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**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: 001-40551

**Acumen Pharmaceuticals, Inc.**

(Exact name of registrant as specified in its charter)

Delaware  
State or other jurisdiction of  
incorporation or organization

36-4108129  
(I.R.S. Employer  
Identification No.)

427 Park St.  
Charlottesville, VA  
(Address of principal executive offices)

22902  
(Zip Code)

Registrant's telephone number, including area code (434) 297-1000

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, par value \$0.0001 per share	ABOS	The Nasdaq Global Select Market

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 Section 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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 Act).  Yes  No

The registrant was not a public company as of the last business day of its most recently completed second fiscal quarter and therefore cannot calculate the aggregate market value of its voting and non-voting common equity held by non-affiliates as of such date. The registrant's common stock began trading on the Nasdaq Global Select Market on July 1, 2021.

The number of the registrant's shares of common stock outstanding as of March 25, 2022 was 40,473,270.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive proxy statement relating to its 2022 annual meeting of the shareholders (the "2022 Proxy Statement") are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The 2022 Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

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**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This Annual Report on Form 10-K contains forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will" or "would" or the negative of these words or other similar terms or expressions. These forward-looking statements include, but are not limited to, statements concerning the following:

- the sufficiency of our existing cash and cash equivalents and marketable securities to fund our future operating expenses and capital expenditure requirements;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize ACU193, subject to necessary regulatory approvals;
- the ability of our clinical trials to demonstrate the safety and efficacy of ACU193, and other positive results;
- the therapeutic potential of ACU193, including its potential for improved safety and efficacy, as compared to other monoclonal antibodies approved and or in development, as well as the expectations concerning the INTERCEPT-AD trial;
- the success, cost and timing of our development activities, nonclinical studies and clinical trials;
- the timing and focus of our future clinical trials, and the reporting of data from those trials;
- our plans relating to commercializing ACU193, subject to obtaining necessary regulatory approvals;
- our ability to attract and retain key scientific and clinical personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our reliance on third parties to conduct clinical trials of ACU193, and for the manufacture of ACU193 for nonclinical studies and clinical trials;
- the success of competing therapies that are or may become available;
- our plans and ability to obtain or protect our intellectual property rights, including extensions of existing patent terms where available or the use of data market exclusivity to provide protection from generic or biosimilar versions of our product;
- the scope of protection we are able to establish and maintain for intellectual property rights covering ACU193 and technology;
- potential claims relating to our intellectual property;
- existing regulations and regulatory developments in the United States and other jurisdictions;
- our ability to obtain and maintain regulatory approval of ACU193, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- our plans relating to the further development and manufacturing of ACU193, including additional therapeutic indications which we may pursue;
- our ability to develop and maintain our corporate infrastructure, including our ability to design and maintain an effective system of internal controls;

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- our financial performance;
- the effects of the ongoing COVID-19 pandemic, geopolitical events such as the pending conflict with Russia and Ukraine; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

You should not rely on forward-looking statements as predictions of future events. The outcome of the events described in these forward-looking statements is subject to risks, uncertainties and other factors described under the header “Risk Factors” and elsewhere in this Annual Report on Form 10-K. Moreover, we operate in a very competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained herein. The results, events and circumstances reflected in the forward-looking statements may not be achieved or occur, and actual results, events or circumstances could differ materially from those described in the forward-looking statements.

The forward-looking statements made in this Annual Report on Form 10-K relate only to events as of the date on which the statements are made, and we undertake no obligation to update them to reflect events or circumstances after the date of this Annual Report on Form 10-K or to reflect new information or the occurrence of unanticipated events, except as required by law.

Unless the context otherwise indicates, references in this report to the terms “Acumen,” “the Company,” “we,” “our” and “us” refer to Acumen Pharmaceuticals, Inc.

We may announce material business and financial information to our investors using our investor relations website ([www.investors.acumenpharm.com](http://www.investors.acumenpharm.com)). We therefore encourage investors and others interested in Acumen to review the information that we make available on our website, in addition to following our filings with the Securities and Exchange Commission, or SEC, webcasts, press releases and conference calls. Our website and information included in or linked to our website are not part of this Annual Report on Form 10-K.

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### **RISK FACTORS SUMMARY**

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are more fully described in “Part I, Item 1A. Risk Factors” of this Annual Report on Form 10-K, including the following:

- We are a clinical-stage biopharmaceutical company with a limited operating history.
- We have no product candidates approved for commercial sale, we have never generated any revenue from product sales and we may never be profitable.
- We will require substantial additional funding to finance our operations, complete the development and commercialization of ACU193 for Alzheimer’s disease, or AD, and evaluate future product candidates. If we are unable to raise this funding when needed, we may be forced to delay, reduce or eliminate our drug development programs or other operations.
- We are substantially dependent on the success of ACU193, our sole product candidate, which will require significant clinical testing before we can seek regulatory approval and potentially launch commercial sales, and which may not be successful in clinical trials, receive regulatory approval or be successfully commercialized, even if approved.
- We have concentrated our research and development efforts on the treatment of AD, a field that has to date seen very limited success in drug development.
- Our approach to the potential treatment of AD is based on a novel therapeutic approach, which exposes us to unforeseen risks.
- Nonclinical and clinical drug development involves a lengthy, expensive and uncertain process. The results of nonclinical studies and early clinical trials are not always predictive of future results. ACU193 or any other product candidate that we advance into clinical trials may not achieve favorable results in later clinical trials, if any, or receive marketing approval.
- Clinical failure can occur at any stage of clinical development and we have never completed a clinical trial or submitted a biologics license application, or BLA, or marketing authorization application, or MAA.
- We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- We currently rely on contract manufacturing organizations, or CMOs, to manufacture and formulate ACU193. The loss of any of these CMOs or the failure of any of them to meet their obligations to us could affect our ability to develop ACU193 in a timely manner.
- We intend to rely on contract research organizations, or CROs, and other third parties to conduct, supervise and monitor a significant portion of our research and nonclinical testing and clinical trials for our product candidates, and if those third parties do not successfully carry out their contractual duties, comply with regulatory requirements or otherwise perform satisfactorily, we may not be able to obtain regulatory approval or commercialize product candidates, or such approval or commercialization may be delayed, and our business may be substantially harmed.
- We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more effective than ours.
- If we are unable to enter into a commercial collaboration or, alternatively, establish internal sales, marketing and distribution capabilities, for ACU193 or any other product candidate that may receive regulatory approval, we may not be successful in commercializing those product candidates if and when they are approved.

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- If we are unable to obtain and maintain sufficient intellectual property protection for ACU193 and any future product candidate, and other proprietary technologies we develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidate, and other proprietary technologies if approved, may be adversely affected.

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### PART I

#### **Item 1. Business.**

##### **Overview**

We are a clinical-stage biopharmaceutical company developing a novel disease-modifying approach to target what we believe to be a key underlying cause of Alzheimer's disease, or AD. Alzheimer's disease is a progressive neurodegenerative disease of the brain that leads to loss of memory and cognitive functions and ultimately results in death. Our scientific founders pioneered research on soluble amyloid-beta oligomers, or A $\beta$ Os, which are globular assemblies of the amyloid-beta, or A $\beta$ , peptide that are distinct from A $\beta$  monomers and amyloid plaques. Based on decades of research and supporting evidence, A $\beta$ Os have gained increasing scientific acceptance as a primary toxin involved in the initiation and propagation of AD pathology. We are currently focused on advancing a targeted immunotherapy drug candidate, ACU193, through clinical proof of mechanism trials in early AD patients. ACU193 is a humanized monoclonal antibody, or mAb, that selectively targets A $\beta$ Os, has demonstrated functional and protective effects in in vitro assays, and has demonstrated in vivo safety and pharmacologic activity in multiple animal species, including transgenic models for AD.

ACU193 is the result of over a decade of research and development undertaken by the company, which included a drug discovery partnership with Merck & Co., Inc., or Merck, from 2003 to 2011. ACU193's mechanism of action is intended to slow disease progression and potentially preserve or improve memory function in early AD patients by binding to A $\beta$ Os and neutralizing their toxicity. A $\beta$ Os have been shown to bind to neurons, contributing to synaptic malfunction, memory deficits, cognitive impairment and, ultimately, neurodegeneration and cell death. As such, we believe A $\beta$ Os are the most toxic and pathogenic form of A $\beta$  in the brains of AD patients relative to other forms of amyloid, including A $\beta$  monomers and amyloid plaques. We believe the development and commercialization of a drug that reduces toxicity of A $\beta$ Os is one of the most promising approaches for the potential treatment and prevention of the progression of AD.

In our nonclinical studies, we observed that ACU193 has over 500-fold greater selectivity for targeting A $\beta$ Os over A $\beta$  monomers and has limited or no binding to amyloid plaques. Also, ACU193 potently prevents binding of A $\beta$ Os to hippocampal neurons. Recent laboratory studies conducted by us and others suggest that inhibiting A $\beta$ Os may enable damaged brain circuits to regain some function and prevent further degeneration from occurring. ACU193 has demonstrated in vivo biochemical and behavioral activity in several AD mouse models, including crossing the blood-brain barrier and forming complexes with A $\beta$ Os in a dose-dependent manner. ACU193 has shown consistent pharmacokinetics and brain penetration properties in four animal species. Safety toxicology studies in rats and monkeys provide acceptable margins for dosing in the clinic. Additionally, studies in transgenic mice indicate low potential for microhemorrhage. Based in part on its binding selectivity for A $\beta$ Os rather than amyloid plaques, ACU193 has the potential to have a lower rate of amyloid-related imaging abnormalities, or ARIA, than the plaque-clearing anti-amyloid antibody therapies currently in development. ARIA is a common adverse event for antibodies targeting amyloid plaque and can be a dose-limiting safety liability for those antibodies.

We initiated a Phase 1 clinical trial of ACU193 in the second quarter of 2021, which we named "INTERCEPT-AD." This trial is enrolling patients with mild dementia or mild cognitive impairment, or MCI, due to AD, conditions referred to as "early AD." INTERCEPT-AD is a U.S.-based, multi-center, randomized, double-blind, placebo-controlled clinical trial with overlapping single ascending dose, or SAD, and multiple ascending dose, or MAD, cohorts involving a total of approximately 62 patients with early AD. The overall objective of the trial is to evaluate the safety and tolerability, and establish clinical proof of mechanism of ACU193 administered intravenously. The primary trial endpoints are focused on safety and immunogenicity. An important safety measure will be the use of magnetic resonance imaging, or MRI, to assess the presence or absence of ARIA. Secondary endpoints include pharmacokinetics in plasma and cerebrospinal fluid, or CSF, and target engagement as evidenced by detection of ACU193 bound to A $\beta$ Os in CSF. Clinical scales typically used in AD trials as well as computerized cognitive testing are included as exploratory measures. In October 2021, we announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients.

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Due to delays in clinical trial site activation and patient enrollment that we believe are principally related to effects of the COVID-19 pandemic, we are expanding the anticipated number of trial sites to support our enrollment objectives and anticipated timelines. Clinical trial site activation and patient recruitment and enrollment is ongoing. At present, INTERCEPT-AD is in the SAD portion of the trial. Based on current site activations and enrollment rates, we anticipate reporting our topline data from this trial in the first half of 2023.

Alzheimer's disease currently affects over 6 million people in the United States and approximately 32 million people worldwide and is the sixth-leading cause of death in the United States. However, due to the aging population, patient populations in the United States impacted by AD are expected to triple by 2050 without effective preventative measures or safe and effective disease-modifying treatments. By 2050, healthcare costs for AD in the United States alone are estimated to exceed \$1 trillion.

Until June 2021, the four approved medications for AD provided only modest improvement in AD symptoms. In June 2021, the FDA granted approval for Biogen's Aduhelm (aducanumab) under the FDA's Accelerated Approval Pathway. Aduhelm is the first new AD product approval since 2004 and the first and only approved disease-modifying product. The FDA decision to approve Aduhelm has stirred significant controversy among various stakeholders. In January 2022, the Centers for Medicare and Medicaid Services, or CMS, published a draft guidance opinion for a National Coverage Decision, or NCD, that took the position that Aduhelm should receive reimbursement under a Coverage with Evidence Development, or CED, designation which would limit reimbursement to use of Aduhelm in the context of placebo controlled clinical trials. The need for a medical breakthrough in AD treatment and prevention becomes more urgent with each passing year, and we believe that our novel approach can potentially help address this pressing need.

### **Understanding the Foundation of Our Therapeutic Approach**

While the pathology of AD was first described by Dr. Alois Alzheimer in 1906, the amyloid hypothesis was not developed until the A $\beta$  peptide was first identified as a major constituent of amyloid plaques in the 1980s. Historically, the primary hypothesis of decades of AD research, known as the amyloid hypothesis, held that AD dementia is the clinical consequence of A $\beta$  peptide monomers accumulating into extracellular amyloid plaques, or amyloid plaques, which in turn contribute to the formation of intracellular neurofibrillary tangles composed of the tau protein and cause inflammation, ultimately leading to neuronal cell loss and progressive dementia. The primary constituent of amyloid plaques is the A $\beta$  peptide, although other proteins are present to lesser degrees.

The amyloid hypothesis was more firmly established when a series of genetic mutations causing AD were discovered in the early to mid-1990s. These mutations were found in genes coding for the Amyloid Precursor Protein, or APP, and the genes coding for one of the enzymes which cleaves APP, creating the A $\beta$  peptide. Based on this hypothesis, a number of monoclonal antibodies currently or previously in clinical development for AD have primarily targeted either A $\beta$  monomers or amyloid plaques; for our purposes, this broadly defined class is referred to as anti-A $\beta$ /plaque antibodies. Several of these antibodies are currently in late-stage development, one having recently received regulatory approval, and collectively they have provided a biological foothold for treating AD. However, the clinical data available to date indicate some of the potential limitations of these approaches with respect to clinically meaningful patient benefit and safety.

Though alternative hypotheses to the amyloid hypothesis propose that amyloid accumulation is a consequence of another process such as infection, the field has now developed an understanding that three predominant pools of A $\beta$  species exist in vivo: A $\beta$  monomers (single A $\beta$  peptide), amyloid plaques (insoluble fibrillar A $\beta$ ), and soluble A $\beta$ Os (dimers and up to 200-mers). The more recent appreciation of the crucial role of A $\beta$ Os in the pathologic process is the central tenet of our therapeutic approach.

