future.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. In the event we do have equity research analyst coverage, we will not have any control over the analysts, or the content and opinions included in their reports. The price of our common stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our common stock could decrease, which in turn could cause our stock price or trading volume to decline.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us more difficult and may prevent attempts our stockholders to replace or remove our management.

Provisions in our amended and restated certificate of incorporation and by-laws may delay or prevent an acquisition or a change in management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders, and the ability of the board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law (the “DGCL”), which prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us in certain circumstances. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then current management by making it more difficult for stockholders to replace members of the board of directors, which is responsible for appointing the members of management.

Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

Our amended and restated by-laws provides that the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) is the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a breach of fiduciary duty owed by any of our directors, officers or other employees or our stockholders to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provisions of the DGCL, or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware, our amended and restated certificate of incorporation or our by-laws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim against us that is governed by the internal affairs doctrine; provided, that these choice of forum provisions do not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. The amended and restated bylaws provide that the federal district courts are the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. The choice of forum provision may limit a stockholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. If a court were to find the choice of forum provision contained in the by-laws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our by-laws described above

We are a California-domiciled public company and are required to have at least two or three women on our board of directors at the end of 2021, depending on the size of our board at the time.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified individuals to our board of directors. As a public company headquartered in California, we were required to have two or three women on our board of directors by the end of 2021, depending on the size of our board of directors at the time. We currently have seven seats on our board of directors which will require us to have at least three women on our

board of directors by the end of 2021. While we currently have two women on the board of directors, recruiting and retaining board members carries uncertainty, and failure to comply with this California requirement may result in financial penalties, ranging from \$100,000 to \$300,000. To date, the Secretary of State of the State of California has neither adopted regulations regarding fines or imposed fines for violations.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable non-U.S. regulators, provide accurate information to the FDA and applicable non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. Employees may also unintentionally or willfully disclose our proprietary and/or confidential information to competitors. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending our self or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters consist of 2,760 square feet of leased office space in Pacific Palisades, California. Our lease expires on February 28, 2025.

We believe our existing facility is adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms for our future growth.

Item 3. Legal Proceedings.

As of the date of this Annual Report on Form 10-K, we are not currently involved in any material legal proceedings. However, from time to time, we could be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Regardless of the outcome, legal proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock began trading on the Nasdaq Capital Market on August 27, 2021, under the symbol "AADI."

Stockholders

As of March 11, 2022, there were 113 stockholders of record of our common stock.

Dividends

We have never declared nor paid any cash dividends to stockholders. We do not intend to pay cash dividends on our common stock for the foreseeable future, and currently intend to retain any future earnings to fund our operations and the development and growth of our business. The declaration of any future cash dividends, if any, would be at the discretion of our board of directors (subject to limitations imposed under applicable Delaware law) and would depend on our earnings, if any, our capital requirements and financial position, our general economic conditions and other pertinent conditions.

Issuer Purchases of Equity Securities

There were no repurchases of shares of common stock made during the year ended December 31, 2021.

Item 6. [Reserved].

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion of our financial condition and results of operations of Aadi Bioscience, Inc. should be read in conjunction with the consolidated financial statements and the related notes to those statements thereto appearing elsewhere in this Annual Report for the year ending December 31, 2021. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risk, uncertainties and assumptions. Our actual results could differ materially from those discussed in our forward-looking statements for many reasons, including those risks. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this Annual Report. You should read this Annual Report completely, including the "Risk Factors" section under Part I, Item 1A of this Annual Report and the "Forward-Looking Statements" sections of this Annual Report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by our forward-looking statements contained in the following discussion and analysis. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

Overview

We are a biopharmaceutical company focused on developing and commercializing precision therapies for genetically defined cancers with alterations in mTOR pathway genes. Our lead drug product, FYARRO, *nab*-sirolimus, (sirolimus protein-bound particles for injectable suspension (albumin-bound)), is a form of sirolimus bound to albumin. Sirolimus is a potent inhibitor of the mTOR biological pathway, the activation of which pathway can promote tumor growth, and inhibits downstream signaling from mTOR.

In May 2021, we completed the filing of a rolling new drug application ("NDA") for FYARRO to the U.S. Food and Drug Administration (the "FDA"), for approval to treat patients with advanced malignant PEComa. The FDA accepted the NDA in July 2021 and granted us priority review designation with a Prescription Drug User Fee Act target action date in November 2021. The NDA was based on results from our Phase 2 registrational study, AMPECT (Advanced Malignant PEComa Trial), in advanced malignant PEComa.

In November 2021, the FDA approved FYARRO sirolimus protein-bound particles for injectable suspension (albumin-bound) for intravenous use for the treatment of adult patients with locally advanced malignant PEComa. During the first quarter of 2022, we launched FYARRO in the United States for treatment of advanced malignant PEComa.

In addition to advanced malignant PEComa, based on data from the completed AMPECT trial and our expanded access program, we have initiated a registration-directed tumor-agnostic Phase 2 study ("PRECISION 1") of FYARRO in patients with Tuberous Sclerosis Complex 1 and 2 (*TSC1* & *TSC2*) alterations. We have completed a Type B meeting with the FDA in which we discussed the initial trial design and the PRECISION 1 trial was opened for enrollment in the first quarter of 2022 in the United States.

For more information regarding our business, including FYARRO, the AMPECT trial and the PRECISION 1 trial, see Part I, Item 1 (Business).

For the fiscal year ended December 31, 2021, we recorded revenue of \$1.1 million and net loss of \$110.1 million. See "Results of Consolidated Operations" for further discussion of our results.

August 2021 Reverse Merger

- On May 16, 2021, at which time we were operating as "Aerpio Pharmaceuticals, Inc.," we entered into: (i) an Agreement and Plan of Merger ("Merger Agreement") with Aspen Merger Subsidiary, Inc., our wholly-owned subsidiary ("Merger Sub"), and Aadi Subsidiary, Inc. (formerly known as Aadi Bioscience, Inc. ("Private Aadi")); and (ii) a subscription agreement ("Subscription Agreement") with certain investors (the "PIPE Investors"), pursuant to which we agreed to sell shares of our common stock to the PIPE Investors concurrently with the closing of the Merger (as defined below) (the "PIPE Financing"). See Note 1 to our audited financial statements for more information about the Merger Agreement and the Subscription Agreement.
- On August 26, 2021, pursuant to the terms of the Merger Agreement and the Subscription Agreement:

- Merger Sub merged with and into Private Aadi, with Private Aadi surviving as our wholly-owned subsidiary (the “Merger”);
- in connection with and immediately prior to the Merger, we effected a reverse stock split of our common stock at a ratio of 15:1 and changed our name from “Aerpio Pharmaceuticals, Inc.” to “Aadi Bioscience, Inc”;
- at the effective time of the Merger, based on an exchange ratio of 0.3172 (after taking into account the Reverse Stock Split), as calculated under the Merger Agreement (the “Exchange Ratio”), we issued an aggregate of 5,776,660 shares of common stock to the holders of Private Aadi common stock immediately prior to the Merger, including shares of Private Aadi common stock issuable upon the conversion of all shares of preferred stock and convertible promissory notes outstanding immediately prior to the Effective Time;
- at the closing of the Merger, we assumed all of the outstanding and unexercised options to purchase shares of Private Aadi common stock, which options were converted into options to purchase shares of our common stock, as adjusted pursuant to the Merger Agreement based on the Exchange Ratio;
- concurrently with the Closing of the Merger, we issued and sold 11,852,862 shares of common stock to the PIPE Investors for total gross proceeds of \$155 million and, immediately after the closing of the Merger and the PIPE Financing, the PIPE Investors and the Private Aadi investors as of immediately prior to the effective time of the Merger owned 55.6% and 29.2%, respectively, of our outstanding common stock on a fully-diluted basis; and
- we entered into a contingent value rights agreement (“CVR Agreement”) pursuant to which each of our stockholders as of immediately prior to the effective time of the Merger became entitled to certain contingent value rights entitling them to receive 90% of the net proceeds (calculated as gross consideration minus certain permitted deductions), if any, received by us under the license agreement, dated June 24, 2018, with Gossamer Bio, Inc., as amended, and certain other covered agreements, as specified in the CVR Agreement (see Note 1 to our audited financial statements for more information about the CVR Agreement).

Celgene License Agreement

In April 2014, Private Aadi entered into a license agreement (the “Celgene License Agreement”) with Abraxis BioScience, LLC, a wholly owned subsidiary of Celgene Corporation, now Bristol Myers Squibb Company (“Celgene”), for exclusive rights for certain patents and a non-exclusive license for certain technology and know-how pertaining to ABI-009 (which we refer to as FYARRO). Under the Celgene License Agreement, as amended, Celgene is entitled to receive certain development milestone payments, royalties on net sales from licensed products under the agreement and any sublicense fees. No payments related to milestones or royalties under this agreement were paid during the twelve months ended December 31, 2021 and December 31, 2020. See Note 2 to the audited financial statements for more information about the Celgene License Agreement.

Under the terms of an August 2021 amendment to the Celgene License Agreement, we paid Celgene \$5.8 million, representing 50% of the previously outstanding payment obligation under the terms of the Celgene License Agreement, following the effective time of the PIPE Financing. Pursuant to the terms of the amendment, the remaining portion of the previously outstanding payment obligation (\$5.8 million), which is recorded on our balance sheet as a “payable to related party,” is due on the third anniversary of the effective time plus any accrued and unpaid interest due thereon.

EOC License Agreement

In December 2020, we entered into a license agreement (“EOC License Agreement”) with EOC Pharma (Hong Kong) Limited (“EOC”) under which we received \$14.0 million in January 2021 in non-refundable upfront consideration as partial payment for the rights and licenses granted to EOC by us for the further development and commercialization of FYARRO in the People’s Republic of China, Hong Kong Special Administration Region, Macao Special Administrative Region and Taiwan (the “Licensed Territory”). See Note 8 to the audited financial statements for more information about the EOC License Agreement.

In accordance with the Celgene License Agreement, we are required to pay 20% of all sublicense fees to Celgene. As such, we recognized \$2.8 million of license expense in the fourth quarter of 2020 and had a corresponding \$2.8 million sublicense payable to Celgene on the balance sheet as of December 31, 2020, which was paid in 2021.

During the fourth quarter of 2021, we recognized license revenue and received \$1.0 million from EOC for achieving the FDA approval milestone in November 2021. In accordance with the Celgene License Agreement, we recognized \$0.2 million of license expense in the fourth quarter of 2021 and had a corresponding \$0.2 million sublicense payable to Celgene on the balance sheet as of December 31, 2021, which was paid in 2022.

Key Trends and Factors Affecting Comparability Between Periods

- Following FDA approval in November 2021, we have been actively engaged in commercial preparations to support the U.S. launch of FYARRO for the treatment of patients with advanced malignant PEComa. We have built a cross-functional commercial team consisting of marketing, market access, commercial operations, and sales to support our launch and are building a commercial infrastructure with capabilities designed to scale when necessary to support future commercial launches. Expenses related to our commercial launch including personnel expenses, sales support, and marketing are included in general and administrative expenses for the year ended December 31, 2021. We expect these expenses will continue to increase as we launch FYARRO and support future launches.
- We expect that our research and development costs will increase in 2022 relative to 2021 as a result of anticipated significant expenses related to the PRECISION 1 trial.
- Following the Merger, we have incurred, and expect to continue to incur, significant additional expenses associated with being a public company that we did not incur as a privately-held company, including (i) costs to comply with the rules and regulations of the SEC and those of Nasdaq, (ii) legal, accounting and other professional services, (iii) insurance, (iv) investor relations activities and (v) other administrative and professional services.
- We accounted for the Merger as a reverse asset acquisition because substantially all of the fair value was concentrated in cash, working capital, and a long-lived contract intangible asset. Due to the significant excess purchase price being allocated over the fair value of the acquired contract intangible asset, we determined that an indicator of impairment was present and recognized in 2021 a non-cash impairment charge of \$74.2 million, to bring the carrying amount of the contract intangible asset down to its estimated fair value of \$3.9 million. The intangible asset is being amortized over the life of the underlying asset, 14.3 years.
- The COVID-19 pandemic has resulted, and is likely to continue to result in, significant national and global economic disruption and may adversely affect our operations. Our clinical trials have been, and may continue to be, affected by the closure of offices, lack of resources or closure of borders, among other measures being put in place around the world. The inability to travel and conduct face-to-face meetings, as well as constraints surrounding hospital infrastructure and staff, can also make it more difficult to enroll and maintain patients in ongoing or planned clinical trials. We are actively monitoring the impact of COVID-19 and the possible effects on our financial condition, liquidity, operations, suppliers, industry and workforce. However, the full extent, consequences and duration of the COVID-19 pandemic and the resulting impact on us cannot currently be predicted. We will continue to evaluate the impact that these events could have on our operations, financial position, results of operations and cash flows in fiscal year 2022.

Liquidity and Capital Resources

We have incurred net losses in each year since inception and as of December 31, 2021 we had an accumulated deficit of \$142.7 million. These losses have resulted principally from costs incurred in connection with research and development activities, general and administrative costs associated with our operations, and costs associated with the Merger. We expect to continue to incur significant expenses and operating losses for the foreseeable future due to the cost of research and development, including identifying and designing product candidates and conducting preclinical studies and clinical trials, the regulatory approval process for our product candidates and the commercial launch of FYARRO. As of December 31, 2021, we had \$149.0 million of cash and cash equivalents. Based on our current plans, we believe our existing cash and cash equivalents will enable us to conduct our planned operations into 2024.

Key Management Changes

Upon the closing of the Merger, Neil Desai, Ph.D. became our President and Chief Executive Officer. Following the Merger, we appointed Brendan Delaney as our Chief Operating Officer (September 2021), Loretta M. Itri, M.D. as our Chief Medical Officer (October 2021), and Scott Giacobello as our Chief Financial Officer (November 2021). Additionally, in September 2021, we appointed Emma Reeve to serve as a Class III director and as Chair of the Audit Committee.

Basis of Presentation

The following discussion highlights our results of operations and the principal factors that have affected our financial condition as well as our liquidity and capital resources for the periods described and provides information that management believes is relevant for an assessment and understanding of the consolidated balance sheets and statements of operation and comprehensive loss presented herein. The following discussion and analysis are based on our consolidated financial statements contained in this Annual Report, which we have prepared in accordance with U.S. generally accepted accounting principles (“GAAP”). You should read the discussion and analysis together with such consolidated financial statements and the related notes thereto.

Components of Statements of Operations and Comprehensive Loss

Revenue

EOC Pharma License Revenue

In December 2020, we entered into the EOC License Agreement with EOC pursuant to which, we granted EOC exclusive rights to develop and commercialize FYARRO in the Licensed Territory for human use in specified indications. EOC is obligated to pay royalties to us on sales of licensed products in the Licensed Territory. Under the terms of the EOC License Agreement, EOC has agreed to use commercially reasonable efforts to develop and commercialize FYARRO in the Licensed Territory and to obtain and maintain regulatory approval.

Unless earlier terminated, the EOC License Agreement will remain in effect until all milestones are achieved and royalty payment obligations are fulfilled as provided for in the EOC License Agreement. Prior to the expiration of the EOC License Agreement, EOC has the right to terminate the agreement for any reason upon a specified number of days advance written notice. Either party may terminate the EOC License Agreement in the event that the other party materially breaches the agreement and fails to cure the breach, or experiences certain events of financial distress. We may terminate the EOC License Agreement if EOC or its affiliates challenge the licensed patents in a legal, administrative or arbitration proceeding.

In December 2020, we recognized revenue of \$14.0 million related to the upfront payment which was paid in January 2021. We are eligible to receive up to an additional \$257.0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties on net sales in the Licensed Territory, which royalties are potentially subject to various reductions. EOC is responsible for controlling the filing for and obtaining all regulatory approvals, with our reasonable cooperation, and for bearing all costs associated with those approvals. In November 2021, we achieved the FDA approval milestone and recognized \$1.0 million of revenue, which was paid in December 2021.

We assessed the EOC License Agreement and concluded that EOC is a customer. Additionally, we identified the license of FYARRO provided to EOC as the sole performance obligation. The \$14.0 million upfront payment received from EOC is non-refundable and non-creditable and is considered fixed consideration.

Both the milestones and royalty payments under the EOC License Agreement are considered variable consideration and, with respect to revenue recognition, are constrained until we receive notification from EOC that the milestones and royalty payments have been achieved.

Grant Revenue

Grant revenue is derived from federal grants, primarily with the FDA. We have determined that the government agencies providing grants to us are not customers. Grant revenue is recognized when there is reasonable assurance of compliance with the conditions of the grant and reasonable assurance that the grant revenue will be received. We recognize grant revenue as reimbursable grant costs are incurred. The costs associated with these reimbursements are reflected as a component of research and development expense in the accompanying statements of operations and comprehensive loss.

With respect to grant revenue derived from reimbursement of direct out-of-pocket expenses for research costs associated with federal contracts, where we act as principal with discretion to choose suppliers, bear credit risk and perform part of the services required in the transaction, we record revenue for the gross amount of the reimbursement. The costs associated with these reimbursements are reflected as a component of research and development expense in the accompanying statements of operations and comprehensive loss.

Operating Expenses

Research and Development Expenses

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, are expensed as incurred. Research and development expenses consist primarily of: (i) employee related costs, including salaries, benefits and stock-based compensation expense for employees engaged in scientific research and development functions; (ii) third-party contract costs relating to research, formulation, manufacturing, nonclinical studies and clinical trial activities; (iii) external costs of outside consultants who assist with technology development, regulatory affairs, clinical development and quality assurance; (iv) payments made under our third-party licensing agreements; and (v) allocated facility-related costs.

Costs for certain activities, such as manufacturing, nonclinical studies and clinical trials are generally recognized based on the evaluation of the progress of completion of specific tasks using information and data provided by our vendors and collaborators. Research and development activities are central to our business. We expect to increase our investment in research and development in order to advance our product candidates through clinical trials. As a result, we expect that our research and development expenses will increase substantially in the foreseeable future as we continue to invest in research and development activities, pursue clinical development of our product candidates and expand our product candidate pipeline.

The process of commercialization and conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and time-consuming. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. Accordingly, to the extent that our product candidates continue to advance into clinical trials, including larger and later-stage clinical trials, our expenses will increase substantially and may become more variable.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, business development, sales and marketing, and other corporate functions. Other general and administrative expenses include professional fees for legal, auditing, tax and business consulting services, insurance costs, intellectual property and patent costs, facility costs and travel costs. We expect that general and administrative expenses will increase in the future as we expand our operating activities. Additionally, we will incur significant additional expenses associated with being a public company that we did not incur as a privately-held company, including (i) costs to comply with the rules and regulations of the SEC and those of Nasdaq, (ii) legal, accounting and other professional services, (iii) insurance, (iv) investor relations activities and (v) other administrative and professional services.

Impairment of Acquired Contract Intangible Asset

Impairment of acquired contract intangible asset relates to a write down of the acquired contract intangible asset to fair value. The contract intangible asset was assessed for recoverability using an undiscounted cash flow model, which resulted in undiscounted cash flows below the carrying amount. We recognized an impairment of \$74.2 million to bring the carrying amount of the contract intangible asset down to its estimated fair value of \$3.9 million at August 26, 2021. The fair value determination of the contract intangible asset was based upon a discounted cash flow valuation of the milestone payments and Monte Carlo valuation for the sales royalties.

Other Income (Expense), Net

Other income (expense) consists of the change in fair value of convertible promissory notes and interest expense related to such notes. These expenses are partially offset by interest income earned on cash and cash equivalents and gain on extinguishment of debt.

Income Taxes

During the years ending December 31, 2021 and 2020, we recognized state tax payments as income tax expense on the statement of operations and comprehensive loss. Since our formation in 2011, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or our earned tax credits, due to our uncertainty of realizing a benefit from those items.

Results of Consolidated Operations

The following table presents the results of operations for the periods indicated (amounts in thousands):

	Years Ended December 31,	
	2021	2020
Revenue		
License revenue	\$ 1,000	\$ 14,000
Grant revenue	<u>120</u>	<u>580</u>
Total revenue	<u><u>1,120</u></u>	<u><u>\$ 14,580</u></u>
Operating expenses		
Research and development	19,670	15,008
General and administrative	<u>18,511</u>	<u>2,121</u>
Impairment of acquired contract intangible asset	<u>74,156</u>	<u>—</u>
Total operating expenses	<u><u>112,337</u></u>	<u><u>17,129</u></u>
Loss from operations	<u>(111,217)</u>	<u>(2,549)</u>
Other income (expense), net	<u>1,129</u>	<u>(927)</u>
Loss before income taxes	<u>(110,088)</u>	<u>(3,476)</u>
Income tax expense	<u>(2)</u>	<u>(2)</u>
Net and comprehensive loss	<u><u>\$ (110,090)</u></u>	<u><u>\$ (3,478)</u></u>

Comparison of Years Ended December 31, 2021 and 2020

License Revenue

License revenue for the years ended December 31, 2021 and 2020 relate to payments received from EOC Pharma as consideration pursuant to the License Agreement. This revenue was recognized when earned. During the year ended December 31, 2021, we recognized \$1.0 million of revenue upon achieving the FDA approval milestone on November 22, 2021.

During the year ended December 31, 2020, we recognized \$14.0 million of revenue, related to the non-refundable upfront payment for the rights and license granted to EOC for the further development and commercialization of FYARRO in the Licensed Territory.

Grant Revenue

Grant revenue amounts can vary from period to period depending on the funding and work performed. Grant revenue decreased by \$0.5 million for the year ended December 31, 2021, compared to the same period in 2020, primarily due to a decrease in the eligible expenses for grant reimbursement incurred during 2021 compared to 2020.

Operating Expenses

Research and Development Expenses

The following table presents our research and development expenses for the periods indicated (amounts in thousands):

	Years Ended December 31,	
	2021	2020
Clinical drug product manufacturing expense	\$ 6,654	\$ 3,803
External clinical development expense	6,697	5,282
License fee	200	2,800
Personnel and other expenses	6,119	3,123
Total research and development expense	<u>\$ 19,670</u>	<u>\$ 15,008</u>

Research and development expenses for the year ended December 31, 2021, were \$19.7 million, an increase of \$4.7 million, compared to \$15.0 million for the year ended December 31, 2020. The increase was primarily driven by a \$2.9 million increase in clinical drug manufacturing costs to prepare for our commercial launch of FYARRO, a \$1.4 million increase for external clinical development, and a \$3.0 million increase in headcount, consultants, and other expenses offset by a reduction of \$2.6 million in license fee expense paid to Celgene.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2021, were \$18.5 million, an increase of \$16.4 million, compared to \$2.1 million for the year ended December 31, 2020.

The increase was primarily driven by the following in support of our increased headcount, preparation of our commercial launch and expenses related to being a public company. We expect these expenses to continue to increase as we commercialize FYARRO and future launches:

- \$2.8 in personnel related expenses due to increased headcount, incentive bonuses and share-based compensation. Sales and administrative headcount increased to 17 employees at December 31, 2021 from two employees at December 31, 2020;
- \$2.0 million of compensation related expenses to former Aerie executives related to the Merger;
- \$3.6 million of consulting expenses to support the growth of the organization;
- \$5.4 million of commercialization readiness and marketing expenses;
- and \$2.6 million of legal, insurance and other office related expenses.

Impairment of Acquired Contract Intangible Asset

During the year ended December 31, 2021, as a result of the excess fair value ascribed to the acquired contract intangible asset related to the Merger, we recorded a \$74.2 million impairment charge to reduce the carrying value of the intangible asset to its fair value at August 26, 2021. No impairments were recognized during the year ended December 31, 2020.

Other Income (Expense), Net

The following table sets forth our other income (expense), net:

	Years Ended December 31,	
	2021	2020
Change in fair value of convertible promissory notes	\$ 1,585	\$ (153)
Gain upon extinguishment of debt	196	—
Interest income	13	41
Interest expense	(665)	(815)
Total other income (expense)	<u>\$ 1,129</u>	<u>\$ (927)</u>

Other income (expense), net for the year ended December 31, 2021, were \$1.1 million of income, compared to \$0.9 million of expense for the year ended December 31, 2020. The change was primarily driven by an increase of \$1.7 million of non-cash income related to the change in fair value of the convertible promissory notes and a \$0.2 million gain recognized on the extinguishment of the Paycheck Protection Program loan forgiven by the Small Business Administration in April 2021.

Liquidity and Capital Resources

We have incurred net losses in each year since inception and as of December 31, 2021, we had an accumulated deficit of \$142.7 million. Our net losses were \$110.1 million and \$3.5 million for the years ended December 31, 2021 and 2020, respectively. These losses have resulted principally from costs incurred in connection with research and development activities, general and administrative costs associated with our operations, and costs associated with the Merger. Additionally, during the year ended December 31, 2021, we recognized a non-cash impairment charge of \$74.2 million on the contract intangible asset acquired in the Merger. We expect to continue to incur significant expenses and operating losses for the foreseeable future due to the cost of research and development, including identifying and designing product candidates and conducting preclinical studies and clinical trials, and the regulatory approval process for our product candidates. We expect our expenses, and the potential for losses, to increase substantially as we conduct clinical trials of FYARRO, seek to expand our pipeline, and operate as a public company.

From inception through December 31, 2021, we received funding of \$25.4 million from our initial seed financing and the sale of Series A convertible preferred stock, \$9.1 million from the issuance of convertible promissory notes, \$145.4 million, net from the PIPE Financing in connection with the Merger and \$29.7 million of cash assumed in the Merger. As of December 31, 2021, we had \$149.0 million of cash and cash equivalents. Based on our current plans, we believe our existing cash and cash equivalents will enable us to conduct our planned operations into 2024.

The following table summarizes our cash flows for the years presented:

	Year Ended December 31,	
	2021	2020
Net cash used in operating activities	\$ (22,423)	\$ (12,701)
Net cash provided by investing activities	25,153	—
Net cash provided by financing activities	141,804	1,194
Net increase (decrease) in cash and cash equivalents	\$ 144,534	\$ (11,507)

Operating Activities

Our net cash used in operating activities primarily results from our net loss adjusted for non-cash expenses, changes in working capital components, amounts due to contract research organizations to conduct our clinical programs and employee-related expenditures for research and development and general and administrative activities. Our cash flows from operating activities will continue to be affected by spending to advance and support our product candidates in the clinic and other operating and general administrative activities, including operating as a public company.

For the year ended December 31, 2021, cash used in operating activities was \$22.4 million and resulted from (i) our net loss of \$110.1 million offset by non-cash adjustments totaling \$75.4 million, which was primarily related to impairment of the acquired contract intangible asset of \$74.2 million, and (ii) a \$12.3 million net increase in our working capital accounts, primarily driven by the receipt of the \$14.0 million upfront payment from EOC under the EOC License Agreement.

For the year ended December 31, 2020, cash used in operating activities was \$12.7 million and resulted from (i) our net loss of \$3.5 million, and (ii) a \$10.5 million net decrease in our working capital accounts, offset by (ii) \$1.3 million in non-cash expenses related to interest expense on convertible promissory notes, stock-based compensation expense, lease expense and depreciation and amortization expense.

Investing Activities

Cash provided by investing activities for the year ended December 31, 2021 related to cash acquired in connection with the Merger partially offset by transaction related expenses and purchases of property and equipment. There were no investing activities for the year ended December 31, 2020.

Financing Activities

Cash provided by financing activities for the year ended December 31, 2021 includes \$155.0 million gross cash proceeds from our PIPE Financing and \$0.8 million from exercise of stock options, partially offset by \$9.6 million of issuance costs related to the PIPE Financing, and \$4.4 million of dividends paid to preferred stockholders. Net cash provided by financing activities for the year ended December 31, 2020 includes \$1.0 million related to the issuance of convertible promissory notes and \$0.2 million related to proceeds from our PPP Loan.

Contractual Obligations and Commitments

In August 2021, we entered into an amendment to extend the lease of our 2,760 square feet of office space in Pacific Palisades, California. We exercised an option, under our prior lease agreement, to extend the term of the lease for an additional three-year period. Included in the renewal were nine months of rent abatement and a rent escalation clause. Rent expense is being recorded on a straight-line basis. Rent expense related to this lease was \$0.2 million for each of the years ended December 31, 2021 and December 31, 2020.

On April 9, 2014, we entered into a license agreement (the “Celgene License Agreement”) with Celgene for exclusive rights for certain patents and a non-exclusive license for certain technology and know-how pertaining to FYARRO. On November 15, 2019, we entered into an amendment to the Celgene License Agreement (“Amended Celgene License Agreement”) to terminate certain of Celgene’s FYARRO product supply obligations and to transfer control over certain regulatory filings under the original Celgene License Agreement to us. This amendment also waived the obligations related to certain development milestone payments and waived the liability related to 2016 and 2017 licensed drug manufacturing costs. On August 30, 2021, we entered into Amendment No. 1 (the “Amendment”) to the Amended Celgene License Agreement related to certain intellectual property rights of Celgene pertaining to the compound known as FYARRO. Celgene is entitled to receive certain development milestone payments, royalties on net sales from licensed products under the agreement and any sublicense fees.

On December 8, 2020, we entered into a license agreement (“EOC License Agreement”) with EOC Pharma (Hong Kong) Limited (“EOC”) for the rights and licenses granted to EOC by us for the further development and commercialization of FYARRO in the People’s Republic of China, Hong Kong Special Administration Region, Macao Special Administrative Region and Taiwan (the “Licensed Territory”). In accordance with the Celgene License Agreement, we are required to pay 20% of all sublicense fees to Celgene.

On January 13, 2022, we entered into a Negotiated Purchase Order Terms and Conditions for Clinical and Commercial Product (the “Fresenius Agreement”) with Fresenius Kabi, LLC (“Fresenius Kabi”) pursuant to which Fresenius Kabi will manufacture FYARRO for us, and we will purchase FYARRO as a finished drug product from Fresenius Kabi, on a purchase-order basis. Under the Agreement, which shall be effective through December 22, 2022 (or such later date as may be agreed between the parties in writing and currently being discussed), we may purchase FYARRO for either clinical or commercial purposes for use in the United States and Canada. In addition to manufacturing, Fresenius Kabi will perform specified labeling, packaging and serialization activities in respect of FYARRO for our benefit. The price of FYARRO will be fixed, subject to the ability of Fresenius Kabi to increase pricing under specified circumstances. We have an obligation to purchase certain minimum quantities of FYARRO. Failure to purchase those minimum quantities will result in an additional payment from us to Fresenius Kabi.

We also have contracts with various organizations to conduct research and development activities, including clinical trial organizations to manage clinical trial activities and manufacturing companies to manufacture the drug product used in the clinical trials. The scope of the services under these research and development contracts can be modified and the contracts cancelled by us upon written notice. In the event of a cancellation, we would be liable for the cost and expenses incurred to date as well as any close out costs of the service arrangement.