Our therapeutic approach focuses on targeting A $\beta$ Os, which we believe are the most toxic and pathogenic form of A $\beta$  relative to A $\beta$  monomers and amyloid plaques. Growing evidence, spurred by advances in AD research and analytic techniques, supports our view that A $\beta$ Os are the main instigators of AD neurodegeneration. A $\beta$ Os have been observed to be potent neurotoxins that cause both acute synaptic toxicity and induce

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neurodegeneration. Experimentally in animal models, the accumulation of A $\beta$ Os is associated with core AD neuropathology, including synapse deterioration and loss, tau hyper-phosphorylation, and inflammation. Research has also shown that the accumulation of A $\beta$ Os is associated with AD-related behavioral deficits, such as learning and memory impairment. In light of this evidence, we believe that blocking the toxicity of A $\beta$ Os is the most promising approach for the treatment of AD, which led us to discover and develop ACU193.

### **Our Product Candidate**

Our product candidate, ACU193, is a humanized monoclonal antibody that targets soluble A $\beta$ Os. We are developing ACU193 for intravenous, or IV, administration every four weeks for the treatment of early AD. We believe that ACU193 represents a differentiated approach from current and prior anti-A $\beta$ /plaque immunotherapies because it is highly selective for soluble A $\beta$ Os. ACU193 has a nanomolar affinity for A $\beta$ Os, over 500-fold greater selectivity for A $\beta$ Os over A $\beta$  monomers, and limited or no binding to dense core amyloid plaques. We believe ACU193 is the most advanced immunotherapy candidate in development that selectively targets A $\beta$ Os.

We believe ACU193 has characteristics that make it a promising potential treatment for AD relative to other antibodies that do not selectively target A $\beta$ Os. ACU193 is engineered to reduce immune effector function signaling and to avoid binding to vascular amyloid plaques, which we expect will reduce the incidence of ARIA observed with amyloid plaque-targeting immunotherapies approved and in development for AD. We are currently assessing ACU193 in INTERCEPT-AD, a proof of mechanism Phase 1 clinical trial involving early AD patients, which we expect to follow with an adaptive Phase 2/3 clinical trial as soon as late 2023 if INTERCEPT-AD is successful.

### **Summary of Clinical Development Plan**

We are currently conducting INTERCEPT-AD, a U.S.-based, multi-center, randomized, placebo-controlled, single and multiple ascending dose Phase 1 clinical trial of ACU193 in patients with early AD. The early AD patient group is comprised of individuals who have mild dementia or MCI due to AD, and our trial excludes patients with moderate to severe AD dementia. We plan to enroll a total of 62 early AD patients across seven cohorts, consisting of a single ascending dose in Part A (32 participants) and an overlapping multiple ascending dose in Part B (30 participants). Part A will contain Cohorts 1 through 4; each cohort will receive a single IV dose between 2mg/kg and 60 mg/kg, or placebo. Part B will contain Cohorts 5 through 7; each cohort will receive a total of three doses of ACU193 or placebo as follows: 10 mg/kg every four weeks (Q4W), 60 mg/kg Q4W, or 60 mg/kg every two weeks (Q2W).

The main objective of INTERCEPT-AD is to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and target engagement of single and multiple ascending doses of ACU193 administered by intravenous infusions. Exploratory outcomes will include cognitive scales and computerized cognitive testing. Our goal is to establish clinical proof of mechanism of ACU193 in early AD patients in order to enable rapid progression into an adaptive Phase 2/3 clinical trial. In October 2021, we announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients. Due to delays in clinical trial site activation and patient enrollment that we believe are principally related to effects of the COVID-19 pandemic, we are expanding the anticipated number of trial sites to support our enrollment objectives and anticipated timelines. Clinical trial site activation and patient recruitment and enrollment is ongoing. At present, INTERCEPT-AD is in the SAD portion of the trial. Based on current site activations and enrollment rates, we anticipate reporting our topline data from this trial in the first half of 2023. Following, and subject to the results of, INTERCEPT-AD, we plan to engage with the FDA in an end-of-Phase 2 meeting, which we anticipate will occur in the second half of 2023, to discuss the Phase 2/3 clinical trial design and pathway for potential approval.

### **Summary of Our Nonclinical Data**

In nonclinical studies, ACU193 has demonstrated promising characteristics that indicate its potential to inhibit A $\beta$ Os as a possible therapeutic treatment of AD. ACU193 has high selectivity, with over 500-fold binding

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selectivity for A $\beta$ Os compared to A $\beta$  monomers and has limited or no binding to amyloid plaques. ACU193 binds to a broad spectrum of small to large soluble A $\beta$ Os. Additionally, ACU193 has been shown to offer protection from synaptic toxicity by inhibiting binding of A $\beta$ Os to primary hippocampal neurons. ACU193 has also demonstrated suitable in vivo pharmacology, target engagement, blood-brain barrier penetration and reduction of behavioral deficits. Based on nonclinical studies, A $\beta$ O target engagement has the potential to be achieved at doses of ACU193 that will be tested in our Phase 1 clinical trial. Lastly, ACU193 has been shown to have an adequate safety margin in Good Laboratory Practice, or GLP, toxicity studies conducted in two animal species. We believe these data indicate that ACU193 has the potential to offer patients a reduction in cognitive decline.

## **Our Strategy**

Our objective is to transform the treatment of AD, and potentially other diseases, by developing innovative therapeutics that target primary drivers of disease pathology. Our initial therapeutic approach is focused on inhibiting and reducing the toxic activity of A $\beta$ Os, which may allow for synaptic protection and decreased neurodegeneration, leading to more effective treatment for patients with early AD. To achieve this objective, we are pursuing the following strategies:

- **Rapidly advance ACU193 through clinical development in patients with early AD.** Based on the strength of the data we observed in our nonclinical studies, we are currently conducting INTERCEPT-AD, which is designed to evaluate safety and tolerability and establish clinical proof of mechanism of ACU193 in early AD patients, which we expect to follow with an adaptive Phase 2/3 clinical trial.
- **Evaluate combination approaches to complement our core ACU193 monotherapy strategy.** Using ACU193 as the foundation of our AD therapy, we plan to evaluate its potential to be used in combination with drugs currently in development that have complementary mechanisms, which, if successful, could provide additive or even synergistic effects when used with ACU193. These other drugs include various antibodies and small molecules targeting tau, investigational drugs targeting inflammation (TREM2), regenerative drugs (hepatocyte growth factor/MET receptor stimulator) and drugs which putatively improve astrocyte function.
- **Selectively explore potential of ACU193 for other diseases.** Toxic A $\beta$ Os have been implicated in several disease pathologies in nonclinical and epidemiological studies (e.g., dementia associated with Down Syndrome, glaucoma and retinopathies associated with age-related macular degeneration). Where both human observational data and nonclinical experiments support its therapeutic potential, we may conduct clinical trials of ACU193 in other indications.
- **Expand our portfolio by developing additional molecules.** In the long term, a key element of our portfolio strategy is to advance additional molecule development through in-licensing or development of alternative formulations for or derivatives of ACU193. Additional molecules may utilize complementary mechanisms to ACU193, making them candidates for combination therapies or as next-generation products.
- **Optimize value of ACU193 and future drug candidates in major markets.** We have an exclusive license from Merck to patents claiming the composition and method of use of ACU193. We plan to develop and pursue approval of ACU193 and other potential future drug candidates in major markets. We anticipate entering into strategic collaborations and partnerships to maximize the commercial potential of ACU193 and any future programs.

## **Impact of AD**

AD represents a significant unmet medical need. AD is a progressive neurodegenerative disease that destroys memory and other important cognitive functions and ultimately leads to patient death. AD is the sixth-leading cause of death in the United States. The disease afflicts more than six million people in the United States and more than 32 million people worldwide, and the patient population in the United States is expected to grow to approximately 13 million people in the United States by 2050. AD can have a significant burden on family and

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caretakers. In 2020, these caregivers provided an estimated 15.3 billion hours of care valued at nearly \$257 billion. The direct costs of caring for individuals with AD and other dementias in the United States were expected to total \$355 billion in 2021, and are projected to increase to \$1.1 trillion by 2050, according to the Alzheimer's Association.

### **Therapeutic Approaches to AD**

The development of effective therapeutics addressing the underlying cause of AD is one of the greatest medical challenges facing society. Existing treatments for AD consist of drugs that provide modest improvements in symptoms but have no impact on the underlying disease and are unable to halt or slow disease progression. While the pathology of AD was first described by Dr. Alois Alzheimer in 1906, the amyloid hypothesis was not developed until the A $\beta$  peptide was first identified as a major constituent of amyloid plaques in the 1980s. The hypothesis was more firmly established when a series of genetic mutations causing the disease were discovered in the early to mid-1990s. These mutations were found in genes coding for APP or in genes coding for one of the enzymes which cleaves APP, creating the A $\beta$  peptide.

#### *Available Treatments: Symptomatic Treatments*

Currently available symptomatic treatments include memantine, an N-methyl-D-aspartate receptor antagonist, and cholinesterase inhibitors, a class of drugs that block the normal breakdown of acetylcholine. The first approved cholinesterase inhibitor, tacrine, was approved in 1993, but was later withdrawn from the market due to liver toxicity. Three other cholinesterase inhibitors were subsequently approved and continue to be used clinically. Memantine is the most recently approved symptomatic treatment drug for AD in 2003 and is indicated for use in moderate to severe AD patients.

#### *Potential Disease-Modifying Approaches focusing on A $\beta$*

Because of the lack of significant improvement provided by these symptomatic drugs, there remains a significant need for therapies that target underlying disease pathology and potentially slow or halt disease progression. Based on the strong linkage between A $\beta$  and AD pathology established by decades of research, a range of treatment modalities focusing on A $\beta$  have been explored as potential disease-modifying treatments, including g-secretase inhibitors,  $\beta$ -site APP-cleaving enzyme, or BACE, inhibitors and monoclonal antibodies.

Initial attempts at disease modification were made using small molecule g-secretase inhibitors and BACE inhibitors, each of which inhibited a different enzyme necessary to produce the A $\beta$  peptide. The first Phase 3 clinical trial results from a g-secretase inhibitor, semagacestat, were reported in 2010 and unexpectedly showed modest cognitive worsening. Development of the other g-secretase inhibitor, avagacestat, was also stopped due to cognitive worsening observed in the clinic. At least four BACE inhibitors have reached clinical trials; however, during 2018 and 2019, Phase 3 clinical trial results for many BACE inhibitors, including verubecestat and elenbecestat, also unexpectedly showed modest clinical worsening.

A third class of potential disease-modifying agents, monoclonal antibodies, or mAbs, have targeted A $\beta$  monomers or amyloid plaques. Some of these monoclonal antibodies, such as solanezumab (an Eli Lilly product), target A $\beta$  monomers, while others, such as Aduhelm (aducanumab) (a Biogen product), target deposited amyloid plaque, and these monoclonal antibodies have been evaluated in Phase 2 and Phase 3 trials over the period from 2012 to 2021. The most advanced monoclonal antibody for the treatment of AD is Aduhelm (aducanumab), which received Food and Drug Administration, or FDA, approval in June 2021 under the FDA's Accelerated Approval Pathway. As shown in Table 1 below, several of these antibodies have demonstrated some degree of slowing of disease progression in clinical trials, as measured by customary assessments of cognition and function.

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**Table 1: Percent Slowing of Cognitive/Functional Decline\***

Measured Outcome**	solanezumab EXPEDITION 3 (Phase 3)	Aduhelm aducanumab EMERGE (Phase 3)	Aduhelm aducanumab ENGAGE† (Phase 3)	lecanamab BAN2401 (Phase 2)	donanemab (Phase 2)
ADAS-cog	-11%	-27%	-12%	-47%	-39%
ADCS-ADL	-15%	-40%	-18%	N.A.	-23%
CDR-SB	-15%	-23%	2%	-26%	-23%
MMSE	-13%	-15%	3%	N.A.	-21%
iADRS	-11%	N.A.	N.A.	N.A.	-32%

\* Percent Slowing= [1- [(endpoint score-baseline score)active/(endpoint score-baseline score)placebo]]\*100%\*(-1)

\*\* ADAS-cog: Alzheimer's Disease Assessment Scale – Cognitive Subscale

ADCS-ADL: Alzheimer's Disease Cooperative Study – Activities of Daily Living

CDR-SB: Clinical Dementia Rating – Sum of Boxes

MMSE: Mini-Mental State Examination

iADRS: Integrated Alzheimer's Disease Rating Scale

†: ENGAGE Post-Protocol Version 4 – patients who received at least 14 doses of 10 mg/kg, High Dose cohort achieved 27% improvement on CDR-SB compared to placebo.

A potential limitation of the amyloid plaque-targeting antibodies under development is an adverse effect known as ARIA. ARIA has two different forms, ARIA-E, or cerebral edema, formerly called vasogenic edema, and ARIA-H, or cerebral microhemorrhages. While the mechanism of ARIA is not known with certainty, the prevailing theory is that ARIAs are related to the presence of amyloid plaques around blood vessels in the vast majority of people with AD, a condition known as cerebral amyloid angiopathy. It is generally believed that the removal of these amyloid plaques by the antibody can result in small hemorrhages, or ARIA-H. ARIA-H occurs in individuals with untreated AD and its occurrence is increased in individuals treated with antibodies that target amyloid plaques. Increased ARIA-H is correlated with worsening cognition. In contrast to ARIA-H, ARIA-E is hypothesized to result from the leakage of fluid from the blood vessels into the interstitial spaces in the brain, causing edema, or ARIA-E. ARIA-E, in particular, is sometimes associated with symptoms that include worsening of cognition, headache, and gait disturbance, which can be severe enough to lead to hospitalization. ARIA-E usually resolves weeks to months following the cessation of treatment. In clinical trials for anti-A $\beta$ /plaque mAbs, surveillance MRI scans are required to detect asymptomatic ARIA. Table 2 below illustrates the rates of ARIA observed in Phase 2 or 3 studies for the most advanced mAbs. Given observed rates of ARIA, from approximately 10% to over 40%, we believe that MRI scans to assess for ARIA are likely to be required in clinical practice for any amyloid plaque-targeting monoclonal antibody that receives regulatory approval.