With respect to our obligations under the CVR Agreement, certain events specified in the CVR Agreement need to occur for us to receive funds, and it is currently uncertain whether any funds will be received under the CVR Agreement. We do not have any commitment or obligation under the CVR Agreement unless and until funds are received.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of financial position and results of consolidated operations are based on consolidated financial statements prepared in accordance with GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosures. On an ongoing basis, we evaluate our estimates and judgments, including those related to prepaid and accrued research and development expenses, revenue recognition and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Merger and Acquired Contractual Intangible Asset

Aerpio issued common stock in the Merger based on the terms of the Merger Agreement. For accounting purposes, however, we concluded under GAAP that Private Aadi has acquired Aerpio. We based this conclusion having evaluated the terms of the Merger Agreement and other factors including: (i) the stockholders of Private Aadi owned approximately 66.8% of the voting rights of the Company as of immediately following the Merger (but prior to the PIPE Financing); (ii) three (3) of seven (7) members of the board of directors of the Company post-Merger were composed of directors designated by Private Aadi under the terms of the Merger Agreement, and one (1) member of the board of directors of the Company post-Merger was a director mutually designated by Private Aadi and Aerpio; (iii) existing members of Private Aadi's management became the management of the Company post-Merger; (iv) the PIPE Investors consist of individuals and funds, and for purpose of this analysis, while they owned approximately 55.6% on a fully-diluted basis, as of immediately following the Merger (and after giving effect to the PIPE Financing), no one individual or fund held more shares than the holders of Private Aadi collectively owned immediately following the Merger and they are not considered to be a single voting group; and (v) following the Merger, the Company is headquartered in Pacific Palisades, California, and all ongoing operations of the combined company are those of Private Aadi.

Further, under GAAP we have accounted for the Merger as a reverse asset acquisition rather than a business combination. Accounting as an asset acquisition is significantly different than the accounting for a merger transaction as a business combination. Among other things, we have not recognized any goodwill on our consolidated balance sheet as there may have been had the Merger been accounted for as a business combination. A central element to the accounting model conclusion is the determination of whether a business or an asset or a group of assets is acquired. A business is defined in ASC 805, Business Combinations, as an integrated set of inputs and processes that are capable of generating outputs that have the ability to provide a return to its investors or owners. Typical inputs include long-lived assets (including intangible assets or rights to use long-lived assets), intellectual property and the ability to obtain access to required resources. Typical processes include strategic, operational and resource management processes that are typically documented or evident through an organized workforce. We considered all of the above factors when determining whether a business was acquired in the Merger and concluded that Aerpio did not meet the definition of a business.

Upon closing of the Merger, substantially all of the fair value is concentrated in cash, working capital and a long-lived contract intangible asset related to Aerpio's license agreement with Gossamer Bio, Inc., under which 90% of any future net cash proceeds will be remitted to CVR Holders and paid through the CVRs. In accordance with GAAP for asset acquisitions, the excess purchase price over the fair value of the acquired assets and liabilities (\$78.1 million) was ascribed to the acquired contract intangible asset. However, due to the significant excess purchase price being allocated over the fair value of the acquired contractual intangible asset, we determined that an indicator of impairment was present, and we assessed the contract intangible asset as compared to expectations of contingent future cash flows. We concluded that our estimate of gross cash flows potentially accruing to us under the license agreement is likely to be less than the excess purchase price of the fair value of the acquired assets and liabilities ascribed to the acquired contract intangible asset. As a result, we performed a valuation of the acquired contract intangible asset and recognized an impairment of \$74.2 million to adjust the carrying amount of the contractual intangible asset to its estimated fair value of \$3.9 million.

The license agreement with Gossamer Bio, Inc. includes potential payments to us in the event of certain development and commercialization milestones and sales-based royalties. Our fair value determination of the intangible asset utilized a scenario-based, risk-adjusted, discounted cash flow model with respect to the potential development milestone payments and a Monte Carlo option-pricing model with respect to the sales-based milestone and royalty payments:

- We determined fair value of the potential development milestone payments under the license agreement with inputs based on certain subjective assumptions, including (a) the probability of clinical success determined with reference to various academic studies reporting probabilities of approval for clinical trials; (b) an estimate of the time to achievement of the clinical milestones; and (c) a counterparty credit risk premium determined with reference to the borrowing costs of a benchmark group of comparable market participants.
- Application of the Monte Carlo simulation model in valuing the potential sales-based milestone and royalties involves making assumptions for (a) the probability of clinical success determined with reference to various academic studies reporting probabilities of approval for clinical trials; (b) our forecast of potential revenues, revenue uptake rate and the period of time from a prospective commercial launch to peak sales, and an estimate of peak sales for each successfully commercialized product covered under the license agreement; (c) drift equal to the risk free rate on revenues following a multivariate Geometric Brownian Motion; (d) a counterparty credit risk premium determined with reference to the borrowing costs of a benchmark group of comparable market participants; and (e) a revenue metric risk premium determined with reference to a long-term risk-free rate, a weighted-average cost of capital, revenue volatility and asset volatility.

Research and Development Costs

We incur substantial expenses associated with clinical trials. Accounting for clinical trials relating to activities performed by CROs and other external vendors requires us to exercise significant estimates in regard to the timing and accounting for these expenses. We estimate costs of research and development activities conducted by service providers, which include, the conduct of preclinical studies, contract manufacturing activities and clinical activities. The diverse nature of services being provided under CRO and other vendor arrangements, the different terms and milestone arrangements that exist for each type of service and the lack of timely information related to certain clinical activities complicates the estimation of accruals for services rendered by CROs and other vendors in connection with clinical trials. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and include these costs in the accrued and other current liabilities or prepaid expenses, as applicable, on the balance sheets and within research and development expense on the consolidated statements of operations. In estimating the duration of a clinical study, we evaluate the start-up, treatment and wrap-up periods, payment arrangements and services rendered attributable to each clinical trial and fluctuations are regularly tested against payment plans and trial completion assumptions.

We estimate these costs based on factors such as estimates of the work completed and budget provided and in accordance with agreements established with our collaboration partners and third-party service providers. We make significant judgments and estimates in determining the accrued liabilities and prepaid expense balances in each reporting period. As actual costs become known, we adjust our estimates and related accounts on the balance sheet. We have not experienced any material differences between accrued costs and actual costs incurred since our inception.

Our expenses related to clinical trials are based on estimates of patient enrollment and related expenses at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that may be used to conduct and manage clinical trials on our behalf. We generally accrue expenses related to clinical trials based on contracted amounts applied to the level of patient enrollment and activity. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis.

Revenue Recognition

We account for revenue related to the EOC License Agreement and Grant Revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers (“ASC 606”). Under ASC 606, we recognize revenue when the defined customer, under ASC 606, transfers promised goods or services in an amount that reflects the consideration

to which we expect to be entitled in exchange for goods or services. To determine revenue recognition for contracts with customers, we perform the following five steps: (i) identify the promised goods or services in the contract; (ii) identify the performance obligation in the contract, including whether they are distinct in the context of the contract; (iii) determine the transaction price, including the constraint on variable consideration; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy the performance obligation. We recognize revenue when our customer obtains control of promised goods or services in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. We only apply the five-step model to contracts when it is probable that we will collect consideration to which we are entitled in exchange for the goods or services we transfer to the customer.

Stock-Based Compensation

We recognize all stock-based payments to employees, including grants of employee stock options in the consolidated statements of operations and comprehensive loss based on their fair values. All of our share-based awards, to employees, non-employees, officers, and directors, are subject only to service-based vesting conditions. We estimate the fair value of its stock-based awards using the Black-Scholes option pricing model, which requires the input of assumptions, including (i) the expected stock price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate based on the U.S. Treasury yield in effect at the time of the grant for zero-coupon U.S. treasury notes with maturities approximately equal to the expected term of the stock options and (iv) expected dividends. Options granted during the year have a maximum contractual term of ten years. Forfeitures are recognized and accounted for as they occur.

Due to the historical lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to ours, including stage of product development and life science industry focus. We believe the group selected has sufficient similar economic and industry characteristics and includes companies that are most representative of us.

We have limited historical stock option activity and therefore estimate the expected term of stock options granted to employees, officers, and directors using the simplified method, which represent the average of the contractual term of the stock option and its weighted-average vesting period, to calculate the expected term, as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term for options granted to employees, and utilize the contractual term for options granted to non-employees. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population.

Compensation expense related to awards to employees is calculated on a straight-line basis by recognizing the grant date fair value over the associated service period of the award, which is generally the vesting term. For the years ended December 31, 2021 and December 31, 2020, we recognized stock-based compensation expense, net of estimated forfeitures, in the statements of operations and comprehensive loss as follows (amounts in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	\$ 657	\$ 94
General and administrative	1,449	45
Total	\$ 2,106	\$ 139

As of December 31, 2021, total unamortized stock-based compensation was \$22.1 million which we expect to recognize over a weighted average period of 2.9 years. The intrinsic value of all outstanding stock options as of December 31, 2021 was \$10.0 million.

Income Taxes

We have accounted for income taxes using the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applicable to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax

assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A valuation allowance against deferred tax assets is recorded if, based upon the weight of all available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

When uncertain tax positions exist, we recognize the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. We recognize interest and penalties related to uncertain tax positions, if any exist, in income tax expense.

During the years ending December 31, 2021 and 2020, we recognized state tax payments as income tax expense on the statement of operations and comprehensive loss. Since our formation in 2011, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or our earned tax credits, due to our uncertainty of realizing a benefit from those items. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses (“NOL”). Pursuant to Section 382 and 383 of the Internal Revenue Code (“IRC”), utilization of our NOL carryforwards and research and development credits may be subject to annual limitations in the event of any significant future changes in our ownership structure. These annual limitations may result in the expiration of NOL carryforwards and research and development credits prior to utilization. As of December 31, 2021, we have completed an IRC Section 382 analysis through the date of the Merger. Ownership changes were identified that will result in annual limitations on future utilization of NOLs and research and development credit carryforwards. To the extent such limitations will cause NOL and R&D credit carryforwards to expire unused, these tax attributes have been removed from deferred tax assets. As of December 31, 2021, we have federal and state net operating loss carryforwards of approximately \$150.9 million and \$55.8 million, respectively. We also have federal and state research credit carryforwards of approximately \$3.1 million and \$1.7 million, respectively, as of December 31, 2021. Ownership changes may occur in the future which can result in future limitations of the available NOL and R&D credit carryforwards.

JOBS Act Accounting Election

We are an “emerging growth company” within the meaning of the JOBS Act. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies that are not emerging growth companies.

Recent Accounting Pronouncements

See Note 3 to the consolidated financial statements for a discussion of recent accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required by this Item.

Item 8. Consolidated Financial Statements and Supplementary Data.

Beginning on the following page are the consolidated financial statements with applicable notes and the related Report of Independent Registered Public Accounting Firm.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors
Aadi Bioscience, Inc.
Pacific Palisades, California

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Aadi Bioscience, Inc. (the “Company”) as of December 31, 2021 and 2020, and the related consolidated statements of operations and comprehensive loss, stockholders’ equity (deficit) and cash flows for the years then ended and the related notes (collectively, referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (“PCAOB”) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ BDO USA, LLP

We have served as the Company’s auditor since 2017

San Diego, California
March 17, 2022

AADI BIOSCIENCE, INC.

Consolidated Balance Sheets

(Amounts in thousands, except share data and par value)

	Year Ended December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	\$ 148,989	\$ 4,455
Accounts receivable	—	14,149
Prepaid expenses and other current assets	2,283	81
Total current assets	151,272	18,685
Property and equipment, net	57	21
Operating lease right-of-use assets	557	119
Intangible asset, net	3,811	—
Other assets	2,213	—
Total assets	\$ 157,910	\$ 18,825
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	\$ 6,439	\$ 2,392
Accrued liabilities	8,445	4,099
Payable to related party	258	14,314
Convertible related party promissory notes payable at fair value	—	9,029
Operating lease liabilities, current portion	131	125
Other current liabilities	—	99
Total current liabilities	15,273	30,058
Convertible promissory notes payable at fair value	—	1,102
Payable to related party	5,757	—
Operating lease liabilities, net of current portion	474	—
Other liabilities	—	97
Total liabilities	21,504	31,257
Commitments and contingencies (Note 15)		
Stockholders' equity (deficit):		
Series Seed preferred stock, \$0.0001 par value, zero and 734,218 shares authorized, issued and outstanding as of December 31, 2021 and 2020, respectively; aggregate liquidation preference of \$0 and \$1,101 as of December 31, 2021 and 2020, respectively	—	—
Series A preferred stock, \$0.0001 par value, zero and 7,211,948 shares authorized, issued and outstanding as of December 31, 2021 and 2020, respectively; aggregate liquidation preference of \$0 and \$28,433 as of December 31, 2021 and 2020, respectively	—	1
Common stock, \$0.0001 par value, 300,000,000 and 20,000,000 shares authorized; 20,894,695 and 2,542,358 shares issued and outstanding as of December 31, 2021 and 2020, respectively	2	1
Additional paid-in capital	279,089	20,161
Accumulated deficit	(142,685)	(32,595)
Total stockholders' equity (deficit)	136,406	(12,432)
Total liabilities and stockholders' equity (deficit)	\$ 157,910	\$ 18,825

The accompanying notes are an integral part of these consolidated financial statements.

AADI BIOSCIENCE, INC.

Consolidated Statements of Operations and Comprehensive Loss
(Amounts in thousands, except share data and earnings per share amounts)

	Year Ended December 31,	
	2021	2020
Revenue		
License revenue	\$ 1,000	\$ 14,000
Grant revenue	120	580
Total revenue	1,120	14,580
Operating expenses		
Research and development (includes related party amounts of \$200 and \$2,461, respectively)	19,670	15,008
General and administrative	18,511	2,121
Impairment of acquired contract intangible asset	74,156	—
Total operating expenses	112,337	17,129
Loss from operations	(111,217)	(2,549)
Other income (expense)		
Change in fair value of convertible promissory notes	1,585	(153)
Gain upon extinguishment of debt	196	—
Interest income	13	41
Interest expense (includes related party amounts of \$600 and \$734, respectively)	(665)	(815)
Total other income (expense), net	1,129	(927)
Loss before income tax expense	(110,088)	(3,476)
Income tax expense	(2)	(2)
Net and comprehensive loss	(110,090)	(3,478)
Cumulative dividends on convertible preferred stock	(647)	(987)
Net and comprehensive loss attributable to common stockholders	\$ (110,737)	\$ (4,465)
Net and comprehensive loss per share attributable to common stockholders, basic and diluted	\$ (12.41)	\$ (1.76)
Weighted average number of common shares outstanding used in computing net and comprehensive loss per share attributable to common stockholders, basic and diluted	8,923,369	2,542,358

The accompanying notes are an integral part of these consolidated financial statements.

AADI BIOSCIENCE, INC.