**Table 2: Percent of ARIA Events for Anti-A $\beta$ /plaque mAbs\***

	Targeting A $\beta$ Monomers		Targeting Amyloid Plaques								
	solanezumab EXPEDITION 3 (Phase 3)	PC	Aduhelm aducanumab EMERGE (Phase 3)			Aduhelm aducanumab ENGAGE (Phase 3)			Leucanamab BAN2401 (Phase 2)	donanemab (Phase 2)	
			Treated	PC	Low	High	PC	Low	High	PC	High
ARIA-E		0.2%	0.1%	2.2%	26.1%	34.4%	3.0%	25.6%	35.7%	0.8%	9.9%
ApoE e4 carriers				1.9%	29.8%	42.5%	2.4%	28.7%	41.8%	1.2%	14.6%
ApoE e4 non-carriers				2.9%	18.1%	17.9%	4.3%	17.5%	27.7%	0.0%	8.0%
Any ARIA E or H				10.3%	32.8%	41.2%	9.8%	30.7%	40.3%	N.A.	8.0%
											38.9%

PC = Placebo, Low = Low Dose; High = High Dose

\* Shows the absence of ARIA after treatment with antibodies targeting A $\beta$  monomers (solanezumab) in comparison to the increasing presence of ARIA after treatment at increasing dose levels with antibodies targeting amyloid plaques (aducanumab, BAN2401, and donanemab), indicating that ARIA results from the removal of amyloid plaques around blood vessels and likely does not result from treatment with antibodies that target other species of A $\beta$ , i.e. A $\beta$  monomers and A $\beta$ Os.

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**Table 3: AD Product Candidates and Target Selectivity and ARIA Profile**

Product Candidate	Target Selectivity+				ARIA Profile Lack of ARIA
	Amyloid plaque	A $\beta$ fibrils	A $\beta$ monomers	A $\beta$ oligomers	
ACU193	x	untested	x	✓	✓
Aduhelm aducanumab	✓	✓	x	✓	x
lecanemab BAN2401	✓	✓	x	✓	x
gantenerumab	✓	✓	x	✓	x
donanemab	✓	untested	x	x	x
solanezumab*	x	x	✓	x	✓
crenezumab*	✓	✓	✓	✓	✓
bapineuzumab*	✓	✓	✓	✓	x

\* Phase 3 discontinued for primary AD indication

+ There have been no head-to-head clinical trials between any of the product candidates listed above. Study designs and protocols for each product candidate were different, and results may not be comparable between product candidates.

### *Additional Treatment Modalities*

While A $\beta$  and amyloid are generally considered to be the proximal cause of AD pathology, and alternative hypotheses to the amyloid hypothesis propose that amyloid accumulation is a consequence of other processes such as infection and that other pathogens lead to amyloid accumulation, downstream targets such as tau, inflammation-related targets, and growth factors may eventually be useful approaches in the treatment of AD and are being explored. Some of these treatment modalities have made nonclinical and early-stage clinical progress, although these efforts are still significantly less advanced than those approaches targeting A $\beta$  or amyloid plaques.

### *Potential Combination Approaches*

The pathology of AD is complex, and many experts in the field expect that combination therapy using drugs with different mechanisms of action, such as tau-based therapies and immune inflammatory modulation, will ultimately prove most successful, similar to cutting edge approaches used in oncology. We believe that a drug targeting A $\beta$ Os will likely be an important component of a combination treatment. In addition, because symptomatic treatments, such as memantine and cholinesterase inhibitors, affect neurotransmitter systems rather than the underlying AD pathology, we believe that it is likely that they will be used together with disease-modifying treatments.

### **Growing Interest in the Anti-A $\beta$ O Hypothesis and A $\beta$ Os as a Drug Target for AD**

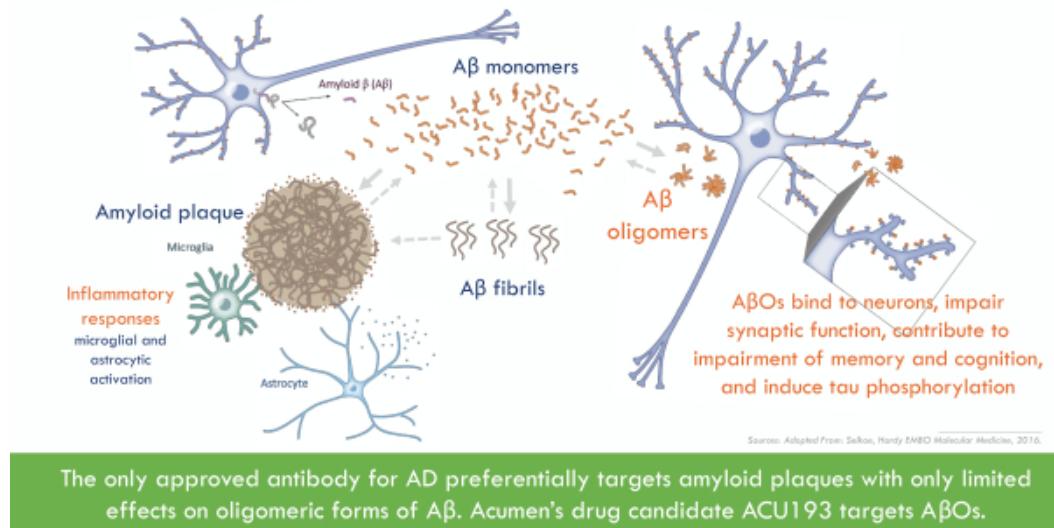
An important refinement of the amyloid hypothesis is the recognition that at least three pools of A $\beta$  species exist in vivo—A $\beta$  monomers, A $\beta$ Os, and amyloid plaques. Because these pools exist in equilibria, manipulation of one pool may have indirect effects on other pools. For example, reduction of A $\beta$  monomers may reduce A $\beta$ Os to some degree. Limited successes in the clinic have been demonstrated with antibodies targeting A $\beta$  monomers, even though A $\beta$  monomers themselves are not widely accepted to have toxic properties. Similarly, limited successes in the clinic have been demonstrated using antibodies that target amyloid plaques, although insoluble fibrillar A $\beta$  and  $\beta$ -amyloid plaques exhibit relatively low in vitro toxicity and may even serve as an in vivo mechanism for removal of the more toxic soluble A $\beta$  species. Both A $\beta$  monomers and amyloid plaques can act as sources of A $\beta$ Os. The positive results of monoclonal antibodies targeting A $\beta$  monomers and amyloid plaques, even in the absence of targeting A $\beta$ Os directly, support the significance of A $\beta$  and amyloid in AD and have led to a growing confidence in the field in the amyloid hypothesis broadly. In contrast to the non-toxic A $\beta$  monomers

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and relatively non-toxic amyloid plaques, A $\beta$ Os are known to bind to neurons, causing synaptic dysfunction and possibly contributing to cognitive impairment, neurodegeneration and cell death. As a result, A $\beta$ Os are now generally believed to be the most toxic form of A $\beta$ . The acute synaptic and chronic neurodegenerative toxicity of A $\beta$ Os, coupled with their very low in vivo levels, suggests that they may be an optimal therapeutic target compared to A $\beta$  monomers and fibrillar A $\beta$  species. Therefore, we believe that drugs that directly target A $\beta$ Os could represent a promising new approach to the potential treatment of AD.

**Figure 1: A $\beta$  related species and pathophysiology of AD**

Growing understanding of disease mechanisms indicate that A $\beta$ O $s$  are the most toxic A $\beta$  species and have the potential to be an ideal target for effective AD therapy



The only approved antibody for AD preferentially targets amyloid plaques with only limited effects on oligomeric forms of A $\beta$ . Acumen's drug candidate ACU193 targets A $\beta$ O $s$ .

The precise mechanism of toxicity of A $\beta$ Os is not fully understood, however numerous studies suggest a mechanism that may include initial reversible memory loss caused by acute A $\beta$ O-induced disruptions of synaptic plasticity, with progressive dementia attributable, at least in part, to neuronal degeneration induced by chronic exposure to A $\beta$ Os. A $\beta$ Os bind to synapses on hippocampal and cortical neurons. In rodent hippocampal slice preparations, A $\beta$ Os cause rapid inhibition of long-term potentiation, or LTP, and direct injection of A $\beta$ O solutions into rodent brains leads to reversible impairment of cognitive function. These findings support the view that A $\beta$ Os may interfere acutely with normal synaptic functions and contribute significantly to the memory loss and cognitive dysfunction characteristic of AD. With regard to neurodegeneration, binding of A $\beta$ Os to neurons also causes damage within neurons, such as calcium influx and the hyperphosphorylation of tau, which leads to neurofibrillary tangles, another downstream hallmark of AD pathology.

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### **Our Differentiated Approach to the Treatment of AD**

We believe that, based on its differentiated mechanism of action, potential for symptomatic improvement and disease modification, and potential for higher dosing, ACU193 has several potential advantages in comparison to other AD drugs that are currently approved or in development:

#### *Differentiated mechanism of action:*

- **Potentially addresses an underlying cause of AD.** A growing body of evidence indicates that A $\beta$ Os, rather than A $\beta$  monomers or amyloid plaques, are the primary toxic species of A $\beta$  that impair neuronal synaptic function and contribute to impairment in memory and cognition and neurodegeneration. We believe that A $\beta$ Os are an optimal therapeutic target relative to other A $\beta$  species and that ACU193 has the potential to be the first anti-A $\beta$ O mAb treatment to prevent or slow the progression of AD.
- **Selectively binds to A $\beta$ O.** ACU193 is the first monoclonal antibody discovered and designed to selectively target A $\beta$ Os. In our nonclinical studies, ACU193 demonstrated a greater than 500-fold affinity to bind to A $\beta$ Os over monomers and did not bind vascular amyloid or dense core amyloid plaques. In comparison, other non-selective anti-A $\beta$ /amyloid antibodies in development bind primarily to A $\beta$  monomers or amyloid plaques.
- **Binds to a broad spectrum of toxic A $\beta$ Os.** A $\beta$ Os are present in the brain in a wide range of sizes. ACU193 has the ability to bind to a broad spectrum of toxic A $\beta$ Os across various molecular weights. Nonclinical data shows that ACU193 binds to low- to mid-sized molecular weight oligomeric species.

#### *Potential for symptomatic improvement and disease modification:*

- **May provide symptomatic improvement in addition to disease modification.** While recent anti-A $\beta$  monoclonal antibody results have established a biological foothold for disease-modifying treatments for AD, they fail to demonstrate clinically meaningful symptomatic improvement as measured by AD clinical assessments. Recent nonclinical studies show that A $\beta$ Os are acutely toxic to neuronal function. By selectively targeting and neutralizing A $\beta$ O toxicity, we believe that ACU193 has the potential to build upon this biological foothold and provide improvements in cognitive function in addition to disease-modifying effects.

#### *Potential for higher dosing:*

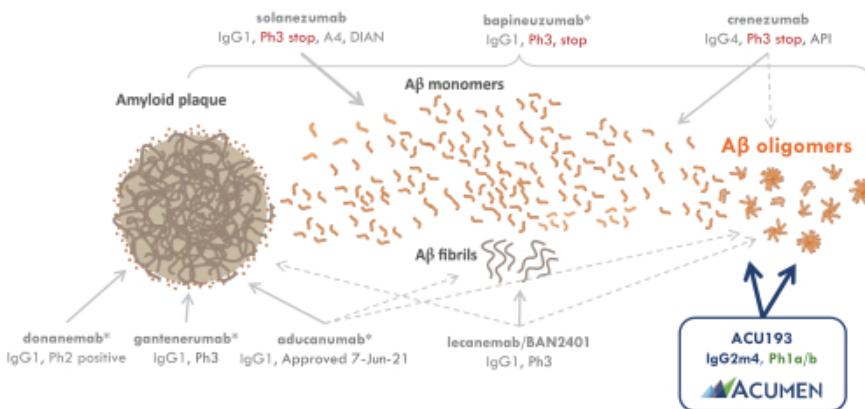
- **Selectivity for A $\beta$ Os is likely to result in greatly reduced rates of ARIA, allowing a broad therapeutic window.** Amyloid plaque binding antibodies have been associated with ARIA, with IgG1 monoclonal antibodies in particular showing elevated rates of ARIA, which presents a safety concern. In contrast, ACU193 was engineered as an IgG2m4 subclass monoclonal antibody, which lacks the inflammatory effector functions of other IgG subclasses. Because ACU193 exhibits limited or no binding to amyloid plaques and lacks inflammatory effector functions, we believe that treatment with ACU193 is likely to result in greatly reduced rates of ARIA adverse events relative to IgG1 monoclonal antibodies that bind to plaque. ACU193 has demonstrated a favorable pharmacokinetic profile in nonclinical studies. Based on the results of GLP safety studies in rats and monkeys, we believe that ACU193 has the potential to be clinically well-tolerated at doses up to 60 mg/kg. While certain anti-A $\beta$ /plaque antibodies have dose limitations due to ARIA, we believe that ACU193 may be well-tolerated at higher doses.

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### **ACU193: First AD Immunotherapy Candidate to Selectively Target A $\beta$ Os**

Our product candidate, ACU193, is a humanized, affinity-matured, immunoglobulin G2m4, or IgG2m4, subclass monoclonal antibody, derived from the murine immunoglobulin G1, or IgG1, parent, ACU3B3. ACU193 lacks the inflammatory effector functions of other IgG subclasses. ACU193 binds with high selectivity to soluble A $\beta$ Os (over 500-fold versus A $\beta$  monomer in a competitive assay), differentiating ACU193 from other therapeutic monoclonal antibodies, which primarily bind A $\beta$  monomers or fibrillar forms of A $\beta$ . Binding of ACU193 to A $\beta$ Os may improve synaptic function and decrease neurodegeneration.

**Figure 2: Summary comparison of ACU193 to anti-A $\beta$ /plaque antibodies in clinical development**



**ACU193's High Selectivity for A $\beta$ Os Combined with an Expected Lack of ARIA-related Safety Concerns Is Anticipated to Provide Superior Cognitive Efficacy Compared to Peers**

\* IgG1 monoclonal antibodies that bind amyloid plaque are associated with high rates of ARIA-E

Despite recognition that A $\beta$ Os are key structures contributing to AD memory dysfunction, cognitive deficits, and neurodegeneration, drug discovery efforts targeting these species have been hampered by technical difficulties of generating physiologically relevant preparations of synthetic A $\beta$ Os, or syn-A $\beta$ Os. Our founders and early-stage researchers were instrumental in the development of well-characterized preparations of syn-A $\beta$ Os, initially termed A $\beta$  Derived Diffusible Ligands, or ADDLs. ADDL preparations were used as the immunogen to generate and discover ACU3B3, the murine IgG1 parent of ACU193.

In December 2003, we entered into an exclusive license and research and development collaboration agreement with Merck for the research, discovery, development, and commercialization of immunotherapies for AD. From 2003 to 2011, Merck carried out extensive research leading to the humanization of ACU3B3 and creation of ACU193. ACU193 emerged as the lead product candidate based on its preferential A $\beta$ O binding, favorable immunogenicity profile, and an absence of off-target binding. In 2011, Merck chose to terminate the program largely based on internal strategic priorities. Consequently, we regained an exclusive, perpetual, irrevocable, royalty-free, worldwide license for the research, development, manufacturing or commercialization of ADDL antibodies, ADDL antigens, or products, including ACU193.

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### **Product Profile**

We are developing ACU193, a humanized monoclonal antibody targeting soluble A $\beta$ Os, as an IV administered treatment for early AD patients. The early AD population is defined as individuals with clinical symptoms consistent with MCI, or consistent with mild dementia who have demonstrated amyloid pathology as assessed with either a positron emission tomography, or PET, or cerebrospinal fluid analysis. A blood test to determine amyloid status may become available in the future. We believe ACU193 has the potential to reduce the rate of cognitive decline by at least 35%, which would be broadly considered as clinically meaningful.

ACU193 is a humanized, affinity-matured, mAb with high selectivity for toxic A $\beta$ Os versus A $\beta$  monomers (greater than 500-fold) and amyloid plaques. With its selective targeting of A $\beta$ Os, we believe that ACU193 could demonstrate a number of potential valuable clinical outcomes, including the slowing of disease progression and downstream changes in tau and neurofibrillary tangles. Additionally, given the acute toxicity of A $\beta$ Os in laboratory studies, we believe that some patients could experience an improvement in cognitive function. ACU193's epitope is composed of a configuration of the N-terminal regions of A $\beta$  monomers within A $\beta$ Os. A $\beta$ Os form when A $\beta$  monomers associate co-linearly along the central alpha helical domains through C-terminal regions via stacking phenylalanine polar bonding associations. This presents an advantage for ACU193 binding because the co-linear association sterically restricts spatial configuration of the N-terminal regions presented by A $\beta$ Os. The N-termini within A $\beta$ Os are anionic and repel one another, resulting in presentation of N-terminal amino acids, which lead to high affinity for ACU193 binding.

In its current formulation, ACU193 deamidates at physiological pH and body temperature. The rate of deamidation is specific to the matrix and temperature, and results in reduced target binding. To prevent deamidation prior to administration of ACU193 in the clinic, the current drug product is stored frozen at -20°C.

ACU193 is an IgG2m4 subclass mAb which lacks the inflammatory effector function signaling stimulated by other IgG subclasses. The product is expected to be given as an IV infusion once every four weeks. Given the indication, ACU193 treatment would be initiated for patients diagnosed with mild dementia or MCI and would likely be continued for several years. Based on the target and lack of inflammatory effector function, we believe the rate of ARIA may be reduced compared to approaches targeting amyloid plaques. Finally, ACU193 could be used in combination with other therapies that might become available for AD, especially those targeting the tau protein or modulating the immune system.

### **Nonclinical Data Package**

#### **Summary of Nonclinical Studies**

In our nonclinical studies, ACU193 has demonstrated: (i) preferential selectivity for binding to A $\beta$ Os versus other forms of A $\beta$  monomers and amyloid plaques in in vitro assays, human AD tissue samples and in vivo transgenic mouse models; (ii) consistent data in support of ACU193 protective effects against A $\beta$ O synaptic toxicity in in vitro and ex vivo assays; (iii) in vivo pharmacology in multiple species confirming blood-brain barrier penetration, target engagement, and behavioral effects; and (iv) safety data in multiple species including GLP toxicology studies in Sprague-Dawley rats and cynomolgus monkeys confirming an adequate safety margin for the first in human clinical trial. Based on the strength of the data we observed in our nonclinical studies, we initiated INTERCEPT-AD, a Phase 1 clinical trial, in the second quarter of 2021.

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### Key Characteristics and Data

Selectivity	<ul style="list-style-type: none"><li>Binding characterization studies of ACU193 and its murine parent ACU3B3 show significant preferential selectivity for A<math>\beta</math>O<sub>s</sub> versus monomeric and amyloid plaques.<ul style="list-style-type: none"><li>Competitive enzyme-linked immunosorbent assay, or ELISA, data show ACU193 binding to A<math>\beta</math>O<sub>s</sub> is 556-fold greater than to A<math>\beta</math> monomer based on monomer equivalent weight. This selectivity value is even higher when adjusted for A<math>\beta</math>O<sub>s</sub>' molecular weight.</li><li>ACU193 binding in brain tissues of transgenic mice following IV dosing shows significant, preferential binding to non-fibrillar, thioflavin-S-negative A<math>\beta</math> structures. The occasional co-localization observed with thioflavin-S-positive fibrillar plaques suggests binding to A<math>\beta</math>O<sub>s</sub> reported to surround amyloid plaques.</li></ul></li><li>ACU193 binds a broad range of synthetic and human-derived low, mid, and higher molecular weight A<math>\beta</math>O<sub>s</sub> (dimers to 200mers).</li></ul>
Protection from A $\beta$ O-induced synaptic toxicity	<ul style="list-style-type: none"><li>ACU193 and ACU3B3 prevent binding of A<math>\beta</math>O<sub>s</sub> to primary hippocampal neurons in vitro (the average IC<sub>50</sub> of ACU193 is 17 nM).</li><li>ACU193 and ACU3B3 block A<math>\beta</math>O<sub>s</sub>' inhibition of long-term potentiation ex vivo.</li><li>ACU3B3 blocks A<math>\beta</math>O mediated intracellular calcium influx in vitro.</li></ul>
In vivo pharmacology	<ul style="list-style-type: none"><li>ACU193 crosses the blood-brain barrier and demonstrates dose-dependent target engagement in the brain following peripheral administration of antibody.</li><li>Blinded studies in transgenic mouse models for AD over a broad range of ages show that treatment with ACU3B3 reduces multiple behavioral deficits.<ul style="list-style-type: none"><li>QPS study of nine- to ten-month-old transgenic mice treated weekly with 20 mg/kg ACU3B3 for four weeks demonstrated significant behavioral improvements during water maze learning test.</li><li>Stanford University study of five- to seven-month-old transgenic mice treated weekly with 20 and 30 mg/kg ACU3B3 showed significant improvements during open field and Y-maze tests after four to five weeks of treatment.</li><li>Gladstone Institute studies of younger three- to five-month-old transgenic mice with sub-chronic weekly administration of ACU3B3 demonstrated significant behavioral improvements to hyperactivity, emotional response alterations and procedural learning deficits.</li></ul></li></ul>
Safety	<ul style="list-style-type: none"><li>GLP studies via IV route established no observed adverse effect level, or NOAEL, of 300 mg/kg/dose in a 14-week cynomolgus monkey study and 250 mg/kg/dose in a 28-day rat study.</li><li>Studies in transgenic mice indicated low potential for cerebral microhemorrhage.</li></ul>

### Selectivity for A $\beta$ O<sub>s</sub>

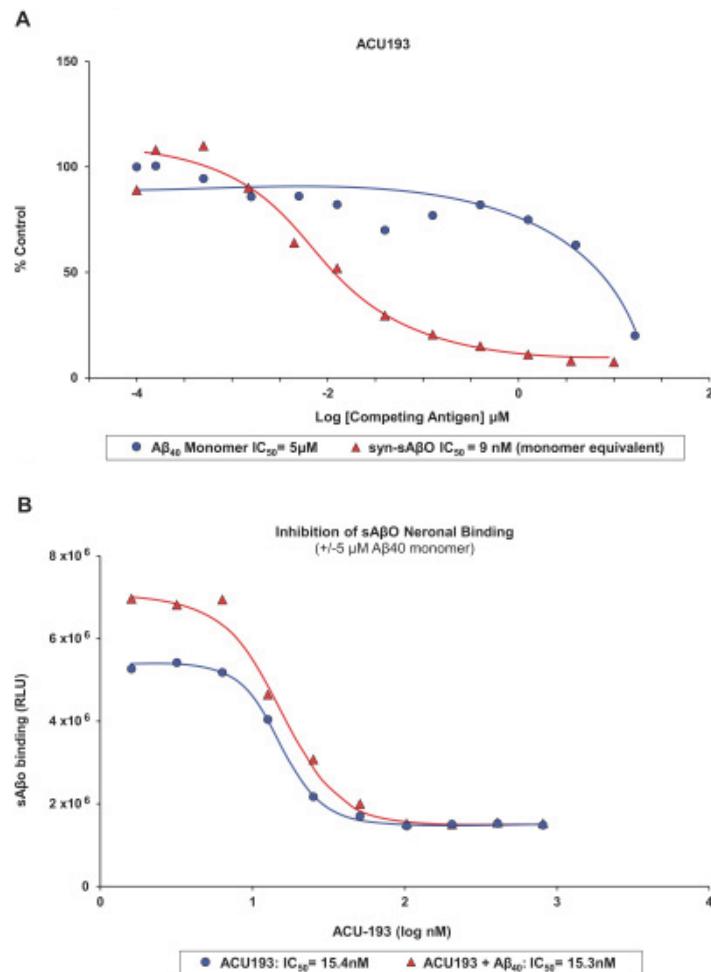
In order to understand ACU193 selectivity for A $\beta$ O<sub>s</sub>, we performed biochemical assays and immunohistochemistry experiments.

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### Selectivity for A $\beta$ Os versus A $\beta$ monomers

We demonstrated that ACU193 shows significant preferential selectivity for A $\beta$ Os compared to A $\beta$  monomers. In a competition ELISA assay, ACU193's binding to A $\beta$ O was 556-fold greater than binding to A $\beta$  monomers. Figure 3A shows comparative syn-A $\beta$ O versus A $\beta$  monomer affinity data for ACU193, and illustrates the high selectivity of ACU193 for A $\beta$ O. Further evidence of ACU193 selectivity for syn-A $\beta$ O was obtained using a very high concentration of monomeric A $\beta$ , 5  $\mu$ M, which did not decrease binding to syn-A $\beta$ O (Figure 3B). We believe ACU193's selectivity for A $\beta$ O in the presence of abundant A $\beta$  monomers is representative of the in vivo levels of these A $\beta$  species in AD patients. Thus, ACU193 does not experience "target distraction" from non-toxic A $\beta$  monomers in an environment simulating brain interstitial fluid.

**Figure 3: [A] Competitive ELISA for ACU193 binding to syn-A $\beta$ O or monomeric A $\beta$ 40 [B] 5  $\mu$ M monomeric A $\beta$  did not substantially change binding to syn-A $\beta$ O**



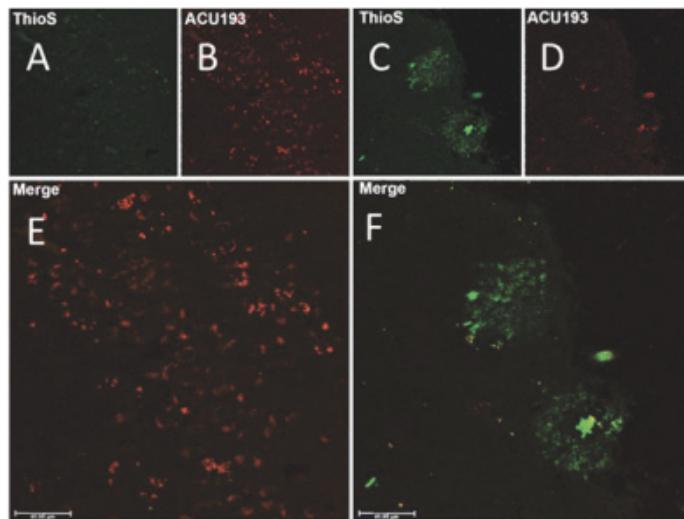
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These results support the conclusion that selectivity of ACU193 for A $\beta$ Os is maintained in a biochemical environment simulating the brain.

### **Selectivity for A $\beta$ Os versus amyloid plaques**

We have shown in our nonclinical data that ACU193 binds A $\beta$ Os from AD patients with limited or no binding to amyloid plaques. In Figure 4 below, thioflavin S-positive  $\beta$ -amyloid plaques are shown in green fluorescence while ACU193 binding is shown in red fluorescence. ACU193 binds significantly in regions that are thioflavin-S-negative, i.e., without amyloid plaques (Figure 4, Panels B and E), but only infrequently and minimally binds to thioflavin-S-positive fibrillar A $\beta$  structures (Figure 4, Panel D); close examination shows possible co-localization of ACU193 with thioflavin-S-positive A $\beta$  deposits in their periphery (Figure 4, Panel F). We believe the most likely explanation of ACU193 infrequent binding near the periphery of some amyloid plaques is due to binding to A $\beta$ Os that surround the periphery of amyloid plaques. Taken together, these results are consistent with the concept that ACU193 binds endogenous A $\beta$ Os, does not block binding by thioflavin-S, and, importantly, preferentially binds A $\beta$ Os versus fibrillar A $\beta$ .