Consolidated Statements of Stockholders' Equity (Deficit)
(Amounts in thousands, including share amounts)

	Stockholders' Equity (Deficit)											
	Series Seed Preferred Stock			Series A Preferred Stock			Common Stock			Additional Paid-In Capital	Accumulated Deficit	Total
	Shares	Par	Value	Shares	Par	Value	Shares	Par	Value			
Balance at December 31, 2019	734	\$ —	—	7,212	\$ 1	—	2,542	\$ 1	20,022	\$ (29,117)	\$ (9,093)	
Share-based compensation expense	—	—	—	—	—	—	—	—	—	139	—	139
Net and comprehensive loss	—	—	—	—	—	—	—	—	—	(3,478)	(3,478)	
Balance at December 31, 2020	<u>734</u>	<u>—</u>	<u>—</u>	<u>7,212</u>	<u>1</u>	<u>—</u>	<u>2,542</u>	<u>1</u>	<u>20,161</u>	<u>\$ (32,595)</u>	<u>\$ (12,432)</u>	
Exercise of stock options to purchase common stock	—	—	—	—	—	—	73	—	833	—	—	833
Issuance of common stock to PIPE Investors, net of issuance costs	—	—	—	—	—	11,853	—	1	145,383	—	—	145,384
Issuance of common stock to former stockholders of Aerpio upon Merger	—	—	—	—	—	3,209	—	—	105,888	—	—	105,888
Conversion of convertible promissory note into common stock upon Merger	—	—	—	—	—	698	—	—	9,130	—	—	9,130
Conversion of convertible preferred stock into common stock upon Merger	(734)	—	(7,212)	(1)	2,520	—	—	—	—	—	—	(1)
Share-based compensation expense	—	—	—	—	—	—	—	—	2,106	—	—	2,106
Cumulative dividends paid on Series A preferred stock	—	—	—	—	—	—	—	—	(4,412)	—	(4,412)	
Net and comprehensive loss	—	—	—	—	—	—	—	—	(110,090)	(110,090)	(110,090)	
Balance at December 31, 2021	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>20,895</u>	<u>\$ 2</u>	<u>\$ 279,089</u>	<u>\$ (142,685)</u>	<u>\$ 136,406</u>	

The accompanying notes are an integral part of these consolidated financial statements.

AADI BIOSCIENCE, INC.

Consolidated Statements of Cash Flows

(Amounts in thousands)

	Year Ended December 31,	
	2021	2020
Cash flows from operating activities:		
Net loss	\$ (110,090)	\$ (3,478)
Adjustments to reconcile net loss to net cash used in operating activities:		
Impairment of acquired contract intangible asset	74,156	—
Change in fair value of convertible promissory notes (includes related party amounts of \$1,404 and \$130, respectively)	(1,585)	153
Non-cash interest expense (includes related party amounts of \$578 and \$734, respectively)	665	815
Gain on forgiveness of Payroll Protection Plan loan	(196)	—
Share-based compensation expense	2,106	139
Non-cash lease expense	171	167
Depreciation and amortization expense	105	9
Changes in operating assets and liabilities:		
Accounts receivable	14,149	(13,864)
Prepaid expenses and other current assets	(2,166)	(22)
Other non-current assets	481	37
Operating lease liability	(129)	(197)
Accounts payable and accrued liabilities	8,290	1,079
Payable to related party	(8,380)	2,461
Net cash used in operating activities	<u>(22,423)</u>	<u>(12,701)</u>
Investing activities:		
Cash acquired in connection with the Merger	29,700	—
Transaction expenses related to the Merger	(4,501)	—
Purchase of property and equipment	(46)	—
Net cash provided by investing activities	<u>25,153</u>	<u>—</u>
Financing activities:		
Proceeds from the exercise of stock options	833	—
Proceeds from the issuance of common stock to PIPE Investors	155,000	—
Costs incurred in connection with issuance of common stock	(9,617)	—
Dividends paid	(4,412)	—
Proceeds from issuance of convertible promissory notes	—	1,000
Proceeds from Payroll Protection Loan Program	—	194
Net cash provided by financing activities	<u>141,804</u>	<u>1,194</u>
Net increase (decrease) in cash and cash equivalents	<u>144,534</u>	<u>(11,507)</u>
Cash and cash equivalents at beginning of year	4,455	15,962
Cash and cash equivalents at end of year	<u>\$ 148,989</u>	<u>\$ 4,455</u>
Supplemental disclosure of cash flow information:		
Interest paid during the period	<u>\$ 22</u>	<u>—</u>
Supplemental disclosure of non-cash activities:		
Issuance of common stock upon Merger	<u>\$ 105,888</u>	<u>—</u>
Operating lease liability arising from obtaining right-of-use asset	<u>\$ 610</u>	<u>—</u>
Conversion of convertible promissory note into common stock upon Merger	<u>\$ 9,130</u>	<u>—</u>

The accompanying notes are an integral part of these consolidated financial statements.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Organization and Operations

Aadi Bioscience, Inc. (together with its subsidiaries, the “Company” or “Aadi”) is a biopharmaceutical company focused on developing and commercializing precision therapies targeted to rare mutation-driven diseases. Aadi’s lead drug product, FYARRO (previously called ABI-009), is *nab*-sirolimus (sirolimus protein-bound particles for injectable suspension (albumin-bound)) for diseases driven by the mTOR pathway activation through mutations or deletions of specific genes such as Tuberous Sclerosis Complex 1 and 2 (“TSC1” and “TSC2”). FYARRO is licensed to Aadi by Abraxis BioScience, LLC, a wholly owned subsidiary of Celgene Corporation, now Bristol Myers Squibb Company (“Celgene”), for all therapeutic areas including oncology, cardiovascular, and metabolic related diseases.

The Company’s historical operations have consisted principally of performing research and development activities and raising capital. The Company’s activities are subject to significant risks and uncertainties, including failing to secure additional funding before sustainable revenues and profit from operations are achieved.

Merger with Aerpio Pharmaceuticals, Inc. and Name Change

On May 16, 2021, the Company, then operating as Aerpio, entered into the Agreement and Plan of Merger (“Merger Agreement”) with Aspen Merger Subsidiary, Inc., a Delaware corporation and a direct, wholly-owned subsidiary of Aerpio (“Merger Sub”) and Aadi Subsidiary, Inc. (formerly known as Aadi Bioscience, Inc. (“Private Aadi”)).

Pursuant to the terms set forth in the Merger Agreement and effective August 26, 2021 (the “Effective Time”): (i) Merger Sub merged with and into Private Aadi, with Private Aadi surviving as a wholly-owned subsidiary of Aerpio (the “Merger”), (ii) Aerpio changed its name to Aadi Bioscience, Inc. in connection with and immediately prior to the Effective Time of the Merger, and (iii) Aerpio effected a 15:1 reverse stock split of the Aerpio common stock (“Reverse Stock Split”) immediately prior to the Effective Time of the Merger. At the Effective Time, each share of Private Aadi common stock outstanding immediately prior to the Effective Time, including the shares of Private Aadi common stock issuable upon the conversion of all shares of preferred stock and convertible promissory notes immediately prior to the closing of the Merger, were converted into the right to receive shares of the Company’s common stock based on an exchange ratio of 0.3172 (the “Exchange Ratio”), after taking into account the Reverse Stock Split.

Pursuant to the Merger Agreement, Aerpio assumed all of the outstanding and unexercised options to purchase shares of Private Aadi capital stock under the Private Aadi Amended and Restated 2014 Equity Incentive Plan (the “Private Aadi Plan”), and, in connection with the Merger, such options were converted into options to purchase shares of the Company’s common stock based on the Exchange Ratio. At the closing of the Merger at the Effective Time, the Company issued an aggregate of 5,776,660 shares of common stock to holders of Private Aadi common stock, including for shares of Private Aadi common stock issuable upon the conversion of all shares of preferred stock and convertible promissory notes outstanding immediately prior to the Effective Time. In connection with the Merger, the Company entered into a Contingent Value Rights Agreement (the “CVR Agreement”) with a legacy director of Aerpio, as Holder Representative (as defined in the CVR Agreement), and American Stock Transfer & Trust Company, LLC, as Rights Agent (as defined in the CVR Agreement), in accordance with the terms of the Merger Agreement. The CVR Agreement entitles each holder of Aerpio common stock as of immediately prior to the closing of the Merger (each, a “CVR Holder”) to receive one contingent value right (“CVR”) for each outstanding share of Aerpio common stock held by such CVR Holder as of immediately prior to the closing of the Merger, each representing the right to receive certain net proceeds, if any, derived from the CVR completed during a CVR Payment Period, which means successive six-month periods, prior to the expiration of the CVR Term (as defined in the CVR Agreement), with any potential payment obligations continuing until the earlier of (a) the 20-year anniversary of the Effective Time and (b) the time at which the license agreement with Gossamer Bio, Inc., the underlying basis for the CVR, has expired or been terminated. Under the terms of the Merger Agreement, as related to the CVR, the Company is entitled to 10% of any proceeds paid from the underlying license agreement plus reimbursement of expenses. There can be no assurances that any proceeds will result therefrom.

The Merger has been accounted for using the reverse asset acquisition method under U.S. generally accepted accounting principles (“GAAP”). For accounting purposes, Private Aadi is considered to have acquired Aerpio and the Merger has been accounted for as a reverse asset acquisition. Private Aadi is considered the accounting acquirer even though Aerpio issued the common stock in the Merger based on the terms of the Merger Agreement and other factors including: (i) following the Merger, the stockholders of Private Aadi collectively owned a substantial portion

of the voting rights of the Company; (ii) three (3) of seven (7) members of the board of directors of the Company post-Merger were composed of directors designated by Private Aadi under the terms of the Merger Agreement, and one (1) member of the board of directors of the Company post-Merger was a director mutually designated by Private Aadi and Aerpio; (iii) existing members of Private Aadi's management became the management of the Company post-Merger; (iv) the PIPE Investors (as defined below) consist of individuals and funds, and for purpose of this analysis, while they owned approximately 55.6% on a fully-diluted basis, as of immediately following the Merger (and after giving effect to the PIPE Financing), no one individual or fund held more shares than the holders of Private Aadi collectively owned immediately following the Merger and they are not considered to be a single voting group; and (v) following the Merger, the Company is named "Aadi Bioscience, Inc." and headquartered in Pacific Palisades, California, and all ongoing operations of the Company are those of Private Aadi. To determine the accounting for this transaction under GAAP, a company must assess whether an integrated set of assets and activities should be accounted for as an acquisition of a business or an asset acquisition. Upon closing of the Merger, substantially all of the fair value is concentrated in cash, working capital and a long-lived contract intangible asset. As such, the acquisition was treated as an asset acquisition. The net assets of Aerpio have been recorded at their relative fair value in the consolidated financial statements of the Company and the reported operating results prior to the Merger will be those of Private Aadi.

Pursuant to the closing of the Merger, Private Aadi's board of directors declared a 4% cumulative dividend on its preferred stock of \$4.4 million which was paid at the Effective Time.

PIPE Financing and Subscription Agreement

On May 16, 2021, the Company entered into a subscription agreement ("Subscription Agreement") with certain investors (the "PIPE Investors"), pursuant to which it would sell shares of its Common Stock concurrently with the closing of the Merger (the "PIPE Financing"). At the closing of the PIPE Financing, the Company entered into a Registration Rights Agreement, dated August 26, 2021 ("Registration Rights Agreement"), with the PIPE Investors. The PIPE Investors purchased an aggregate of 11,852,862 shares of common stock of the Company (the "PIPE Shares") for an aggregate purchase price of \$155.0 million pursuant to the Subscription Agreement ("PIPE Financing"). The aggregate net proceeds for the issuance and sale of the PIPE Shares was \$145.4 million, after deducting certain expenses incurred that were direct and incremental to the issuance of the PIPE Shares.

Immediately following the Effective Time, and after giving effect to the Reverse Stock Split and the PIPE Financing, there were approximately 20.8 million shares of common stock of the Company outstanding. Immediately following the Effective Time and after giving effect to the Reverse Stock Split and the PIPE Financing: (i) the Private Aadi stockholders owned approximately 29.2% of the outstanding shares of common stock; (ii) Aerpio's stockholders immediately prior to the Merger, whose shares of common stock, as adjusted for the Reverse Stock Split, remain outstanding after the Merger, owned approximately 15.2% of the outstanding shares of common stock; and (iii) the PIPE Investors owned approximately 55.6% of the outstanding shares of common stock, in each case as calculated on a fully-diluted basis.

Liquidity

Since inception, the Company has devoted substantially all of its resources to research and development activities, business planning, establishing and maintaining its intellectual property portfolio, hiring personnel, raising capital and providing general and administrative support for these operations and has not realized revenues from its planned principal operations.

The Company has experienced net losses since its inception and expects to continue to incur net losses into the foreseeable future. The Company had an accumulated deficit of \$142.7 million as of December 31, 2021 and net loss of \$110.1 million and \$3.5 million for the years ended December 31, 2021 and 2020, respectively. To date, these operating losses have been funded primarily from outside sources of invested capital through the issuance of convertible promissory notes, grant funding, the sale of securities, and proceeds from license agreements.

During the year ended December 31, 2021, the Company raised capital through the PIPE Financing of \$155.0 million which netted \$145.4 million after financing expenses. Additionally, the Company assumed \$29.7 million of cash from Aerpio in the Merger, which netted to \$27.7 million after \$2.0 million of compensation related expenses for former Aerpio executives related to the Merger. The Company had cash and cash equivalents of \$149.0 million at December 31, 2021. Management believes that the Company's current cash and cash equivalents, including the aggregate net proceeds from the PIPE Financing, will provide sufficient funds to enable the Company to meet its obligations for at least twelve months from the filing date of this report.

COVID-19

In December 2019, a strain of coronavirus was reported in Wuhan, China and began to spread globally, including to the United States and Europe, in the following months. The World Health Organization has declared COVID-19 to be a global pandemic. The full impact of the COVID-19 pandemic is inherently uncertain at the time of this report. The COVID-19 pandemic has resulted in travel restrictions and, in some cases, prohibitions of non-essential activities, disruption and shutdown of businesses, and greater uncertainty in global financial markets. As COVID-19 has spread, it has significantly impacted the health and economic environment around the world, and many governments have closed most public establishments, including restaurants, workplaces, and schools. Aadi's clinical trials have been, and may continue to be, affected by the closure of offices, or country borders, among other measures being put in place around the world. The inability to travel and conduct face-to-face meetings, as well as constraints surrounding hospital resources, infrastructure, staff and other resources, can also make it more difficult to enroll new patients in ongoing or planned clinical trials. Any of these circumstances will potentially have a negative impact on the Company's financial results and the timing of its clinical trials.

The COVID-19 pandemic has caused the Company to modify business practices (including but not limited to curtailing or modifying employee travel, moving to full remote work, and cancelling physical participation in meetings, events, and conferences), and may take further actions as may be required by government authorities or that are determined to be in the best interests of the Company's employees, patients, and business partners.

The extent of the impact of the COVID-19 pandemic on Aadi's future liquidity and operational performance will depend on certain developments, including the duration and spread of the outbreak, the availability and effectiveness of vaccines, the impact on the Company's clinical trials, patients, and collaboration partners, and the effect on its suppliers.

2. Related Party Transactions

Presented below are the details of a license agreement with Celgene, an entity which was a stockholder of Private Aadi prior to the Merger and became a stockholder of the Company as a result of the Merger.

Celgene License Agreement

On April 9, 2014, the Company entered into a license agreement (the "Celgene License Agreement") with Celgene for exclusive rights for certain patents and a non-exclusive license for certain technology and know-how pertaining to FYARRO.

The Celgene License Agreement will remain in effect from the effective date of April 9, 2014 until expiration of all milestone and royalty payment obligations under the agreement, unless terminated by either of the parties upon giving an advance notice as specified in the Celgene License Agreement. Under the terms of the Celgene License Agreement, Celgene agreed to supply the Company with licensed products of FYARRO necessary for clinical or non-clinical development.

Celgene had the option to terminate the Celgene License Agreement and all of the Company's related rights and licenses upon the occurrence of each of the following: (a) successful completion of the first Phase 2 Trial for a licensed product ("First Trigger Event"), or (b) if Celgene elects not to exercise its option upon the First Trigger Event, then upon the acceptance by the Food and Drug Administration or the European Medicines Agency, as applicable, of the first New Drug Application either in the United States or European Union, whichever occurs first, for a licensed product ("Second Trigger Event"). On May 1, 2019, Celgene terminated its rights to elect an option to terminate the Celgene License Agreement upon the occurrence of a First Trigger Event, Second Trigger Event or Early Exercise. As a result, the Company is free to negotiate and enter into any agreement with respect to an acquisition of all or substantially all of the business or assets of the Company whether by merger, sale of equity or assets, or otherwise and to consummate the same as it sees fit.