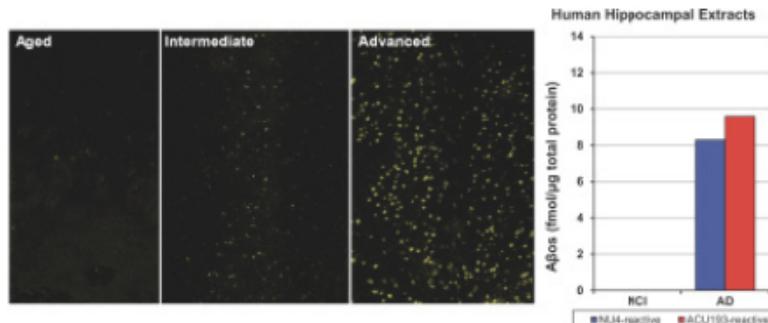
**Figure 4: ACU193 binding to A $\beta$ Os versus amyloid plaques**



The upper left portion of the immunohistochemistry figure shows that in areas with no amyloid plaque binding (no green fluorescence staining, A) there is substantial binding by ACU193 (red fluorescence staining, B) that is not related to amyloid plaque. The merge of these panels (Panel E) shows ACU193 binding with no amyloid plaque present. On the upper right portion of the Figure, the area that is positive for amyloid plaque (green fluorescence staining, C) shows minimal ACU193 binding (red fluorescence staining, D). The merge of these panels (F) shows the minimal binding of ACU193 (red fluorescence staining) on the periphery of the amyloid plaque (green fluorescence staining), most likely related to A $\beta$ O binding in the halo of the amyloid plaque.

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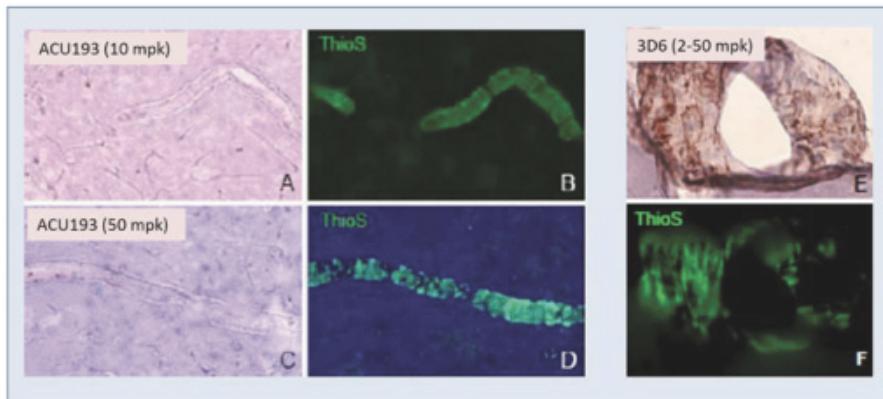
**Figure 5: AD stages based on AD neuropathic change, or ADNC, scoring**



ADNC scoring is a combination of amyloid plaque levels, neuritic plaque levels, and neurofibrillary tangle pathology, or NFT, levels (Braak stage). In human tissue samples, ACU193 shows a disease state-relevant signal based on immunohistochemistry shown on the left from aged controls, intermediate AD pathology, and advanced AD pathology. On the far-right panel, ACU193 detects A<sub>β</sub>Os in soluble hippocampal extracts from an autosomal dominant AD patient, but not from a cognitively normal patient.

Furthermore, we have demonstrated that ACU193 does not bind to amyloid plaque surrounding blood vessels (cerebral amyloid angiopathy). In a study of transgenic mice, we did not observe binding to vascular amyloid, in contrast to hu3D6 (bapineuzumab), which displayed significant binding at all dose levels.

**Figure 6: ACU193 versus hu3D6 binding to vascular amyloids**



ACU193 (A and C) shows no binding to the vascular amyloid that is visible in the vessels stained by thioflavin-S (green fluorescence, B and D) in the brain 24 hours following IV dosing of 10 or 50 mg/kg in seven- to eight-month-old Tg2576 mice. In contrast, hu3D6 (bapineuzumab) binds vascular amyloid (E) at all dose levels assessed.

The data above related to vascular plaque binding support our belief that ACU193 is unlikely to have an ARIA liability. Given that the amyloid plaque-binding properties of multiple antibodies have been associated with ARIA (e.g., aducanumab, lecanemab, gantenerumab, and donanemab), we believe that ACU193's negligible binding of amyloid plaques, including amyloid plaques associated with cerebral amyloid angiopathy, provides evidence that ARIA is unlikely to be associated with ACU193.

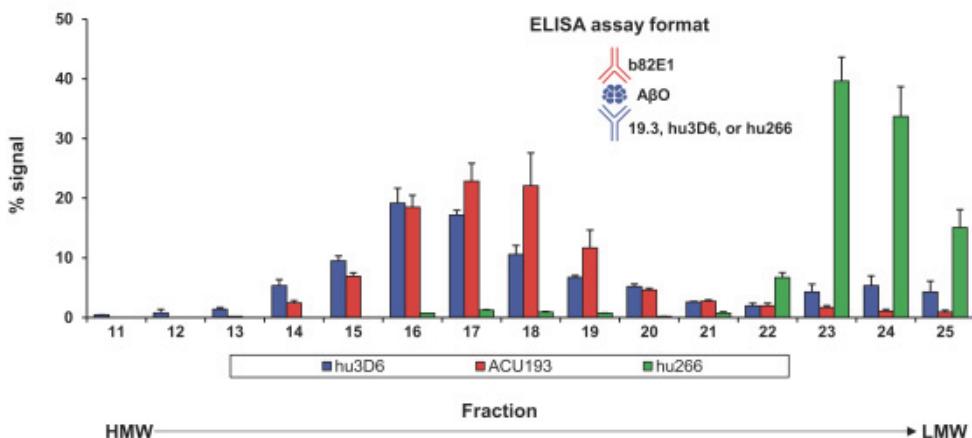
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### **Binding to a broad spectrum of molecular weight A $\beta$ O**

In addition, we demonstrated that ACU193 binds a broad spectrum of A $\beta$ O across various molecular weights. In another series of experiments, syn-A $\beta$ O were fractionated by size exclusion chromatography and characterized by ELISA using ACU193, hu3D6 (bapineuzumab) or hu266 (solanezumab) as the capture antibody and biotinylated anti-human A $\beta$  antibody 82E1 for detection. These data show ACU193 binds mid to higher molecular weight A $\beta$ O, with preferential binding to mid-molecular weight oligomers compared to hu266. This range of molecular weights is very similar to the range of molecular weights of oligomers thought to be most toxic.

**Figure 7. Binding of humanized antibodies to size exclusion chromatography fractions of synthetic A $\beta$  species**

Comparison of ELISA signals across size exclusion chromatography fractions of synthetic sA $\beta$ O



Size exclusion chromatography fractionation of syn-A $\beta$ O prep with sandwich ELISA detection. hu3D6 is also known as bapineuzumab; hu266 is also known as solanezumab. These data demonstrate the specificity of ACU193 for oligomers versus monomers, and also demonstrate a range of oligomers that are bound by ACU193.

Collectively the data show that ACU193 binds A $\beta$ O with 556-fold selectivity versus A $\beta$  monomers and demonstrates limited to no binding to amyloid plaques, but does bind to a broad range of synthetic and endogenous low, mid, and higher molecular weight A $\beta$ O. Based on these and other data, we believe that ACU193 can target therapeutically relevant A $\beta$ O in the brain of early AD patients.

### **Protection from A $\beta$ O-induced synaptic toxicity**

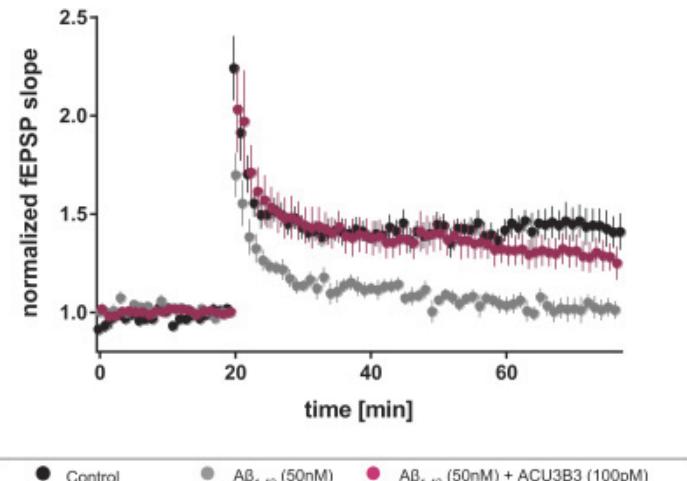
In order to understand ACU193's ability to either neutralize or limit A $\beta$ O-induced physiological changes, we performed ex vivo studies using brain slices or cell cultures.

### **Prevention of A $\beta$ O toxic effects on neuronal electrophysiology**

In ex vivo studies using the murine hippocampal slice long term potentiation, or LTP, model, pre-incubation with ACU193 or ACU3B3 has been shown to prevent the LTP deficit caused by A $\beta$ O (formed by administration of 50nM A $\beta$ <sub>1-42</sub>). LTP is an electrophysiological phenomenon demonstrated in neurons that may be associated with memory formation and other important neurological functions. Disruption of LTP has been associated with animal models in a variety of central nervous system disease states.

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**Figure 8. Effects of ACU3B3 and ACU193 on A $\beta$ O-induced change in LTP**

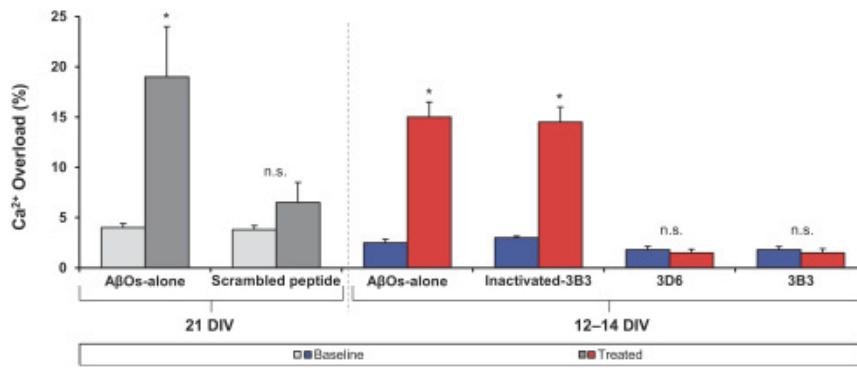


Note that A $\beta$ Os disrupted normal LTP findings, but that pre-incubation with ACU3B3 prevented that disruption.

### ***Prevention of toxic effects of A $\beta$ Os on calcium homeostasis***

Exposure to ACU3B3 has been shown to prevent calcium overload in cortical neuronal cultures induced by direct application of syn-A $\beta$ Os (Figure 9). Disruptions in calcium homeostasis that cause cellular dysfunction have been implicated in a number of disease states, including myocardial infarction and stroke. Further, A $\beta$ Os have been shown to cause disruption of calcium homeostasis, and thus, restoration of intracellular calcium to normal levels could serve as a functional indicator of potential treatment effect in AD. Multiphoton microscopy was used to examine the relationship of syn-A $\beta$ O and neuronal calcium homeostasis in vitro (Figure 9). Direct application of syn-A $\beta$ Os elicited calcium elevations in cortical neuronal cultures. Prior exposure to antibodies ACU3B3 and 3D6 prevented this calcium elevation (Figure 9). These results demonstrate that syn-A $\beta$ Os induce elevated concentrations of intracellular neuronal calcium and that ACU3B3 prevented the syn-A $\beta$ O-induced calcium overload.

**Figure 9: Effect of ACU3B3 on calcium homeostasis**



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The relationship of syn-A $\beta$ O and neuronal calcium homeostasis in the presence and absence of ACU3B3 was studied in primary cultures of transgenic APP-PS1 mouse cortical neurons. Multiphoton microscopy was used to obtain images of neuronal cultures at 12–14 days in vitro, or DIV, or 21 DIV. Cortical regions were identified and reimaged before and after topical applications of syn-A $\beta$ Os to allow comparison of resting calcium within the same neuronal compartments. After baseline calcium was obtained, the cultures were treated with antibody-immunodepleted syn-A $\beta$ Os (1 mL of 3 nM syn-A $\beta$ Os with 9  $\mu$ g of antibody) or syn-A $\beta$ Os alone for 45 minutes. The cultures were then re-imaged in the same areas in the dish. Taken together, these studies show that ACU3B3 prevents the toxic effect of A $\beta$ Os on calcium homeostasis.

## In Vivo Pharmacology

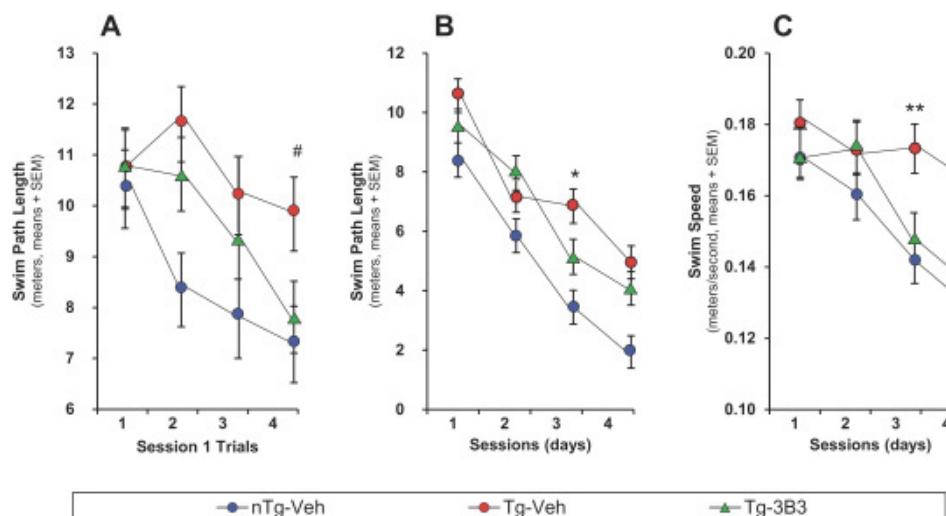
In order to understand the effects of ACU193 in intact animals, we performed behavioral studies in transgenic mice with genetic alterations that overproduce a mutant amyloid precursor protein that forms amyloid plaques. The transgenic mouse models are generally based on autosomal dominant mutations in the APP gene causing rare forms of human AD. Transgenic mouse models using these mutations may not cause the full spectrum of AD pathology, but they do provide relevant animal models for drug development in AD.