Celgene is entitled to receive certain development milestone payments, royalties on net sales from licensed products under the agreement and any sublicense fees. No payments related to milestones or royalties under this agreement were paid during the years ended December 31, 2021 and December 31, 2020. See below for discussion on sub-license fee.

On November 15, 2019, Celgene and the Company entered into an amendment to the Celgene License Agreement (the "Amended Celgene License Agreement") to terminate certain of Celgene's FYARRO product supply obligations and to transfer control over certain regulatory filings under the original Celgene License Agreement

from Celgene to the Company. The Amended Celgene License Agreement also waived the obligations related to certain development milestone payments and waived the liability related to 2016 and 2017 licensed drug manufacturing costs of \$1.2 million and \$2.7 million, respectively.

On August 30, 2021, the Company and Celgene entered into Amendment No. 1 (the “Amendment”) to the Amended Celgene License Agreement related to certain intellectual property rights of Celgene pertaining to the compound known as FYARRO. Under the terms of the Amendment, the Company paid Celgene \$5.8 million representing 50% of the previously outstanding payment obligation under the terms of the Amended Celgene License Agreement, following the Effective Time of the PIPE Financing. Pursuant to the terms of the Amendment, the remaining previously outstanding payment obligation of \$5.8 million, is due on the third anniversary of the Effective Time, or August 26, 2024 plus any accrued and unpaid interest due thereon (“Balloon Payment”). The Balloon Payment shall accrue interest, beginning August 26, 2021 until paid in full, at a rate equal to 4.0% per annum based on the weighted average amount outstanding during the applicable calendar quarter, and interest is payable quarterly in arrears. In addition, the parties agreed to amend the royalty rates payable to Celgene based on net sales of products subject to the Amended Celgene License Agreement.

On December 8, 2020, the Company entered into a license agreement (“EOC License Agreement”) with EOC Pharma (Hong Kong) Limited (“EOC”) under which the Company received \$14.0 million in January 2021 in non-refundable upfront consideration as partial payment for the rights and licenses granted to EOC by the Company for the further development and commercialization of FYARRO in the People’s Republic of China, Hong Kong Special Administration Region, Macao Special Administrative Region and Taiwan (the “Licensed Territory”). In accordance with the Celgene License Agreement, the Company is required to pay 20% of all sublicense fees to Celgene. As such, the Company recognized \$2.8 million of license expense in the year ended December 31, 2020 and had a corresponding \$2.8 million sublicense payable to Celgene on the balance sheet as of December 31, 2020, which was paid in 2021.

During the year ended December 31, 2021, the Company recognized license revenue and received \$1.0 million from EOC for achieving the FDA approval milestone on November 22, 2021. In accordance with the Celgene License Agreement, the Company recognized \$0.2 million of license expense in the year ended December 31, 2021 and had a corresponding \$0.2 million sublicense payable to Celgene on the balance sheet as of December 31, 2021, which was paid in 2022. Refer to Note 8 for additional information on the EOC License Agreement.

3. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements, and the related disclosures, have been prepared in accordance with generally accepted accounting principles in the United States (“GAAP”) and U.S. Securities and Exchange Commission (“SEC”) regulations and, in the opinion of management include all adjustments necessary for a fair presentation of the results of operations, financial position, changes in stockholders’ equity and cash flows for each period presented. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) of the Financial Accounting Standards Board (“FASB”). All adjustments are of a normal and recurring in nature. The Company’s consolidated financial statements are stated in U.S. Dollars.

On August 26, 2021, when the Company closed the Merger, all outstanding shares of common stock along with preferred stock of Private Aadi were exchanged for new shares of common stock of the Company and the approximately 8.1 million shares of Private Aadi capital stock held by stockholders of Private Aadi immediately prior to the Merger were exchanged for approximately 2.5 million shares of common stock of the Company based on the Exchange Ratio. The authorized number of shares of common stock was not reduced and remains at 300.0 million. The par value of the Company’s common stock remains unchanged at \$0.0001 per share.

Also on August 26, 2021, and immediately prior to the closing of the Merger, Aerpio effected the Reverse Stock Split. Accordingly, all share and per share amounts for the period presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect the Reverse Stock Split. No fractional shares were issued in connection with the Reverse Stock Split. Unless otherwise noted, all references to shares of the Company’s common stock and per share amounts have also been adjusted to reflect the Exchange Ratio.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing proprietary therapeutics. All the assets and operations of the Company's sole operating segment are located in the United States.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities, revenues and expenses, and the disclosure of contingent assets and liabilities in the Company's consolidated financial statements and accompanying notes. In the opinion of management, all adjustments, consisting of normal recurring accruals, considered necessary for a fair presentation have been included. The most significant estimates in the Company's consolidated financial statements relate to fair value of the intangible asset, fair value of the convertible promissory notes, stock-based compensation expense and accrued research and development costs. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may materially differ from these estimates and assumptions.

Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentration of credit risk, consist primarily of cash and cash equivalents and certain investments in money market funds. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has not experienced any losses on deposits since inception.

Cash and Cash Equivalents

The Company considers all highly liquid marketable securities purchased with original maturities of three months or less at the time of purchase date to be cash equivalents. At December 31, 2021 and 2020, cash and cash equivalents included money market investments totaling \$140.0 million and \$3.0 million, respectively.

Fair Value Option

The Company has elected the fair value option to account for its convertible promissory notes issued. The Company records these convertible promissory notes at fair value with changes in fair value recorded in the statements of operations and comprehensive loss. As a result of applying the fair value option, direct costs and fees related to the convertible promissory notes were recognized in earnings as incurred and not deferred. As of December 31, 2021, there were no Convertible Notes outstanding as they were converted to shares of Private Aadi common stock immediately prior to the closing of the Merger.

Fair Value of Financial Instruments

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value, and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is defined as an exit price representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs, such as quoted prices in active markets

Level 2: Inputs, other than the quoted prices in active markets that are observable either directly or indirectly

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions which reflect those that a market participant would use. The valuation of the Level 3 intangible asset was based on fair value measurements including discounted cash flow methodologies when valued at the time of the Merger.

Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement requires judgment and may affect the valuation of fair value assets and liabilities and their placement within the fair value hierarchy levels.

In determining the fair value of its financial instruments, the Company considers the source of observable market data inputs, liquidity of the instrument, the credit risk of the counterparty to the contract, and its risk of nonperformance. In the case fair value is not observable, for the items subject to fair value measurements, the Company applies valuation techniques deemed the most appropriate under the GAAP guidance based on the nature of the assets and liabilities being measured.

The carrying amounts of cash and cash equivalents, accounts receivable, prepaid expenses and other current assets and accounts payable are reasonable estimates of their fair value because of the short maturity of these items.

The following table sets forth the recurring and non-recurring fair value of the Company's financial assets and liabilities, allocated into the Level 1, Level 2 and Level 3 hierarchy that were measured at fair value on a recurring basis (amounts in thousands):

Recurring fair value measurements:

	Fair Value Measurements as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds (1)	\$ 140,032	\$ —	\$ —	\$ 140,032
Fair Value Measurements as of December 31, 2020				
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds (1)	\$ 3,041	\$ —	\$ —	\$ 3,041
Liabilities:				
Convertible promissory notes	\$ —	\$ —	\$ 10,131	\$ 10,131

(1) Included in cash and cash equivalents in the accompanying balance sheets.

Non-Recurring fair value measurement:

	Fair Value Measurements as of December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Intangible asset	\$ -	\$ -	\$ 3,811	\$ 3,811

Intangible Asset

The Company recognized an impairment of the contract intangible asset acquired in connection with the Merger and reduced the contract intangible asset to its estimated fair value which represented a Level 3 fair value measurement as factors used to develop the estimated fair value are unobservable inputs that are not supported by market activity. The total contract intangible asset was valued at \$3.9 million utilizing a scenario-based, risk-adjusted, discounted cash flow model with respect to the potential development milestone payments within the underlying license agreement and a Monte Carlo option-pricing model with respect to the sales-based milestone and royalty payments:

- The Company determined fair value of the potential development milestone payments under the license agreement with inputs based on certain subjective assumptions, including (a) the probability of clinical success determined with reference to various academic studies reporting probabilities of approval for clinical trials; (b) an estimate of the time to achievement of the clinical milestones; and (c) a counterparty credit risk premium determined with reference to the borrowing costs of a benchmark group of comparable market participants.

- Application of the Monte Carlo simulation model in valuing the potential sales-based milestone and royalties involves making assumptions for (a) the probability of clinical success determined with reference to various academic studies reporting probabilities of approval for clinical trials; (b) a forecast of potential revenues, revenue uptake rate and the period of time from a prospective commercial launch to peak sales, and an estimate of peak sales for each successfully commercialized product covered under the license agreement; (c) drift equal to the risk free rate on revenues following a multivariate Geometric Brownian Motion; (d) a counterparty credit risk premium determined with reference to the borrowing costs of a benchmark group of comparable market participants; and (e) a revenue metric risk premium determined with reference to a long-term risk-free rate, a weighted-average cost of capital, revenue volatility and asset volatility

See Notes 4 and 5 for further discussion of the Intangible Asset acquired through the Merger.

Convertible Note

As further described in Note 9, Private Aadi issued convertible notes in October 2019 and January 2020 (collectively the “Convertible Notes”). The Company elected the fair value option to account for the Convertible Notes. The fair value was estimated using a scenario-based analysis based on the probability-weighted value of expected future investment returns, considering possible outcomes available to the noteholders including conversions in subsequent equity financings, change of control transactions, settlement, and dissolution. The Company adjusts the carrying value of its Convertible Notes to their estimated fair value at each reporting date, with any related increases or decreases in the fair value recorded as a change in fair value of convertible promissory notes in the statements of operations and comprehensive loss.

As of December 31, 2021, there were no Convertible Notes outstanding as the Convertible Notes were converted to shares of Private Aadi common stock immediately prior to the closing of the Merger, which were concurrently exchanged for common stock of the Company based on the Exchange Ratio in connection with the closing of the Merger. As of December 31, 2020, the significant unobservable inputs used in the fair value measurement of the Convertible Notes included an expected settlement date in August 2021 and June 2021, respectively, and an estimated discount rate of 25%. Other significant unobservable inputs include the relative weighting applied to the possible outcomes available to the noteholders including conversions in subsequent equity financings, change of control transactions, settlement, and dissolution.

There are significant judgments, assumptions and estimates inherent in the determination of the fair value of the Convertible Notes described above. These include determination of a valuation method and selection of the possible outcomes available to the Company, including the determination of timing and expected future investment returns for such scenarios, as well as the likelihood of repayment, conversion, and dissolution. The related judgments, assumptions and estimates are highly interrelated and changes in any one assumption could necessitate changes in another. Any changes in the probability of a particular outcome would require a related change to the probability of another outcome.

The following table provides a reconciliation of the Convertible Notes (refer to Note 9) measured at fair value using significant unobservable inputs (Level 3) (amounts in thousands):

Convertible Notes (Level 3)	
Balance as of December 31, 2019	\$ 8,165
Issuance of convertible promissory notes	1,000
Accrued interest	813
Change in fair value of convertible promissory notes	153
Balance as of December 31, 2020	\$ 10,131
Issuance of convertible promissory notes	-
Accrued interest	584
Change in fair value of convertible promissory notes	(1,585)
Converted into common stock	(9,130)
Balance as of December 31, 2021	\$ —

There have been no transfers between levels during the reporting periods.

Accounts Receivable

Accounts receivable represents revenue recognized, but for which payment has not yet been received. Accounts receivable at December 31, 2020 includes \$14.0 million receivable related to the EOC upfront payment and \$0.1 million grant revenue. These amounts were subsequently collected in 2021. Estimates for allowances for doubtful accounts are determined based on existing contractual obligations and historical payment patterns. No allowance for doubtful accounts was recorded as of December 31, 2021 and 2020.

Inventory

The Company capitalizes inventory costs associated with its products upon regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed. Prior to FDA approval of FYARRO, all costs related to the manufacturing of FYARRO were charged to research and development expense in the period incurred.

Property and Equipment, Net

Property and equipment, consisting of computers, furniture and fixtures, and office equipment, are stated at cost, less accumulated depreciation. Property and equipment is depreciated using the straight-line method over the estimated useful lives of the assets, generally five years. Such costs are periodically reviewed for recoverability when impairment indicators are present.

Intangible Asset

The Company's intangible asset consists of a single asset, Aerpio's license agreement with Gossamer Bio., Inc. acquired in the Merger. The intangible asset is stated at fair value and is amortized using the straight-line method over its estimated useful life of 14.3 years. The intangible asset is reviewed for potential impairment when events or circumstances indicate that carrying amounts may not be recoverable.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, including property, equipment, and the intangible asset for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets may not be recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than the carrying amount. The impairment loss, if recognized, would be based on the excess of the carrying value of the impaired asset over its respective fair value. An impairment was recorded for the long-lived intangible asset during the year ended December 31, 2021 (see Note 5).

Leases

At the inception of a contractual arrangement, the Company determines whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. If both criteria are met, the Company records the associated lease liability and corresponding right-of-use asset upon commencement of the lease using the implicit rate or a discount rate based on a credit-adjusted secured borrowing rate commensurate with the term of the lease. The Company does not recognize assets or liabilities for leases with lease terms of less than 12 months.

The Company additionally evaluates leases at their inception to determine if they are to be accounted for as an operating lease or a finance lease. A lease is accounted for as a finance lease if it meets one of the following five criteria: (i) the lease has a purchase option that is reasonably certain of being exercised, (ii) the present value of the future cash flows is substantially all of the fair market value of the underlying asset, (iii) the lease term is for a significant portion of the remaining economic life of the underlying asset, (iv) the title to the underlying asset transfers at the end of the lease term, or (v) if the underlying asset is of such a specialized nature that it is expected to have no alternative uses to the lessor at the end of the term. Leases that do not meet the finance lease criteria are accounted for as an operating lease. Operating lease assets represent a right to use an underlying asset for the lease term and operating lease liabilities represent an obligation to make lease payments arising from the lease. Operating lease liabilities with a term greater than one year and their corresponding right-of-use assets are recognized on the balance sheet at the commencement date of the lease based on the present value of lease payments over the expected lease term.

Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received. As the Company's leases do not typically provide an implicit rate, the Company utilizes the appropriate incremental borrowing rate, determined as the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term and in a similar economic environment. For finance leases, depreciation expense is recognized for the leased asset acquired and interest expense is recognized related to the portion of the financing in the statements of operations. For operating leases, lease cost is recognized on a straight-line basis over the lease term and variable lease payments are recognized as operating expense in the period in which the obligation for those payments is incurred. Variable lease payments primarily include common area maintenance, utilities, real estate taxes, insurance, and other operating costs that are passed on from the lessor in proportion to the space leased by the Company. The Company has elected the practical expedient to not separate between lease and non-lease components.

Commitments and Contingencies

The Company recognizes a liability with regard to loss contingencies when it believes it is probable a liability has been incurred, and the amount can be reasonably estimated. If some amount within a range of loss appears at the time to be a better estimate than any other amount within the range, the Company accrues that amount. When no amount within the range is a better estimate than any other amount the Company accrues the minimum amount in the range. The Company has not recorded any such liabilities as of December 31, 2021 and 2020.

Revenue Recognition

Grant Revenue

The Company's grant revenues are derived from federal grants with the U.S. Food and Drug Administration. The Company has determined that the government agencies providing grants to the Company are not customers. Grant revenue is recognized when there is reasonable assurance of compliance with the conditions of the grant and reasonable assurance that the grant revenue will be received. The Company recognizes grant revenues as reimbursable grant costs are incurred. The costs associated with these reimbursements are reflected as a component of research and development expense in the accompanying statements of operations and comprehensive loss.

With respect to grant revenue derived from reimbursement of direct out-of-pocket expenses for research costs associated with federal contracts, where the Company acts as principal with discretion to choose suppliers, bears credit risk, and performs part of the services required in the transaction, the Company records revenue for the gross amount of the reimbursement. The costs associated with these reimbursements are reflected as a component of research and development expense in the accompanying statements of operations and comprehensive loss.

Revenue Under License Agreement

The Company generates revenues from payments received under a license agreement. Under such license agreement, the Company recognizes revenue when it transfers promised goods or services to partners in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. To determine revenue recognition for contracts with partners, the Company performs the following five steps: (i) identifies the promised goods or services in the contract; (ii) identifies the performance obligations in the contract, including whether they are distinct in the context of the contract; (iii) determines the transaction price, including the constraint on variable consideration; (iv) allocates the transaction price to the performance obligations in the contract; and (v) recognizes revenue when (or as) the Company satisfies the performance obligations.

For revenue from such license agreement, the Company generally collects an upfront license payment from the license partner and is also entitled to receive event-based payments subject to the license partner's achievement of specified development, regulatory and sales-based milestones. In addition, the Company is generally entitled to royalties if products under the license agreement are commercialized.

Transaction price for a contract represents the amount to which the Company is entitled in exchange for providing goods and services to the partner. Transaction price does not include amounts subject to uncertainties unless it is probable that there will be no significant reversal of revenue when the uncertainty is resolved. Apart from the upfront license payment, all other fees the Company may earn under such license agreements are subject to significant uncertainties of product development. Achievement of many of the event-based development and regulatory milestones may not be probable until such milestones are actually achieved. This generally relates to milestones such as obtaining regulatory approvals and successful completion of clinical trials. With respect to other development milestones, e.g., dosing of a first patient in a clinical trial, achievement could be considered probable

prior to its actual occurrence, based on the progress towards commencement of the trial. The Company does not include any amounts subject to uncertainties into the transaction price until it is probable that the amount will not result in a significant reversal of revenue in the future. At the end of each reporting period, the Company re-evaluates the probability of achievement of such milestones and any related constraint, and if necessary, adjusts the estimate of the overall transaction price.

Because such agreements generally only have one type of performance obligation, a license, which is generally all transferred at the same time as agreement inception, allocation of the transaction price among multiple performance obligations is not required. Upfront amounts allocated to licenses are recognized as revenue when the licenses are transferred to the partners. Development milestones and other fees are recognized in revenue when their occurrence becomes probable.

Research and Development

Research and development expenses consist of costs incurred in performing research and development activities, including salaries and benefits, materials and supplies, preclinical expenses, stock-based compensation expense, contract services, and other external development expenses. The Company records research and development activities conducted by third-party service providers, which include work related to preclinical studies, clinical trials, and contract manufacturing activities, to research and development expense as incurred. The Company is required to estimate the amount of services provided but not yet invoiced and include these expenses in accrued expenses on the balance sheet and within research and development expenses in the statements of operations and comprehensive loss. These expenses are a significant component of the Company's research and development expenses and require significant estimates and judgments. The Company accrues for these expenses based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. As actual expenses become known, the Company adjusts its accrued expenses.

Share-Based Compensation

The Company recognizes all stock-based payments to employees, including grants of employee stock options in the consolidated statements of operations and comprehensive loss based on their fair values. All the Company's share-based awards, to employees, non-employees, officers, and directors, are subject only to service-based vesting conditions. The Company estimates the fair value of its stock-based awards using the Black-Scholes option pricing model, which requires the input of assumptions, including (i) the expected stock price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. Options granted during the year have a maximum contractual term of ten years. Forfeitures are recognized and accounted for as they occur.

Due to the historical lack of a public market for the trading of the Company's securities and a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. The Company believes the group selected has sufficient similar economic and industry characteristics and includes companies that are most representative of the Company.

The Company has limited historical stock option activity and therefore estimates the expected term of stock options granted to employees, officers, and directors using the simplified method, which represents the average of the contractual term of the stock option and its weighted-average vesting period, to calculate the expected term, as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term for options granted to employees, and utilizes the contractual term for options granted to non-employees. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of the grant for zero-coupon U.S. treasury notes with maturities approximately equal to the expected term of the stock options. Compensation expense related to awards to employees is calculated on a straight-line basis by recognizing the grant date fair value over the associated service period of the award, which is generally the vesting term.

Income Taxes

Income taxes have been accounted for using the asset and liability method. Under the asset and liability method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applicable to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A valuation allowance against deferred tax assets is recorded if, based upon the weight of all available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. The Company recognizes interest and penalties related to uncertain tax positions, if any exist, in income tax expense.

Net and Comprehensive Loss per Share Attributable to Common Stockholders

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding for the period. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares and common share equivalents outstanding for the period. Common stock equivalents are only included when their effect is dilutive. The Company's potentially dilutive securities, which include convertible promissory notes, convertible preferred stock, outstanding stock options and warrants under the Company's equity incentive plans have been excluded from the computation of diluted net loss per share as they would be anti-dilutive.

Net loss per share is presented as the more dilutive of the treasury stock and as-converted method or the two-class method required for participating securities. The Series A convertible preferred stock is considered a participating security and does not have a contractual obligation to share in Private Aadi's losses. As such, the two-class method was not required.

The following table sets forth the outstanding potentially dilutive securities that have been excluded in the calculation of diluted net loss per share because their inclusion would be anti-dilutive (amounts in thousands):

	Year Ended December 31,	
	2021	2020
Options to purchase common stock	1,750	391
Warrants to purchase common stock	37	—
Series Seed convertible preferred stock	—	734
Series A convertible preferred stock	—	7,212

The table above excludes the conversion of the principal balance and accrued interest on the convertible promissory notes which converted into 698,018 shares of common stock in conjunction with the closing of the Merger.

Accounting Pronouncements Not Yet Adopted

In August 2020, the FASB issued ASU 2020-06, “Debt – Debt with Conversion and Other Options” (Subtopic 470-20) and “Derivatives and Hedging – Contracts in Entity’s Own Equity” (Subtopic 815-40). This new guidance is intended to reduce the complexity of accounting for convertible instruments. The guidance also addresses how convertible instruments are accounted for in the diluted earnings per share calculation and requires enhanced disclosures about the terms of convertible instruments. Entities may adopt ASU 2020-06 using either a partial retrospective or fully retrospective method of transition. This ASU is effective for fiscal years beginning after December 15, 2023, including interim periods within those fiscal years for smaller reporting companies. The Company is currently evaluating the impact the adoption of ASU 2020-06 will have on the Company’s consolidated financial statements.

In April 2021, the FASB issued ASU 2021-04, which included Topic 260 “Earnings Per Share.” This guidance clarifies and reduces diversity in an issuer’s accounting for modifications or exchanges of freestanding equity-classified written call options due to a lack of explicit guidance in the FASB Codification. ASU 2021-04 is effective

for all entities for fiscal years beginning after December 15, 2021. Early adoption is permitted. The Company has evaluated the impact of adopting ASU 2021-04 and does not expect this will have a material impact on the Company's consolidated financial statements.

4. Merger

The Merger was accounted for as a reverse asset acquisition because substantially all of the fair value was concentrated in cash, working capital, and a long-lived contract intangible asset (See Note 1).

The estimated fair value of total consideration given was \$110.4 million as detailed below and is based on 3,208,718 shares of common stock, after taking into account the Reverse Stock Split, outstanding immediately prior to the Effective Time.

Number of common shares of the combined company to be owned by Aerpio shareholders	3,208,718
Multiplied by the fair value per share of Aerpio common stock on August 26, 2021	\$ 33.00
Fair value of Aerpio common stock	105,887,694
Aadi transaction costs	4,500,864
Purchase price	<u><u>\$ 110,388,558</u></u>

The allocation of the purchase price is as follows (amounts in thousands):

	August 26, 2021
Cash and cash equivalents	\$ 29,700
Other current assets	2,709
Intangible asset (1)	78,062
Deposits	20
Accounts payable and accrued liabilities	<u>(103)</u>
Purchase price	<u><u>\$ 110,388</u></u>

- (1) The long-lived intangible asset represents Aerpio's out-licensing agreement with Gossamer Bio., Inc. Should payment be received from the underlying license agreement, in accordance with milestones or royalties, the Company will retain 10% of the proceeds with the balance being distributed to the CVR Holders. In accordance with GAAP for asset acquisitions, the excess purchase price over the fair value of the acquired assets and liabilities was ascribed to the acquired contract intangible asset. See Note 5 below for additional discussion of the subsequent impairment recognized.

5. Intangible Asset

In conjunction with the Merger, the Company recorded a long-lived contract intangible asset related to Aerpio's license agreement with Gossamer Bio. Inc., which was assumed in the Merger. In accordance with GAAP, for asset acquisitions, the excess purchase price over the fair value of the acquired assets and liabilities was ascribed to the acquired contract intangible asset. Due to the significant excess purchase price being allocated over the fair value of the acquired contract intangible asset, the Company determined that an indicator of impairment was present. The contract intangible asset was assessed for recoverability using an undiscounted cash flow model, which resulted in undiscounted cash flows below the carrying amount. The Company therefore recognized an impairment of \$74.2 million to bring the carrying amount of the contract intangible asset down to its estimated fair value of \$3.9 million. The fair value estimate of the intangible asset relates to contingent cash flows expected from Aerpio's out-licensing arrangement, of which 90% of any future net cash proceeds will be remitted to CVR Holders and paid through the CVRs. The fair value determination of the intangible asset was based upon a discounted cash flow valuation of the milestone payments and Monte Carlo valuation for the sales royalties. The estimated useful life of the intangible asset is 14.3 years. Amortization expense was \$95,000 for the year ended December 31, 2021. No intangible asset or amortization expense was recorded in 2020.

The estimated amortization expense related to this finite lived intangible asset for the five succeeding years is as follows (amounts in thousands):

	December 31, 2021
Intangible asset	\$ 3,906
Less amortization	(95)
Intangible asset, net	<u><u>\$ 3,811</u></u>
2022	\$ 273
2023	273
2024	273
2025	273
2026	273
Amounts thereafter	2,446
	<u><u>\$ 3,811</u></u>

As of December 31, 2021, all development milestones, sales-based milestones and royalty payments within the license agreement are constrained. There can be no assurance that any proceeds will be received under the license agreement.

6. Accrued Liabilities

Details of accrued liabilities are presented as follows (amounts in thousands):

	December 31,	
	2021	2020
Accrued clinical	\$ 2,507	\$ 2,017
Accrued contract manufacturing	2,287	1,301
Accrued bonus	1,465	597
Accrued professional fees	1,948	11
Accrued other	238	173
Total accrued liabilities	<u><u>\$ 8,445</u></u>	<u><u>\$ 4,099</u></u>

7. Operating Lease

In April 2019, the Company entered into a twenty-eight-month facility lease agreement for 2,760 square feet of office space in Pacific Palisades, California. The lease commenced on May 1, 2019, included four months of rent abatement and a rent escalation clause and was set to expire on August 31, 2021. In August 2021, the Company exercised its option to extend the term of the lease for an additional three-year period and entered into an amendment to the lease agreement (the “Lease Amendment”). Pursuant to the Lease Amendment, the Company and the landlord agreed to extend the term for an additional period of three (3) years and six (6) months, until February 28, 2025, with an option to renew for an additional three (3) years in accordance with the terms of the lease agreement. Included in the Lease Amendment were nine months of rent abatement and a rent escalation clause. Rent expense is being recorded on a straight-line basis.

The following table summarizes information related to the Company’s lease (amounts in thousands):

	December 31,	
	2021	2020
Assets:		
Operating lease right-of-use assets	\$ 557	\$ 119
Total right-of-use assets	<u><u>\$ 557</u></u>	<u><u>\$ 119</u></u>
Liabilities:		
Operating lease liabilities, current	\$ 131	\$ 125
Operating lease liabilities, non-current	<u><u>474</u></u>	<u><u>—</u></u>
Total operating lease liabilities	<u><u>\$ 605</u></u>	<u><u>\$ 125</u></u>

Rent expense related to this lease each of the twelve months ended December 31, 2021 and December 31, 2020 is presented on the following table (amounts in thousands):

	December 31,	
	2021	2020
Cash paid included in operating cash flows	\$ 146	\$ 195
Operating leases rent expense	<u><u>\$ 188</u></u>	<u><u>\$ 183</u></u>

The future minimum lease payments required under the operating lease as of December 31, 2021, are summarized below (amounts in thousands):

Future Minimum Lease Payments:	
2022	\$ 169
2023	231
2024	238
2025	40
Total minimum lease payments	<u><u>\$ 678</u></u>
Less: amount representing interest	<u><u>(73)</u></u>
Present value of operating lease liabilities	<u><u>\$ 605</u></u>
Less: operating lease liabilities, current	<u><u>(131)</u></u>
Operating lease liabilities, non-current	<u><u>\$ 474</u></u>
Remaining lease term (in years)	3.17
Incremental borrowing rate	6.80%

8. EOC License Agreement

In December 2020, the Company entered into the EOC License Agreement with EOC for the further development of ABI-009, now called FYARRO, and commercialization of FYARRO in Greater China, including the Republic of China, Hong Kong, Macau and Taiwan (the “Licensed Territory”). Under the terms of the EOC License Agreement, the Company granted to EOC an exclusive, royalty-bearing license to develop and commercialize the product in the Licensed Territory.

Unless earlier terminated, the term of the EOC License Agreement continues until the expiration of the royalty obligations. EOC has the right to terminate the agreement for any reason upon 120 days advance written notice. Either party may terminate the EOC License Agreement in the event that the other party breaches the agreement and fails to cure the breach, becomes insolvent or challenges certain of the intellectual property rights licensed under the agreement.

The Company assessed the EOC License Agreement and concluded that EOC is a customer and identified the license of FYARRO provided to EOC as the sole performance obligation. The \$14.0 million upfront payment received from EOC is non-refundable and non-creditable and is considered fixed consideration. The Company recognized revenue of \$14.0 million in the year ended December 31, 2020 when the EOC License Agreement was signed, and the \$14.0 million upfront payment was received in January 2021.

The potential milestone payments and royalty payments under the EOC License Agreement are considered variable consideration and are constrained with respect to revenue recognition notification from EOC that the milestone and royalty payments have been achieved.

The Company is eligible to receive an additional \$257.0 million in the aggregate upon achievement of certain development, regulatory, and sales milestones, as well as tiered royalties on net sales in the Licensed Territory. Under the terms of the EOC License Agreement, EOC will fund all research, development, regulatory, marketing and commercialization activities in the defined Licensed Territory. The Company earned \$1.0 million in milestone revenue upon achievement of the FDA approval milestone on November 22, 2021. EOC paid the \$1.0 million milestone payment in December 2021. In accordance with the Company's agreement with Celgene, 20% of the \$1.0 million payment, or \$0.2 million was accrued at December 31, 2021, for payment to Celgene in January 2022.