### ***In vivo behavioral studies in multiple transgenic mouse models for AD***

The behavioral studies described below, performed at three different laboratories, indicate in vivo central pharmacologic activity of peripherally administered ACU3B3. The behavioral effects seen in these studies indicate that sufficient amounts of ACU3B3 cross the blood-brain barrier to engage the target, resulting in behavioral improvements in these transgenic mice. The Phase 1 clinical trial includes doses in the range used in these nonclinical studies.

A study conducted at QPS and using nine- to ten-month-old APP/SL transgenic mice treated weekly with 20 mg/kg ACU3B3 for four weeks demonstrated statistically significant behavioral improvements in swim path length and swim speed during the water maze learning test (Figure 10).

**Figure 10: Results of ACU3B3 treatment in mice study**

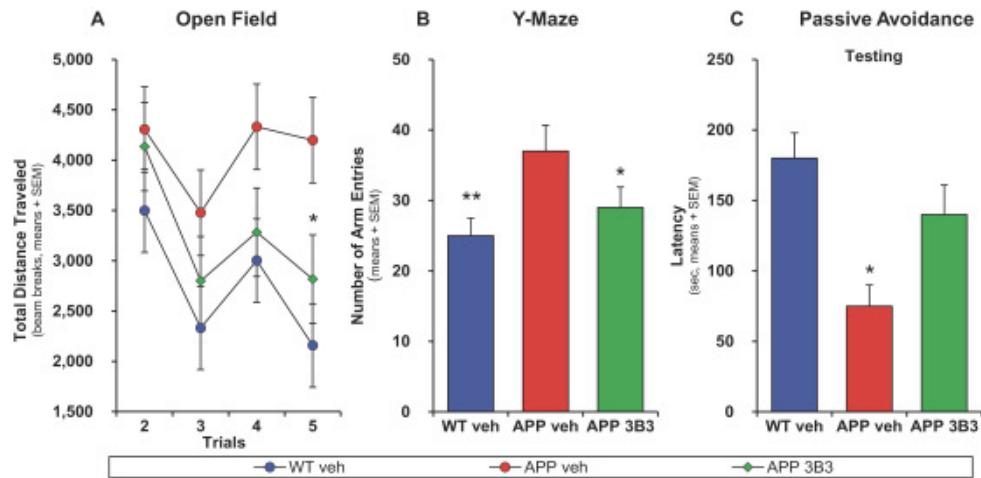


ACU3B3 treatment in nine- to ten-month-old APP/SL mice (n=10/group) improves performance on the first day of water maze training (A; p=0.057), decreases swim path length (B; p=0.034), and reverses a swim speed abnormality (C; p<0.02).

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In a separate study conducted at Stanford University, the hyperactivity phenotype of five- to seven-month-old Thy1-hAPP/SL transgenic mice in the open field and Y-maze tests was also significantly reduced after four to five weeks of treatment with ACU3B3 (20 and 30 mg/kg, weekly). Prior to dosing, Thy1-hAPP/SL mice showed increased activity in the activity chamber compared to wild-type mice. After treatment with ACU3B3, Thy1-hAPP/SL mice activity fell to a level comparable to wild-type mice, particularly activity in the center of the test arena (Figure 11A). Similar effects of ACU3B3 were found with changes in Y-maze behavior (Figure 11B) and passive avoidance (Figure 11C).

**Figure 11: ACU3B3 treatment at 20 mg/kg in five- to seven-month-old Thy1-hAPP/SL mice (n=13-14/group, means + SEM)**

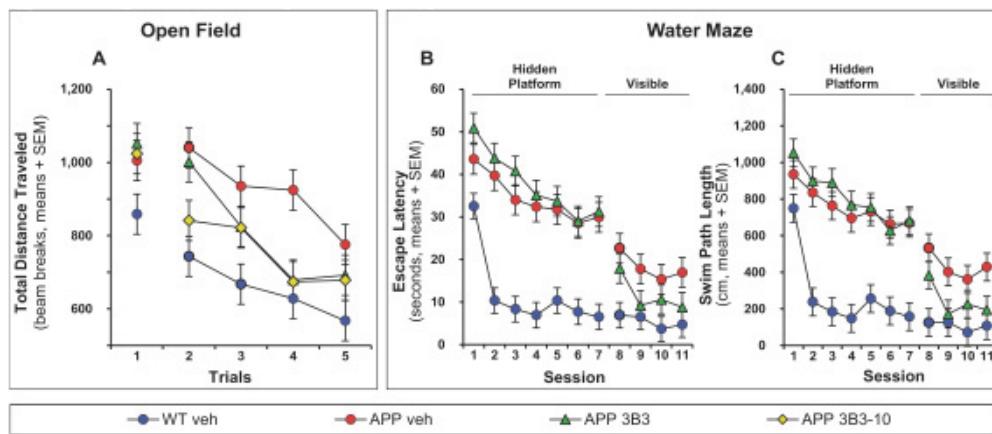


[A] Open field total distance measurement, APP-Veh vs. APP-3B3, \*p=0.029. [B] Y-maze arm entries, APP-Veh vs APP-3B3, \*p=0.045; APP-Veh vs WT-Veh, \*\*p=0.007. [C] Passive avoidance latency, APPSL-APP3B3 vs. APPSL-Veh tended for drug effect, but was not statistically significant.

In separate studies conducted at the Gladstone Institute in young three- to five-month-old hAPP/J20 mice, behavioral abnormalities in these mice were reduced after chronic treatment with ACU3B3. Treatment ameliorated the hyperactivity phenotype, emotional response alterations and procedural learning deficits in this mouse model and hyperactivity in the Y-maze test was reduced dose-dependently (5 < 10 = 20 mg/kg) (Figure 12).

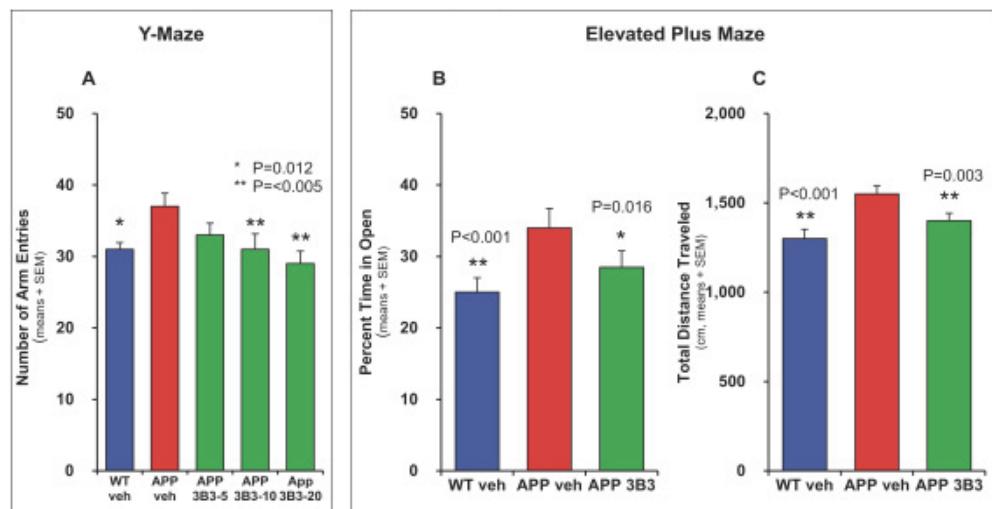
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**Figure 12: Open field and water-maze behavior in three- to five-month-old hAPP/J20 mice following repeat weekly IP dosing with ACU3B3 (n=13-14/group)**



[A] Open field activity after four weekly doses. [B], [C] Water-maze behavior following eight weekly doses.

**Figure 13: Y-maze and elevated plus-maze behavior in three- to five-month-old hAPP/J20 mice following repeat, weekly IP dosing with ACU3B3 (n=13-14/group)**



[A] Y-maze activity after six weekly doses. [B], [C] Elevated plus-maze behavior following nine weekly doses.

Taken together, these behavioral studies, performed at three different laboratories, indicate in vivo central pharmacologic activity of peripherally administered ACU3B3. The behavioral effects seen in these studies indicate that sufficient amounts of ACU3B3 cross the blood-brain barrier to engage the target, resulting in behavioral improvements in these transgenic mice. The range of doses used in these nonclinical studies are expected to be covered in INTERCEPT-AD.

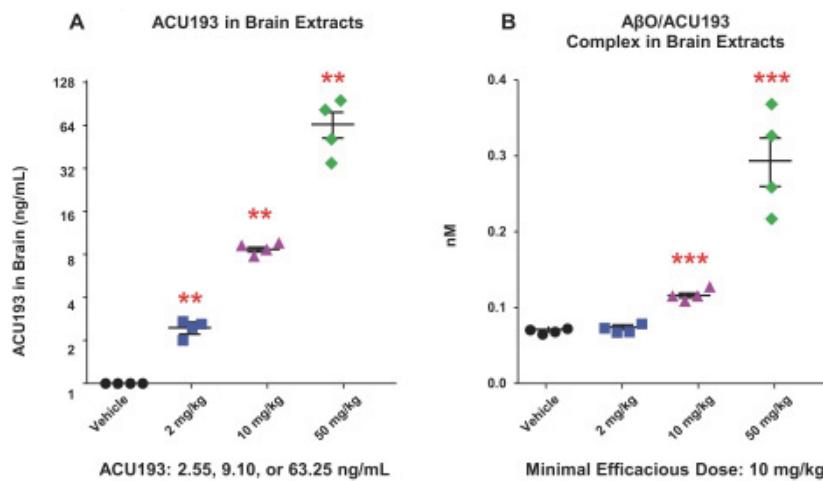
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### **Pharmacokinetics and Pharmacodynamics**

ACU193 has demonstrated favorable pharmacokinetics and pharmacodynamics based on a number of nonclinical studies. ACU193 could be detected in plasma, CSF, and brain tissue of Tg2576 mice, rats, dogs, and rhesus monkeys following IV injection. Penetration of ACU193 into the brain was demonstrated by direct measurements of brain levels in Tg2576 mice, rats, and dogs, and by measurements of CSF levels in rats and rhesus monkeys. Brain levels were approximately 0.02% of plasma levels and CSF levels ranged from 0.05 to 0.15% of plasma levels, showing penetration of ACU193 into the brain. Toxicokinetic data collected as part of GLP toxicity studies in Sprague Dawley rats and cynomolgus monkeys showed clearance of 1 to 3 mL/h/kg and terminal half-life of approximately seven days.

Brain penetration and in vivo binding of ACU193 was explored in seven-month-old Tg2576 mice dosed intravenously with 2, 10 and 50 mg/kg of ACU193 or hu3D6 (bapineuzumab), and perfused brain tissue was collected 24 hours after dosing for analysis. A dose dependent increase in brain levels of ACU193 (Figure 14A) and ACU193/A $\beta$ O complex (Figure 14B) was demonstrated, with a minimum effective dose for target engagement of 10 mg/kg.

**Figure 14: Levels of ACU193 and A $\beta$ O/ACU193 complexes in the brain 24 hours following IV dosing in seven-month-old Tg2576 mice (n = 4/cohort)**

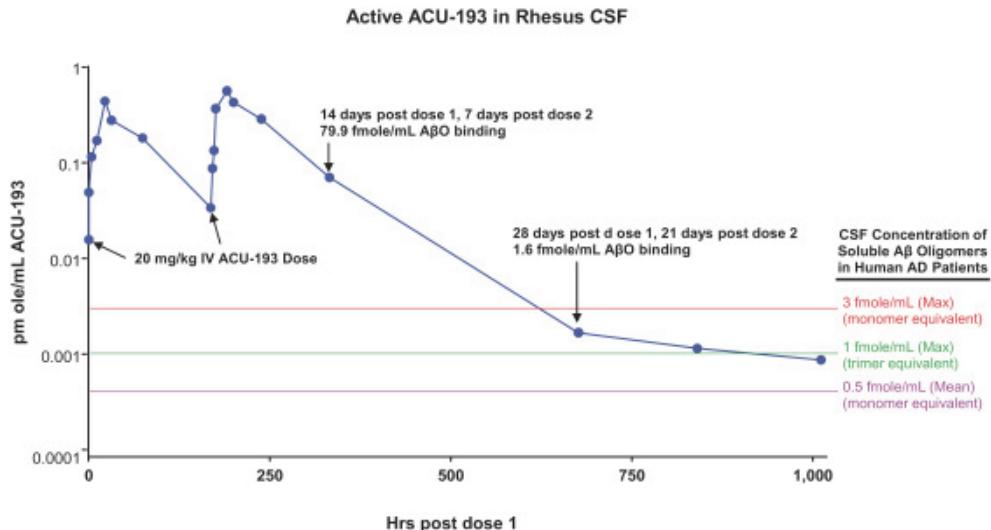


These results show ACU193 can penetrate the blood-brain barrier and bind endogenous A $\beta$ O<sub>1-42</sub>.

Additionally, a study of pharmacokinetics in CSF was conducted in rhesus monkeys. An intrathecal catheter was implanted in the monkeys, and two doses at 20 mg/kg IV were administered. As shown in Figure 15, the concentrations of ACU193 in CSF should provide adequate target engagement with every four week dosing.

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**Figure 15: Comparison of ACU193 levels in rhesus CSF to CSF Levels of A $\beta$ O in human AD patients**



Following two doses of 20 mg/kg ACU193 CSF concentrations were sufficient to provide target engagement at 28 days. An estimate of 1 fmole/mL for oligomer concentration is conservative given that it is based on A $\beta$ Os consisting of trimers.

### **Safety Profile**

GLP studies using IV administration of ACU193 established a no-observed-adverse-effect level, or NOAEL, of 250 mg/kg/dose, which was the maximum feasible dose, given every two weeks in a 28-day study in Sprague-Dawley rats. The NOAEL in cynomolgus monkeys was 300 mg/kg/dose in a 14-week study in cynomolgus monkeys using IV dosing every two weeks. In Sprague Dawley rats, no adverse findings were noted. In the 14-week study in cynomolgus monkeys, doses of 60, 300, or 600 mg/kg/dose ACU193 once every two weeks were administered. Three animals administered the highest 600 mg/kg/dose were sacrificed early for humane reasons on Days 43 or 60 due to ACU193-related, anaphylactoid-type reactions.

Thus, the 300 mg/kg/dose is considered the NOAEL for cynomolgus monkeys. The NOAELs of 300 mg/kg and 250 mg/kg compare favorably to the highest dose of ACU193 being used in our Phase 1 clinical trial (60 mg/kg).