9. Convertible Notes

Private Aadi received \$8.1 million in October 2019 and \$1.0 million in January 2020 for the proceeds in connection with the issuance of Convertible Notes. The October 2019 Convertible Notes were issued to existing equity holders of Private Aadi. The Convertible Notes issued in October 2019 and January 2020 originally had a maturity date of one year from the date of issuance and an escalating interest rate of 6% per annum for the first four months following the effective date of the loan agreement, 8% per annum for the fifth and sixth months, and 10% per annum for the remaining six months of the note term until maturity at twelve months. The Convertible Notes contain certain redemption features, including conversion to preferred stock upon the closing of Private Aadi's next issuance of preferred stock resulting in net proceeds to the Company of at least \$25.0 million ("Qualified Financing"). The Convertible Notes would convert into a variable, whole number of preferred shares equal to the number obtained by dividing the principal plus accrued interest of the Convertible Notes by 80% of the price per share paid by cash investors in the Qualifying Financing if converted in the first four months following the effective date of the loan agreement, 75% if converted in months five or six, and 70% if converted later than six months. The Convertible Notes also contained a mandatory prepayment provision that required Private Aadi to pay the outstanding principal, plus accrued and unpaid interest together with a premium in the event that a qualified liquidity event occurred. The premium was equal to 120% of the outstanding principal amount to be prepaid in the event the liquidity event occurs within four months of the note date, 130% between the fifth and sixth month, and 140% if after the sixth month but prior to maturity.

In November 2020, Private Aadi entered into an amendment to the October 2019 and January 2020 Convertible Notes, whereby the term was extended from one year to two years. The amendment was accounted for as a debt modification.

In May 2021, Private Aadi entered into an amendment to the October 2019 and January 2020 Convertible Notes, whereby upon the closing of the Merger (see Note 1), the outstanding principal amount of the Convertible Notes and all accrued and unpaid interest as of immediately prior to the closing of the Merger would automatically convert into fully paid and nonassessable shares of Private Aadi common stock at a price per share equal to \$4.80 and would be concurrently exchanged for shares of the Company's common stock based on the Exchange Ratio. In conjunction with the closing of the Merger on August 26, 2021, the outstanding Convertible Notes were converted into shares of Private Aadi common stock which were concurrently exchanged for 698,018 shares of the Company's common stock after taking into account the Exchange Ratio. At the date of conversion, the convertible notes were marked to market.

10. Payroll Protection Program Loan

On March 27, 2020, President Trump signed into law the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act"). The CARES Act, among other things, includes provisions relating to refundable payroll tax credits, deferment of employer side social security payments, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations and technical corrections to tax depreciation methods for qualified improvement property. The CARES Act also appropriated funds for the Small Business Administration ("SBA") Paycheck Protection Program ("PPP") loans that are forgivable in certain situations to promote continued employment, as well as Economic Injury Disaster Loans to provide liquidity to small businesses harmed by COVID-19.

In May 2020, Aadi was approved for a \$0.2 million SBA PPP loan, as provided for in the CARES Act ("PPP Loan"). Under certain conditions, the PPP Loan and accrued interest are forgivable after a twenty-four-week covered period as long as the loan proceeds were used for eligible expenses, including payroll, benefits, rent and

utilities, and the company maintains certain payroll levels. The amount of loan forgiveness is subject to reduction if the Company terminates employees or reduces salaries during the twenty-four-week covered period. The unforgiven portion of the loan is payable over two years at an interest rate of 1%, with a deferral of payments for the ten months following the end of the twenty-four-week covered period. On April 29, 2021, the Company received notification from the SBA that the Company's Forgiveness Application of the PPP Loan and accrued interest was approved in full, and the Company had no further obligations related to the PPP Loan. Accordingly, the Company recorded a gain on the forgiveness of the PPP Loan totaling \$0.2 million.

The SBA has stated that all PPP loans in excess of \$2 million, and other PPP loans as appropriate, will be subject to review by the SBA for compliance with program requirements. If the SBA determines in the course of its review that a borrower lacked an adequate basis for the required certification concerning the necessity of the loan request or the subsequent use of loan proceeds, the SBA will seek repayment of the PPP loan, including interest and potential penalties. While the Company believes the loan was properly obtained and forgiven, there can be no assurance regarding the outcome of an SBA review. The Company has not accrued any liability associated with the risk of an adverse SBA review.

11. Common Stock

Preferred Stock

As of December 31, 2021, under the Company's certificate of incorporation, as amended and restated, the Company has 10,000,000 shares of preferred stock, par value \$0.0001 per share, in authorized capital with no shares outstanding.

Series Seed Preferred Stock

On February 23, 2017, Private Aadi converted from a limited liability company to a corporation and at that time converted 734,218 membership units into shares of Series Seed Preferred Stock. All outstanding shares of Series Seed Preferred Stock were converted into Private Aadi's common stock and concurrently exchanged for the Company's common stock based on the Exchange Ratio in connection with the closing of the Merger.

Series A Preferred Stock

In February and March 2017, Private Aadi sold and issued in a private placement 5,847,940 shares of Series A Preferred Stock at \$3.42 per share (the "Series A Financing"). Upon the closing of the Series A Financing, convertible notes issued in 2015 converted into 482,426 shares of Series A Preferred Stock at 85% of the \$3.42 price per share (the "Series A Original Issue Price") paid by the Series A Financing investors. Convertible notes issued in 2017 converted into 881,286 shares of Series A Preferred Stock at the Series A Original Issue Price. All outstanding shares of Series A Preferred Stock were converted into shares of Private Aadi common stock and concurrently exchanged for the Company's common stock based on the Exchange Ratio in connection with the closing of the Merger. Upon the closing of the Merger, Private Aadi's board of directors declared a 4% cumulative dividend on its preferred stock of \$4.4 million which was paid at the Effective Time.

Common Stock

As of December 31, 2021 and 2020, the Company had 300,000,000 and 20,000,000 shares of authorized common stock with par value of \$0.0001 per share, respectively, under the Company's certificate of incorporation, as amended and restated. As of December 31, 2021 and 2020, the shares of common stock outstanding were 20,894,695 and 2,542,358, respectively.

In conjunction with the closing of the Merger, the Company issued an aggregate of 2,558,218 shares of common stock to holders of Private Aadi common stock in exchange for all of the Private Aadi capital stock outstanding immediately prior to the closing of the Merger. Concurrently with the closing of the Merger, the PIPE Investors purchased an aggregate of 11,852,862 shares of the Company's common stock for an aggregate purchase price of \$155.0 million pursuant to the Subscription Agreement entered into with the Company on May 16, 2021. The aggregate net proceeds, after deducting certain expenses incurred that were direct and incremental to the issuance of the PIPE shares, was \$145.4 million.

Dividends

The holders of common stock are entitled to receive dividends, if and when declared by the board of directors of the Company (the “board of directors”). Since the Company’s inception, no dividends have been declared or paid to the holders of common stock.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution, or winding-up of the Company, the holders of common stock are entitled to share ratably in the Company’s assets.

Voting

The holders of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings.

12. Stock-Based Compensation

Stock Option Plan – 2014 Plan (“Private Aadi Plan”)

In connection with the Merger, the Company assumed Private Aadi Plan, which was amended and restated in February 2017, and the issued and outstanding stock options under the Private Aadi Plan (the Private Aadi common stock underlying the awards was adjusted for shares of the Company’s common stock pursuant to the Merger Agreement). The Private Aadi Plan allowed for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock unit awards and other stock awards. In connection with the closing of the Merger and the adoption of the 2021 Plan (as defined below), no further awards will be issued under the Private Aadi Plan.

The options that are granted from the Private Aadi Plan are exercisable at various dates as determined upon grant and will expire no more than ten years from their date of grant. The Private Aadi Plan stock options generally vest over a four-year term.

Stock Option Plan – 2011 Plan and 2017 Plan

In connection with the closing of the Merger, the Company assumed the Aerpio 2011 Equity Incentive Plan (the “2011 Plan”) and the Aerpio 2017 Stock Option and Incentive Plan (the “2017 Plan,” and collectively with the 2011 Plan, the “Prior Plans”). No new awards will be granted under the Prior Plans effective upon the closing of the Merger and adoption of the 2021 Plan (as defined below).

Stock Option Plan – 2021 Plan

At the closing of the Merger, the Company adopted the Aadi Bioscience, Inc. 2021 Equity Incentive Plan (the “2021 Plan”), which also permits stock options and restricted stock unit grants to employees, members of the board of directors, and outside consultants.

Subject to the adjustment provisions contained in the 2021 Plan and the evergreen provision described below, a total of 2,070,784 shares of common stock were initially reserved for issuance pursuant to the 2021 Plan. In addition, the shares reserved for issuance under the 2021 Plan include any shares of common stock (i) subject to awards of stock options or other awards granted under the Prior Plans that expire or otherwise terminate without having been exercised in full and shares of common stock granted under the Prior Plans that are forfeited or repurchased by the Company, and (ii) any shares of common stock subject to stock options or similar awards granted under the Private Aadi Plan that were assumed in the Merger (provided that the maximum number of shares that may be added to the 2021 Plan pursuant to this sentence is 764,154 shares).

The number of shares available for issuance under the 2021 Plan also will include an annual increase, or the evergreen feature, on the first day of each of the Company’s fiscal years, beginning with the Company’s fiscal year 2022, equal to the least of:

- 2,070,784 shares of common stock;
- a number of shares equal to 4% of the outstanding shares of common stock on the last day of the immediately preceding fiscal year; or
- such number of shares as the Board or its designated committee may determine.

As a result of the evergreen increase, a total of 835,787 shares were added to the 2021 Plan on January 1, 2022.

Shares issuable under the 2021 Plan are authorized, but unissued, or reacquired shares of common stock. If an award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an exchange program, or, with respect to restricted stock, restricted stock units, performance units or performance shares, is forfeited to or repurchased by the combined company due to failure to vest, the unpurchased shares (or for awards other than stock options or stock appreciation rights, the forfeited or repurchased shares) will become available for future grant or sale under the 2021 Plan (unless the 2021 Plan has terminated).

As of December 31, 2021, zero, 432,978, 126,267 and 1,190,631 shares were subject to awards outstanding under the 2011 Plan, Private Aadi Plan, 2017 Plan and 2021 Plan, respectively.

The following table summarizes the stock option activity during the twelve months ended December 31, 2021 and December 31, 2020:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value (in thousands)
Outstanding, January 1, 2021	390,949	\$ 2.11	7.26	\$ 505
Granted	1,248,520	26.05		
Assumed through Merger	248,258	29.20		
Exercised	(72,316)	11.52		
Expired/cancelled	(65,535)	53.99		
Outstanding as of December 31, 2021	<u>1,749,876</u>	<u>\$ 20.71</u>	<u>8.48</u>	<u>\$ 10,007</u>
Vested and exercisable as of December 31, 2021	444,700	\$ 8.63	\$ 5.05	\$ 7,585
Vested and expected to vest as of December 31, 2021	1,749,876	\$ 20.71	8.48	\$ 10,007

As of December 31, 2021, the aggregate intrinsic value of options outstanding was \$10.0 million. The intrinsic value for stock options is calculated based on the difference between the exercise prices of the underlying awards and the quoted stock price of the Company's common stock as of the reporting date.

As of December 31, 2021, there was \$22.1 million of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted average period of 2.9 years.

As of December 31, 2021, zero and 1,390,606 shares were reserved for issuance under the Private Aadi Plan and 2021 Plan, respectively.

Compensation Expense Summary

The Company recognized the following compensation cost related to employee and non-employee stock-based compensation activity for the periods presented (amounts in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	\$ 657	\$ 94
General and administrative	1,449	45
Total	<u>\$ 2,106</u>	<u>\$ 139</u>

Included in the twelve months ended December 31, 2021 is \$0.3 million of expense related to the acceleration of vesting associated with individual awards assumed in the Merger.

The Company uses the Black-Scholes option pricing model to determine the estimated fair value for stock-based awards. Option pricing models require the input of various assumptions, including the option's expected life, expected dividend yield, price volatility and risk-free interest rate of the underlying stock. Accordingly, the weighted-average fair value of the options granted during the twelve months ended December 31, 2021 and 2020 was \$18.88 and \$2.56 per share, respectively.

The calculation was based on the following assumptions:

	Year Ended December 31,	
	2021	2020
Weighted average grant date fair value (per share)	\$ 18.88	\$ 2.56
Risk-free interest rate	0.84% - 1.38%	0.34% - 0.80%
Expected volatility	85.21% - 87.88%	89.57% - 92.52%
Expected term (in years)	5.1 - 6.3	5.3 - 6.3
Expected dividend yield	—	—

The Company determines the assumptions used in the option pricing model in the following manner:

Risk-Free Interest Rate – For the determination of the risk-free interest rates, the Company utilizes the U.S. Treasury yield curve for instruments in effect at the time of measurement with a term commensurate with the expected term assumption.

Expected Volatility – Due to the Company's limited historical stock price volatility data, the Company based its estimate of expected volatility on the estimated and expected volatilities of a guideline group of publicly traded companies. For these analyses, the Company selected companies with comparable characteristics including enterprise value, risk profiles, and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company computes the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of its stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Expected Dividend – The expected dividend yield is assumed to be zero since the Company has never paid dividends and does not have current plans to pay any dividends on its common stock.

Expected Term – The Company estimates the expected term of its stock options granted to employees and non-employee directors using the simplified method, whereby, the expected term equals the average of the vesting term and the original contractual term of the option. The Company utilizes this method since it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term.

Prior to the Company's Merger, given the absence of a public trading market for the Company's common stock, its board of directors exercised their judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of the Company's common stock underlying the stock options, such as: contemporaneous valuations performed by independent third-party specialists, its stage of development, including the status of its research and development efforts of its therapeutic candidates and the material risks related to its business and industry, its results of operations and financial condition, including its levels of capital resources, the prices at which its sold shares of its convertible preferred stock, the rights, preferences and privileges of its convertible preferred stock relative to those of its common stock, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable life sciences public companies, as well as recently completed mergers and acquisitions of peer companies, the likelihood of achieving a liquidity event for the holders of its common stock or convertible preferred stock, such as an IPO or a sale of the Company given prevailing market conditions, trends and developments in its industry, external market conditions affecting the life sciences and biotechnology sectors, and the lack of liquidity of its common stock, among other factors.

Subsequent to the Company's Merger, the fair value of the Company's common stock is determined based on its closing market price on the date of the grant. The Company's board of directors intended all options granted to be exercisable at a price per share not less than the per share fair value of its common stock underlying those options on the grant date.

Warrants to Purchase Common Stock

The Company had warrants outstanding for the purchase of 36,666 shares of the Company's common stock at December 31, 2021. There were no warrants outstanding as of December 31, 2020. These warrants were assumed in the Merger and were issued by Aerpio in October 2019, for the purchase of 40,000 shares (after taking into account the Reverse Stock Split) of the Company's common stock at an exercise price of \$7.29 per share (after taking into account the Reverse Stock Split). These warrants were fully vested as of the date of the Merger and expire on October 24, 2024.

The number of shares and the exercise price shall be adjusted for standard anti-dilution events such as stock splits, combinations, reorganizations, or issue shares as part of a stock dividend. The warrants meet the criteria to be classified within stockholders' equity (deficit).

13. Employee Stock Purchase Plan

On August 17, 2021, a special meeting of the Company's stockholders was held to approve the Merger and related matters which included, among others, an employee stock purchase plan ("Special Meeting"). At the Special Meeting, the Company's stockholders considered and approved the Company's 2021 Employee Stock Purchase Plan (the "2021 ESPP"). Upon approval of the 2021 ESPP by the stockholders, Aerpio's Amended and Restated 2017 Employee Stock Purchase Plan terminated. An aggregate of 310,617 shares of common stock have been reserved and are available for issuance under the 2021 ESPP. The number of shares of common stock available for issuance under the 2021 ESPP will be increased on the first day of each fiscal year beginning with the 2022 fiscal year in an amount equal to the least of (i) 310,617 shares of common stock, (ii) one percent (1%) of the outstanding shares of all classes of common stock on the last day of the immediately preceding fiscal year, or (iii) an amount to be determined by the Board or its designated committee no later than the last day of the immediately preceding fiscal year. On January 1, 2022, 208,946 shares of common stock were added to the 2021 ESPP. Shares of common stock issuable under the 2021 ESPP will be authorized, but unissued, or reacquired shares of common stock. If the Company's capital structure changes because of a stock dividend, stock split or similar event, the number of shares that can be issued under the 2021 ESPP will be appropriately adjusted. No shares were issued under the 2021 ESPP as of December 31, 2021.