Based in part on binding to A $\beta$ Os rather than amyloid plaque, ACU193 has the potential to have a lower rate of ARIA than plaque-clearing anti-amyloid antibodies. Additionally, ACU3B3 showed no apparent increased risk of microhemorrhage when administered *in vivo* for three months in aged Tg2576 mice, as compared with 3D6, a plaque binding antibody used as a positive control.

With regard to effector function and possible inflammatory effects generally, ACU193 is an IgG2m4 subclass antibody which lacks inflammatory effector function signaling stimulated by other IgG subclasses. Thus, the risk for inflammatory effector function using ACU193 is considered to be low.

### **Investigational New Drug Application**

In October 2020, we submitted an investigational new drug, or IND, application for ACU193 to the FDA. The FDA initially placed the IND on clinical hold until we were able to address the FDA's concerns regarding potential off-target binding of ACU193 with an additional nonclinical tissue cross reactivity (TCR) study in

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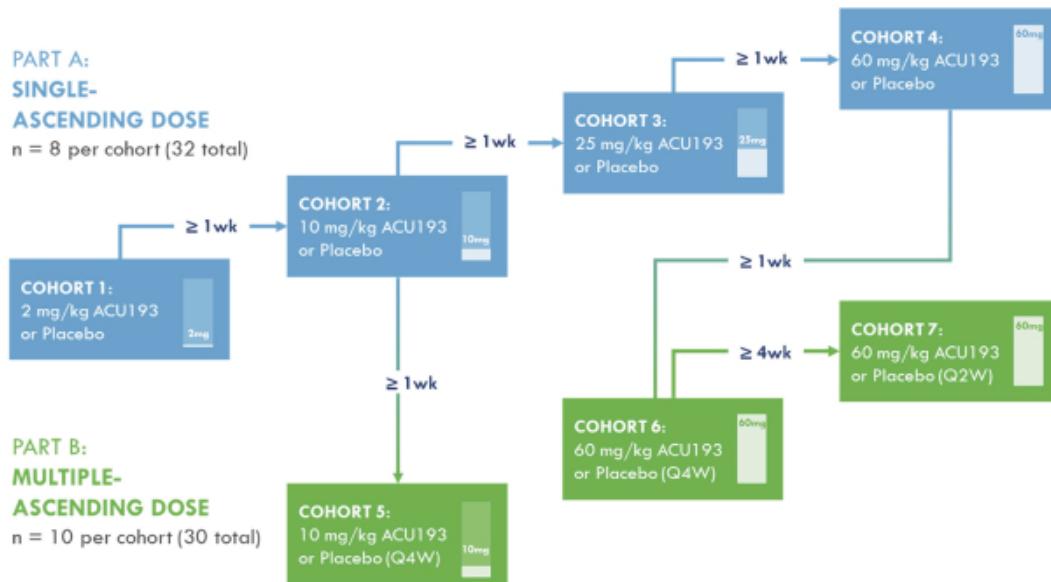
human, monkey, and rat samples. The supplemental TCR study supported the in-vivo GLP safety results. On April 9, 2021, we received an FDA letter advising us that the clinical hold had been removed and authorizing us to proceed with a first-in-human, Phase 1 clinical trial.

### Clinical Development Plan

#### Phase 1 Clinical Trial in AD

In the second quarter of 2021, we initiated a multi-center, randomized, placebo-controlled, single and multiple ascending dose Phase 1 clinical trial of ACU193, which we named “INTERCEPT-AD,” in 62 patients with early AD. The early AD patient set is comprised of individuals who have mild dementia or MCI due to AD. Patients with moderate to severe dementia will not be included. The main objectives of the trial are to evaluate the safety, tolerability, pharmacokinetics, and target engagement of single and multiple ascending doses of ACU193 administered by IV infusion. Pharmacodynamics effects including cognitive testing are expected to be performed on an exploratory basis. The trial is designed to be conducted in two overlapping parts: Part A (the single ascending dose portion) and Part B (the multiple ascending dose portion).

**Figure 16: Design of INTERCEPT-AD**



#### Trial Design Part A – Single Ascending Dose

We expect to enroll 32 participants in Part A of our clinical trial, with the participants randomized in a 6:2 ratio into one of four cohorts to receive a single dose of ACU193 or placebo as follows:

- Cohort 1: One IV dose of ACU193 (2 mg/kg) or placebo.
- Cohort 2: One IV dose of ACU193 (10 mg/kg) or placebo.
- Cohort 3: One IV dose of ACU193 (25 mg/kg) or placebo.
- Cohort 4: One IV dose of ACU193 (60 mg/kg) or placebo.

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The double-blind treatment period for Cohorts 1-4 of Part A will be approximately 20 weeks and will include ten visits (four inpatient and six outpatient). A sequential dosing scheme will be followed for each cohort in Part A. Dosing of Cohorts 1-3 will begin at least one week after all participants in the immediately preceding lower-dose cohort have received one administration of study drug and safety data have been reviewed by our internal blinded safety team. Dosing of Cohort 4 will begin at least one week after all participants in Cohort 3 have received one administration of study drug and these safety data, along with Cohort 2 aggregate pharmacokinetic data, have been reviewed by our internal blinded safety team. An unblinded, independent Data Monitoring Committee, or DMC, will also monitor the trial and can review safety data on an ad hoc basis if requested by the blinded study team.

### *Trial Design Part B – Multiple Ascending Dose*

We expect to enroll 30 participants in Part B of our clinical trial, with the participants randomized in an 8:2 ratio into one of three cohorts to receive a total of three doses of ACU193 or placebo as follows:

- Cohort 5: One IV dose of ACU193 (10 mg/kg) or placebo once every four weeks.
- Cohort 6: One IV dose of ACU193 (60 mg/kg) or placebo once every four weeks.
- Cohort 7: One IV dose of ACU193 (60 mg/kg) or placebo once every two weeks.

Participants in Cohorts 5 and 6 will be evaluated over approximately 35 weeks, consisting of a seven-week screening period followed by a 28-week, double-blind treatment period. A follow-up safety check will be performed approximately eight weeks after the final visit of the double-blind treatment period.

Participants in Cohort 7 will be evaluated over approximately 31 weeks, consisting of a seven-week screening period, followed by a 24-week, double-blind treatment period. A follow-up safety check will be performed approximately eight weeks after the final visit of the double-blind treatment period.

In order to maintain participant safety for Part B of the clinical trial, dosing of Cohort 5 will begin at least one week after all participants in Cohort 2 of Part A have received one administration of ACU193 or placebo and the Cohort 2 safety data have been reviewed by our internal blinded safety team. For Cohort 6, dosing will begin at least one week after all participants in Cohort 4 of Part A have received one administration of ACU193 or placebo and the Cohort 4 safety data have been reviewed by our internal blinded safety team. Dosing of Cohort 7 will begin after four or more participants in Cohort 6 have been administered two doses of ACU193 or placebo and the Cohort 6 safety data, along with aggregated pharmacokinetic data from Cohort 4, have been reviewed by our internal blinded safety team. If a potential safety signal, an unexpected adverse reaction, or higher than expected exposure occurs, our internal blinded safety team will notify the independent, unblinded DMC to review the safety and pharmacokinetic data and advise on dose escalation. Cohort 7 will allow for additional pharmacokinetic modeling to more accurately determine the half-life of ACU193 if every two-week dosing is necessary.

### *Endpoints*

Our goal for the Phase 1 trial is to establish clinical proof of mechanism of ACU193 in patients with early AD. The endpoints we will measure as part of this trial include:

#### *Primary Endpoint*

- safety and immunogenicity, including assessment for ARIA;

#### *Secondary Endpoints and Exploratory Objectives*

- pharmacokinetics in plasma;
- determination of CSF concentrations of ACU193;

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- evaluation of central target engagement as measured by levels of ACU193 A $\beta$ O complex in CSF;
- evaluation of possible changes in concentration of biomarkers for AD in CSF or blood;
- evaluation of possible changes in amyloid plaque load as determined by PET imaging;
- evaluation of possible changes in cerebral blood flow as determined by MRI imaging, using Arterial Spin Labeling (ASL) pulse sequence; and
- evaluation of possible changes in cognitive, functional, and behavioral measures using computerized testing and standard clinical measures for AD.

In October 2021, we announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients. Due to delays in clinical trial site activation and enrollment that we believe are principally related to effects of the COVID-19 pandemic, we are expanding the anticipated number of trial sites to support our enrollment objectives and anticipated timelines. Clinical trial site activation and patient recruitment and enrollment is ongoing. At present, INTERCEPT-AD is in the SAD portion of the trial. Based on current site activations and enrollment rates, we anticipate reporting our topline data from this trial, including assessments of safety, ARIA-E, pharmacokinetics and target engagement through the full 168 day follow-up period for Cohort 7, in the first half of 2023.

### **Future Clinical Trials**

Subject to establishment of proof of mechanism of ACU193 and the safety and immunogenicity results of INTERCEPT-AD, we intend to advance ACU193 into later stage clinical trials. We plan to explore a proposed therapeutic dose of ACU193 in a future Phase 2/3 clinical trial based on safety, pharmacokinetics and pharmacodynamics assessments of the various dosing cohorts in INTERCEPT-AD. Following, and subject to the results of, INTERCEPT-AD, we plan to engage with the FDA in an end-of-Phase 2 meeting, which we anticipate will occur in the second half of 2023, to discuss the Phase 2/3 clinical trial design and pathway for potential approval. The Phase 2/3 trial is being designed as an adaptive trial, such that after a planned interim analysis of clinical and biomarker changes, a decision could be made to increase the enrollment of the trial to be adequately powered as a Phase 3 pivotal trial, or to continue the trial as a Phase 2 clinical trial. The Phase 2/3 trial will utilize standard cognitive measures that are widely employed in AD trials and most highly sensitive to changes in mild AD patients, including ADAS-COG 13, CDR-sb, ADCS-iADL, iADRS, MMSE, and potentially others including computerized neuropsychological testing. Additionally, a number of biomarkers may be studied including blood flow as determined by ASL pulse sequence on MRI, plasma or CSF p-tau, amyloid PET scanning, and tau PET scanning. Selected endpoints will be used to inform the interim decision whether to expand the trial and whether to initiate a second Phase 3 clinical trial.

### **Combination Potential**

While we believe ACU193, if successful, will likely be a foundational treatment for people with early AD, it also could be used as part of a combination treatment regimen. The pathology of AD is complex, and many experts in the field expect that combination therapy using drugs with different mechanisms of action, such as tau, immune modulation, glial cells such as microglia and astrocytes, and growth factors, will ultimately prove most successful, similar to cutting edge approaches used in oncology. In addition, because symptomatic treatments, such as memantine and cholinesterase inhibitors, affect neurotransmitter systems rather than the underlying AD pathology, we believe that it is likely that they will be used together with disease-modifying treatments.

### **Manufacturing**

We do not currently own or operate facilities for product manufacturing, storage and distribution, or testing. We contract with third parties for the manufacture of ACU193. Because we rely on contract manufacturers, we employ personnel with extensive technical, manufacturing, analytical and quality experience. Our staff has strong project management discipline to oversee contract manufacturing and testing activities, and to compile manufacturing and quality information for our regulatory submissions.



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Manufacturing is subject to extensive regulation that imposes various procedural and documentation requirements and that governs record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, and more. Our systems and our contractors are required to be in compliance with these regulations, and compliance is assessed regularly through monitoring of performance and a formal audit program.

Our current supply chains for ACU193 involve several manufacturers that specialize in specific operations of the manufacturing process, including raw materials manufacturing, drug substance manufacturing and drug product manufacturing. We currently operate under work order programs for ACU193 with master services agreements in place that include specific supply timelines, volume and quality specifications. We believe our current manufacturers have the scale, the systems, and the experience to supply our currently planned clinical trials.

## **Competition**

We face competition from several different institutions, including pharmaceutical and biotechnology companies, research institutions, governmental organizations and universities developing novel therapies for AD. We believe that the key factors affecting the clinical and commercial success of ACU193 will include safety profile, efficacy, cost, method of administration, level of marketing activity, insurance reimbursement and intellectual property protection.

If approved, ACU193 will compete with therapies currently approved for the treatment of AD, which have primarily been developed to treat the symptoms of AD rather than the underlying cause of the disease, such as memantine and cholinesterase inhibitors. ACU193 may also compete with one or more potentially disease-modifying therapeutics that target A $\beta$  or amyloid plaques, the most advanced of which is Biogen Inc.'s Aduhelm (aducanumab), which the FDA approved in June 2021 under the accelerated approval pathway, which allows for earlier approval of drugs that treat serious conditions, and that fill an unmet medical need based on a surrogate endpoint. Regulatory approval of aducanumab is pending in Europe and Japan. Eisai Co., Ltd. (lecanamab), Eli Lilly and Company (donenamab), and Roche Holding AG (gantenerumab), are anticipated to complete Phase 3 studies in 2022 and 2023 with their amyloid plaque targeting monoclonal antibody drugs and may obtain FDA approval under the accelerated approval pathway or full approval based on Phase 3 results.

Other companies known to be developing therapies with A $\beta$ , A $\beta$ O-, and amyloid plaque-related targets include Alzheon, Inc., Alzinova AB, Chugai Pharmaceutical Co. Ltd., Cognition Therapeutics, Inc., Grifols, S.A., KalGene Pharmaceuticals, Inc., Neurimmune AG, Novartis AG, ProMIS Neurosciences, Inc., Prothena Biosciences, Inc., Vaxinity, Inc., Vivoryon Therapeutics N.V. and Wren Therapeutics, Inc. Additionally, ACU193, if approved, may also compete with other potential therapies intended to address underlying causes of AD that are being developed by several companies, including AbbVie Inc., AC Immune SA, Alector, Inc., Anavex Life Sciences Corp., Annovis Bio, Inc., Athira Pharma, Inc., Biohaven Pharmaceuticals, Inc., Cassava Sciences, Inc., Cortexyme, Inc., Denali Therapeutics, Inc., Johnson & Johnson (including Janssen, its wholly-owned subsidiary) and Takeda Pharmaceutical Co. Ltd.