14. Income Taxes

The Company did not record a current or deferred income tax expense or benefit for the years ended December 31, 2021 and 2020, due to the Company's net and comprehensive losses and increases in its deferred tax asset valuation allowance. A reconciliation of the statutory federal income tax with the provision for income taxes are as follows:

	Year Ended December 31,			
	2021	%	2020	%
Federal tax at statutory rate	21.0		21.0	
State income tax, net of federal benefit	0.5		2.5	
Nondeductible interest	(0.1)		(4.9)	
Other permanent items	0.4		(1.6)	
Nondeductible impairment	(13.8)		—	
Research credit	0.9		28.8	
Change in valuation allowance	(8.9)		(45.7)	
Effective tax rate	\$ —	%	0.1	%

Significant components of the Company's deferred tax assets and liabilities are as follows (amounts in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	\$ 34,228	\$ 7,265
Research and development tax credits	3,732	2,782
Other	1,214	227
Total deferred tax assets	39,174	10,274
Valuation allowance	(38,410)	(10,255)
Total gross deferred tax assets, net of valuation allowance	764	19
Deferred tax liabilities:		
Other	(764)	(19)
Total gross deferred tax liabilities	(764)	(19)
Net deferred tax assets / (liabilities)	\$ —	\$ —

Deferred income tax assets and liabilities are recorded for differences between the financial statement and tax basis of the assets and liabilities that will result in taxable or deductible amounts in the future based on enacted laws and rates applicable to the periods in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized in future periods.

The Company has evaluated the available evidence supporting the realization of its gross deferred tax assets, including the amount and timing of future taxable income and has determined it is more likely than not that the assets will not be realized. As a result, the Company has concluded that a full valuation allowance against its deferred tax asset is necessary at this time.

As of December 31, 2021, the Company has federal and state net operating loss (“NOL”) carryforwards of \$150.9 million and \$55.8 million, respectively. Of the amount of federal NOL carryforwards, \$106.6 million can be carried forward indefinitely. The remaining federal and state NOL carryforwards begin to expire in 2030, unless previously utilized. The Company also has federal and state research credit carryforwards of approximately \$3.1 million and \$1.7 million, respectively, unless previously utilized. The federal and New Jersey research credit carryforwards will begin to expire in 2037 and 2027, respectively, unless previously utilized. The California research and development (“R&D”) credit will carry forward indefinitely. The increase in the valuation allowance is \$28.2 million and \$1.6 million for the years ended December 31, 2021 and 2020, respectively.

Pursuant to Section 382 and 383 of the Internal Revenue Code (“IRC”), utilization of the Company’s NOL carryforwards and R&D credits may be subject to annual limitations in the event of any significant future changes in its ownership structure. These annual limitations may result in the expiration of NOL carryforwards and R&D credits prior to utilization. As of December 31, 2021, the Company has completed an IRC Section 382 analysis through the date of the Merger. Ownership changes were identified that will result in annual limitations on future utilization of NOL and R&D credit carryforwards. To the extent such limitations will cause NOL and R&D credit carryforwards to expire unused, these tax attributes have been removed from deferred tax asset table above.

Uncertain tax positions are evaluated based upon the facts and circumstances that exist at each reporting period. Subsequent changes in judgement based upon new information may lead to changes in recognition, derecognition, and measurement. Adjustment may result, for example, upon resolution of an issue with the taxing authorities or expiration of a statute of limitations barring an assessment for an issue.

The Company recognizes a tax benefit from an uncertain tax position when it is more likely than not that the position will be sustained upon examination by tax authorities.

The following table summarizes the changes to the Company’s gross unrecognized tax benefits for the years ended December 31, 2021 and 2020 (amounts in thousands):

	December 31,	
	2021	2020
Balance at the beginning of the year	\$ 2,404	\$ 2,210
Decrease related to prior year positions	(24)	—
Increase related to current year positions	294	194
Balance at the end of the year	<u>\$ 2,674</u>	<u>\$ 2,404</u>

Due to the existence of the valuation allowance, future recognition of previously unrecognized tax benefits will not impact the Company’s effective tax rate. The Company’s practice is to recognize interest and penalties related to income tax matters in income tax expense. The Company is subject to taxation in the United States federal and certain state jurisdictions. The Company’s tax years from inception are subject to examination by the United States federal and state authorities due to the carryforward of unutilized NOLs and R&D credits.

The Company had no accrued interest and no penalties related to income tax matters in the Company’s balance sheet as of December 31, 2021 and has not recognized interest or penalties in the Company’s statement of operations and loss for the year ended December 31, 2021. Further, the Company is not currently under examination by any federal, state or local tax authority.

The CARES Act provides sweeping tax changes in response to the COVID-19 pandemic. Some of the more significant provisions are removal of certain limitations on utilization of NOL’s, increasing the loss carryback period

for certain losses to five years, and increasing the ability to deduct interest expense, as well as amending certain provisions of the previously enacted Tax Cuts and Jobs Act. As of December 31, 2021, the Company has not recorded any material adjustments to its income tax provision related to the provisions with the CARES Act. The Company will continue to analyze the impact that the CARES Act will have, if any, on its financial positions, results of operations or cash flows.

15. Commitments and Contingencies

Litigation

The Company is not party to any material legal proceedings. From time to time, it may be involved in legal proceedings or subject to claims incident to the ordinary course of business. Regardless of the outcome, such proceedings or claims can have an adverse impact on the Company because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Purchase Commitments

The Company has ongoing contracts with vendors for clinical trials and contract manufacturing. These contracts are generally cancellable, with notice, at the Company's option. The Company recorded accrued expenses of \$4.8 million and \$3.3 million in its consolidated balance sheet for expenditures incurred by clinical and contract manufacturing vendors as of December 31, 2021 and 2020, respectively.

At December 31, 2021 the Company does not have any significant contracts that contain specific activities such as non-cancellable commitments, minimum purchase commitments, or binding annual forecasts.

16. Employee Retirement Plan

The Company maintains a 401(k) plan (the "401k Plan") created in 2015 for the benefit of its employees. All employees who have attained the age of 21 are eligible to participate in the 401k Plan as of the first Entry Date, as defined by the 401k Plan document, following the employment date. Each employee can contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary. No contributions were made during 2021 or 2020.

17. Subsequent Events

On January 13, 2022, the Company entered into a Negotiated Purchase Order Terms and Conditions for Clinical and Commercial Product (the “Fresenius Agreement”) with Fresenius Kabi, LLC (“Fresenius Kabi”) pursuant to which Fresenius Kabi will manufacture FYARRO for the Company, and the Company will purchase FYARRO as a finished drug product from Fresenius Kabi, on a purchase-order basis. Under the Agreement, which shall be effective through December 22, 2022 (or such later date as may be agreed between the parties in writing and currently being discussed), the Company may purchase FYARRO for either clinical or commercial purposes for use in the United States and Canada. In addition to manufacturing, Fresenius Kabi will perform specified labeling, packaging and serialization activities in respect of FYARRO for the Company’s benefit. The price of FYARRO will be fixed, subject to the ability of Fresenius Kabi to increase pricing under specified circumstances. The Company has an obligation to purchase certain minimum quantities of FYARRO. Failure to purchase those minimum quantities will result in an additional payment from the Company to Fresenius Kabi.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.***Evaluation of Disclosure Controls and Procedures.***

We maintain disclosure controls and procedures that are designed to provide reasonable assurance that information required to be disclosed in our Company's reports under the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. Management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

In connection with the preparation of this Annual Report for the year ended December 31, 2021, an evaluation was performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of December 31, 2021. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded based upon the evaluation described above that, as of December 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting for us. Internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) is a process to provide reasonable assurance regarding the reliability of our financial reporting for external purposes in accordance with U.S. generally accepted accounting principles. Internal control over financial reporting includes maintaining records that in reasonable detail accurately and fairly reflect our transactions; providing reasonable assurance that transactions are recorded as necessary for preparation of our consolidated financial statements; providing reasonable assurance that receipts and expenditures of company assets are made in accordance with management authorization; and providing reasonable assurance that unauthorized acquisition, use or disposition of company assets that could have a material effect on our consolidated financial statements would be prevented or detected on a timely basis. Because of its inherent limitations, internal control over financial reporting is not intended to provide absolute assurance that a misstatement of our consolidated financial statements would be prevented or detected.

Management conducted an evaluation of the effectiveness, as of December 31, 2021, of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013. Based on this evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2021.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act during the fourth quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

Part III

Item 10. Directors, Executive Officers and Corporate Governance

The other information required by this item is omitted from this Annual Report on Form 10-K and is incorporated herein by reference from our definitive proxy statement relating to our 2022 Annual Meeting of Stockholders (the “Definitive Proxy Statement”).

Code of Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Our code of business conduct and ethics is available on our website, which is located at www.aadibio.com. We intend to disclose any amendments to the code, or any waivers of its requirements, on our website, or in a current report on Form 8-K as may be required by law.

Item 11. Executive Compensation

The information required by this Item 11 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this Item 14 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statements.

(a)(1) Financial Statements.

The consolidated financial statements required by this item are submitted in a separate section beginning on page 122 of this Annual Report.

(a)(2) Exhibits.

The exhibits filed as part of this Annual Report are set forth on the Exhibit Index immediately preceding the signature page of this Annual Report. The Exhibit Index is incorporated herein by reference.

Exhibit Index

Exhibit Number	Description
2.1	<u>Agreement and Plan of Merger, dated May 16, 2021, by and among the registrant, Aadi Bioscience, Inc. and Aspen Merger Subsidiary, Inc. (incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on May 17, 2021).</u>
3.1	<u>Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
3.2	<u>Amended and Restated Bylaws of the Company (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
4.1*	<u>Description of common stock</u>
10.1	<u>Contingent Value Rights Agreement dated August 26, 2021, by and between Aerpio Pharmaceuticals, Inc., Cheryl Cohen, as Holder Representative, and American Stock Transfer & Trust Company, LLC, as Rights Agent (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.2	<u>Subscription Agreement, dated May 16, 2021, by and among Aerpio Pharmaceuticals, Inc. and each purchaser identified on Exhibit A thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on May 17, 2021.</u>
10.3	<u>Registration Rights Agreement dated August 26, 2021, by and between Aadi Bioscience, Inc. (formerly known as Aerpio Pharmaceuticals, Inc.) and certain purchasers listed therein (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.4#	<u>Amended and Restated Employment Agreement, dated August 26, 2021, by and between Aadi Bioscience, Inc. and Neil Desai, Ph.D. (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.5*#	<u>Executive Employment Agreement, dated October 28, 2021, by and between Aadi Bioscience, Inc. and Scott Giacobello.</u>
10.6#	<u>Aadi Bioscience, Inc. 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.7#	<u>Form of Stock Option Agreement under the Aadi Bioscience, Inc. 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.8#	<u>2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.9#	<u>Aadi Bioscience, Inc. Amended and Restated 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.10#	<u>Form of Stock Option Agreement under the Aadi Bioscience, Inc. Amended and Restated 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.10 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>
10.11#	<u>Form of Indemnification Agreement between Aadi Bioscience, Inc. and each of its directors and executive officers (incorporated by reference to Exhibit 10.11 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 27, 2021).</u>

10.12+	<u>Asset Purchase Agreement dated August 17, 2021, by and between Aerpio Pharmaceuticals, Inc. and EyePoint Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on August 23, 2021).</u>
10.13+	<u>Amended and Restated License Agreement by and between Abraxis BioScience, LLC and Aadi Bioscience, Inc. dated November 15, 2019 (incorporated by reference to Exhibit 10.13 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38560) filed with the SEC on November 10, 2021).</u>
10.14+	<u>Amendment No. 1 to the Amended and Restated License Agreement between Abraxis BioScience, LLC and Aadi Bioscience, Inc. Amended and Restated License Agreement by and between Abraxis BioScience LLC and Aadi Bioscience, Inc. dated November 15, 2019 (incorporated by reference to Exhibit 10.14 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38560) filed with the SEC on November 10, 2021).</u>
10.15	<u>First Amendment to Office Lease dated August 30, 2021 by and between BRE Sunset Coast, LLC and Aadi Bioscience, Inc. (incorporated by reference to Exhibit 10.15 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38560) filed with the SEC on November 10, 2021).</u>
10.16#	<u>Employment Agreement dated September 14, 2021, by and between Brendan Delaney and Aadi Bioscience, Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-38560) filed with the SEC on September 20, 2021).</u>
10.17#	<u>Employment Agreement dated October 19, 2021, by and between Loretta Itri and Aadi Bioscience, Inc. (incorporated by reference to Exhibit 10.17 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38560) filed with the SEC on November 10, 2021).</u>
10.18+	<u>License Agreement by and between Aadi Bioscience, Inc. and EOC Pharma (Hong Kong) Limited dated December 8, 2020. (incorporated by reference to Exhibit 10.18 to the Registrant's Quarterly Report on form 10-Q (File No. 001-38560) filed with the SEC on November 10, 2021).</u>
10.19#	<u>Senior Cash Incentive Bonus Plan. (incorporated by reference to Exhibit 10.15 in the Registrant's Annual Report on Form 10-K (File No. 000-53057) filed with the SEC on March 15, 2017).</u>
23.1*	<u>Consent of BDO USA LLP</u>
31.1*	<u>Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
31.2*	<u>Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.</u>
32.1**	<u>Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
32.2**	<u>Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>
101.INS	IXBRL Inline Instance Document
101.SCH	IXBRL Inline Taxonomy Extension Schema Document
101.CAL	IXBRL Inline Taxonomy Extension Calculation Linkbase Document
101.DEF	IXBRL Inline Taxonomy Extension Definition Linkbase Document
101.LAB	IXBRL Inline Taxonomy Extension Label Linkbase Document
101.PRE	IXBRL Inline Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)

* Filed herewith.

- ** Indicates the exhibit is being furnished, not filed, with this report
- # Indicates a management contract or any compensatory plan, contract or arrangement.
- + Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

Item 16. Form of 10-K Summary

We may voluntarily include a summary of information required by Form 10-K under this Item 16. We have elected not to include such summary information.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

AADI BIOSCIENCE, INC.

Date: March 17, 2022

By: /s/ Neil Desai, Ph.D.

Neil Desai, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
<u>/s/ Neil Desai, Ph.D.</u> Neil Desai, Ph.D.	Chief Executive Officer and Director Principal Executive Officer	March 17, 2022
<u>/s/ Scott Giacobello</u> Scott Giacobello	Chief Financial Officer and Principal Financial and Accounting Officer	March 17, 2022
<u>/s/ Caley Castelein, M.D.</u> Caley Castelein	Chairman	March 17, 2022
<u>/s/ Emma Reeve</u> Emma Reeve	Director	March 17, 2022
<u>/s/ Behzad Aghazadeh, Ph.D.</u> Behzad Aghazadeh	Director	March 17, 2022
<u>/s/ Anupam Dalal, M.D.</u> Anupam Dalal	Director	March 17, 2022
<u>/s/ Karin Hehenberger, M.D., Ph.D.</u> Karin Hehenberger	Director	March 17, 2022
<u>/s/ Richard Maroun, J.D.</u> Richard Maroun	Director	March 17, 2022