## **Collaboration Agreement with Merck**

In December 2003, we entered into an exclusive license and research and development collaboration agreement with Merck to research, discover and develop certain technology related to amyloid beta-derived diffusible ligands, or ADDL, which agreement was amended and restated in October 2006. The agreement generally provided that, during the course of the collaboration, Merck would be responsible for the preclinical and clinical development and commercialization of any products covered by the agreement and, in return, we were eligible to receive potential nonclinical, clinical and regulatory milestone payments and royalties on future product sales. During the collaboration, Merck developed ACU193, an ADDL antibody, and intellectual property related to ACU193 was filed by Merck. In 2011, Merck elected to voluntarily terminate the collaboration agreement. Pursuant to the surviving provisions of the agreement, effective upon termination of the collaboration, Merck

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granted us an exclusive, perpetual, irrevocable, royalty-free, worldwide license, with right to sublicense, under Merck's interest in the patent rights and know-how necessary for the research, development, manufacturing or commercialization of ADDL antibodies, ADDL antigens or products, including ACU193.

### **Intellectual Property**

Our intellectual property is critical to our business and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidate. We also rely on the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how that is not patentable, we rely on confidentiality agreements to protect our interests. We require our employees, consultants, scientific advisors and contractors to enter into confidentiality agreements prohibiting the disclosure of confidential information and requiring disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

The main form of commercial exclusivity for our product candidate, ACU193, is expected to come from biologic regulatory exclusivity. We expect that once approved by regulatory agencies, ACU193 will receive the benefit of 12 years of market exclusivity in the U.S. and 10 to 11 years of data and market exclusivity in Europe, in each case, against competitors seeking approval for a biosimilar product.

We have an exclusive license grant from Merck to patents claiming the composition and method of use of our product candidate, ACU193. The license grant arose from our collaboration agreement with Merck to research, discover, and develop technology related to ADDLs. During our collaboration, ACU193, an ADDL antibody, was developed and intellectual property was filed by Merck. In 2011, the collaboration agreement terminated and Merck exclusively licensed to Acumen, Merck's interest in patent rights claiming ADDL antibodies, including ACU193, ADDL Antigens and/or Products to Acumen. In the nine years subsequent to the termination of the collaboration with Merck, Acumen has controlled and directed and continues to control and direct prosecution of the licensed ACU193 patent portfolio. Acumen has also paid for and continues to pay all costs and fees associated with the prosecution and maintenance of the licensed ACU193 patent portfolio.

As of March 25, 2022, Acumen licenses from Merck one issued U.S. patent, 18 issued foreign patents including issued patents in Brazil, China, Canada, Australia, Japan, South Korea, France, Germany and the UK drawn to our product candidate, ACU193. These patents are projected to expire in July of 2031, without taking into account any possible extensions and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees.

Throughout the development of our product candidate, we seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including by protecting inventions related to additional methods of use, processes of making, formulation, and dosing regimens.

### **Patent Term and Term Extensions**

The terms of individual patents are determined based primarily on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, utility patents issued for applications filed in the United States are granted a term of 20 years from the earliest effective filing date of a non-provisional patent application. In addition, in certain instances, the term of a U.S. patent can be extended to recapture a portion of the United States Patent and Trademark Office, or USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the restoration period cannot extend the patent term beyond 14 years from FDA approval for the product covered by that patent. In addition, only one patent applicable to an approved drug may receive the extension, and the extension applies only to coverage for the approved drug, methods for using it and methods of manufacturing it,

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even if the claims cover other products or product candidate. Where one patent covers multiple products or product candidate, it may only receive an extension for one of the covered products; any extension related to a second product or product candidate must be applied to a different patent. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date of a non-provisional patent application, such as a Patent Cooperation Treaty, or PCT, application. All taxes, annuities or maintenance fees for a patent, as required by the USPTO and various foreign jurisdictions, must be timely paid in order for the patent to remain in force during this period of time.

The actual protection afforded by a patent may vary on a product-by-product basis, from country to country, and can depend upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions and the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Our patents and patent applications may be subject to procedural or legal challenges by others. We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see the section titled “Risk Factors—Risks Related to Our Intellectual Property.”

### ***Trademarks and Know-How***

In connection with the ongoing development and advancement of our products and services in the United States and various international jurisdictions, we seek to create protection for our marks and enhance their value by pursuing trademarks and service marks where available and when appropriate. We rely upon know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by using confidentiality agreements with our commercial partners, collaborators, employees and consultants, and invention assignment agreements with our employees and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed by our employees and through relationships with third parties. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our contractors, commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For more information, see the section titled “Risk Factors—Risks Related to Our Intellectual Property.”

### **Government Regulation**

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of biologics such as those we are developing. We, along with our third-party contractors, will be required to navigate the various preclinical, clinical, manufacturing and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable 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 or post-approval may subject an applicant to delays in development or approval, as well as administrative and judicial sanctions.

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### **U.S. Biologics Regulation**

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and other federal, state, local and foreign statutes and regulations. The process required by the FDA before biologics may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practice requirements, or GLPs;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical trials may begin and must be updated annually and when certain changes are made;
- approval by an institutional review board, or IRB, or independent ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice, or GCP, requirements and other clinical trial-related regulations to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a biologics license application, or BLA, after completion of all pivotal clinical trials;
- payment of user fees for FDA review of the BLA;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with current Good Manufacturing Practices, or cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

### *Preclinical and Clinical Trials*

Prior to beginning the first clinical trial with a product candidate in the United States, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of chemistry, formulation and stability, as well as *in vitro* and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety and toxicology studies. In the United States, the results of the preclinical studies, together with manufacturing information and analytical data must be submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational new drug 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.

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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 dosing procedures, subject selection and exclusion criteria, and the parameters and criteria to be used in monitoring safety and effectiveness. 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.

While clinical trials are ongoing, the FDA may impose a partial or complete clinical hold based on concerns for patient safety and/or noncompliance with regulatory requirements. This order issued by the FDA would cause the suspension of an ongoing study, or part of an ongoing study, until all outstanding concerns have been adequately addressed, and the FDA has notified the company that investigations may proceed. Imposition of a clinical hold could cause significant delays or difficulties in completing planned clinical studies in a timely manner. In addition, 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 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 provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may 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. In the United States, information about applicable clinical trials, including clinical trials results, must be submitted within specific timeframes for publication on the [www.clinicaltrials.gov](http://www.clinicaltrials.gov) website.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing suggest a significant risk for human participants exposed to the drug or biologic, or for 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 also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1—The investigational product is initially introduced into a limited population of healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dose response, 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.
- Phase 2—The investigational product 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 investigational product 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

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are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may also be made a condition to approval of the BLA.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life and to identify appropriate storage conditions for the product candidate.

### ***BLA Submission and Review by the FDA***

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include data available from preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by independent investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the investigational biologic, to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States. The submission of a BLA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the filing date, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process may also be extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may also convene an advisory committee to provide clinical insight on application review questions. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides 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.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

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If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter, or CRL. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

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 BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy implemented to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and 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. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. 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 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.

### *Expedited Development and Review Programs*

The FDA offers a number of expedited development and review programs for qualifying product candidates. These programs include fast track designation, breakthrough therapy designation, priority review, and accelerated approval.

The fast track program is intended to expedite or facilitate the process for reviewing new products that 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. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a fast track product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, 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

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FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any marketing application for a drug or biologic submitted to the FDA for approval, including a product candidate with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product candidate is eligible for priority review if it is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to ten months under standard review).

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive 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 accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. 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.

Fast track designation, breakthrough therapy designation, and priority review, accelerated approval do not change the standards for approval but may expedite the development or approval process. Even if a product candidate 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.

### *Orphan Drug Designation and Exclusivity*

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

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A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

### *Post-approval Requirements*

Biologics are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and complying with advertising and promotion requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as “off-label use”) and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe approved products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, including not only by Company employees but also by agents of the Company or those speaking on the Company’s behalf, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Promotional materials for approved biologics must be submitted to the FDA in conjunction with their first use or first publication.

After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Biologic manufacturers and their subcontractors 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, which impose certain procedural and documentation requirements up. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. 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;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- 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;

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- mandated modification of promotional materials and labeling and the issuance of corrective information; and
- and the imposition of civil or criminal penalties.

### *United States Biosimilars and Exclusivity*

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act, or BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars in the United States. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, a reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the Patient Protection and Affordable Care Act, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and regulatory interpretation of the BPCIA remain subject to significant uncertainty.

### *Other Healthcare Laws*

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business and may constrain the financial arrangements and relationships through which we research, as well as, sell, market and distribute any products for which we obtain marketing approval. Such laws include, without limitation, federal and state anti-kickback, fraud and abuse, false claims, data privacy and security and physician and other health care provider transparency laws and regulations. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind in return for, or to induce, either the referral of an individual, or the purchase, lease, order or arrangement for or recommendation of the purchase, lease, order or arrangement for any good, facility, item or service for

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which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term “remuneration” has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly;

- the federal civil and criminal false claims laws, including, without limitation, the federal False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. 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;
- the federal Health Insurance Portability and Accountability Act, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. 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 and their implementing regulations, also imposes obligations, including mandatory contractual terms, on “covered entities,” including certain healthcare providers, health plans, healthcare clearinghouses, and their respective “business associates,” that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, as well as analogous state and foreign laws that 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;
- the federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the State Children’s Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare and Medicaid Services, or CMS, information related to: (i) payments or other “transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, and (ii) ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or that otherwise restrict payments that may be made to healthcare providers; and state and local laws that require the registration of pharmaceutical sales representatives.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of

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such laws. 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. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, 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. 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, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

### *Coverage and Reimbursement*

In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs (e.g., Medicare, Medicaid, TRICARE), commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. The principal decisions about reimbursement for new medicines are typically made by CMS, an agency within the U.S. Department of Health and Human Services, or HHS. CMS decides whether and to what extent products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Third-party payors determine which products and procedures they will cover and establish reimbursement levels. These third-party payors are increasingly reducing reimbursements for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Patients who are treated in-office for a medical condition generally rely on third-party payors to reimburse all or part of the costs associated with the procedure, including costs associated with products used during the procedure, and may be unwilling to undergo such procedures in the absence of such coverage and adequate reimbursement. In addition, for products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs.

Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a procedure is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental nor investigational. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

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### *Healthcare Reform*

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, each as amended, collectively known as the ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, the ACA:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70 percent 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; and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is also unclear how other such challenges and the healthcare reform measures of the Biden administration will impact the ACA or our business.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2% per year, which began in 2013, and due to subsequent legislative amendments to the statute, will remain in effect through 2031, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. 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. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries, proposed and enacted legislation and executive orders issued by the prior presidential administration 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, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. However, several lawsuits have been brought against HHS challenging various aspects of the rules implemented during the Trump administration. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these

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Trump-era policies. In July 2021, the Biden administration released an executive order, “Promoting Competition in the American Economy,” with multiple provisions aimed at prescription drugs. In response to Biden’s executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic. Individual states in the United States have also become increasingly active in implementing 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.

### **Employees and Human Capital Resources**

Our human capital objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of stock-based compensation awards.

As of March 1, 2022, we had 17 employees, 14 of which were full time. Of the 17 employees, there were 11 in research and development and six in general and administrative functions. We also utilized 12 consultants, nine in various roles related to research and development and three in general and administrative functions. We believe our employee relations are good.

### **Corporate Information**

We were incorporated under the laws of the State of Delaware in 1996. Our principal executive offices are located at 427 Park St., Charlottesville, Virginia 22902 and our telephone number is (434) 297-1000.

### **Available Information**

Our website address is <http://www.acumenpharm.com/>. In addition to the information about us contained in this Annual Report on Form 10-K, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report on Form 10-K.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the SEC. Additionally, the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC’s website is [www.sec.gov](http://www.sec.gov).

### **Item 1A. Risk Factors.**

*The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and our other public filings. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.*

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### **Risks Related to our Financial Position and Capital Needs**

#### ***We are a clinical stage biopharmaceutical company with a limited operating history.***

We are a clinical-stage biopharmaceutical company with a limited operating history focused on pioneering a novel disease-modifying therapeutic approach to treat AD. We were incorporated in 1996 and were party to an exclusive license and research collaboration with Merck in 2003. Although we acquired the exclusive rights to ACU193 from Merck in 2011, following Merck's strategic decision to focus its AD development efforts on a different product candidate, we did not recommence meaningful operations until we completed our first institutional fundraising in 2018. As a result, we have a very limited operating history, which may make it difficult to evaluate the success of our business to date and assess our future viability. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We received clearance of our Investigational New Drug application, or IND, for our sole product candidate, ACU193, and initiated our Phase 1 clinical trial in the second quarter of 2021. In October 2021, we announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients. Due to delays in clinical trial site activation and patient enrollment that we believe are principally related to effects of the COVID-19 pandemic, we are expanding the anticipated number of trial sites to support our enrollment objectives and anticipated timelines. However, we cannot assure that we will not experience additional delays in site activation or enrollment. Clinical trial site activation and patient recruitment and enrollment is ongoing. To date, we have not completed a clinical trial, initiated a pivotal trial, obtained marketing approval for any product candidate, manufactured a commercial scale product candidate, arranged for a third party to do so on our behalf or conducted sales or marketing activities necessary for successful product candidate commercialization. Our short operating history makes any assessment of our future success and viability subject to significant uncertainty. We will likely encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to overcome such risks and difficulties successfully. If we do not address these risks and difficulties successfully, our business will suffer.

#### ***We have no product candidates approved for commercial sale, we have never generated any revenue from sales and we may never be profitable.***

We have no product candidates approved for sale, have never generated any revenue from sales, have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses in each year since our inception. For the years ended December 31, 2021 and 2020, our net losses were \$100.6 million and \$7.3 million, respectively. As of December 31, 2021, we had an accumulated deficit of \$127.6 million.

To date, we have devoted most of our financial resources to research and development of ACU193, including our nonclinical development activities of ACU193, and corporate overhead. We expect that it will be several years, if ever, before we have a product candidate approved and ready for commercialization. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, ACU193 and any other product candidate we may develop in the future, prepare for and begin the commercialization of any approved product candidates and add infrastructure and personnel to support our drug development efforts and operations as a public company. We anticipate that any such losses could be significant for the next several years. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. Further, these net losses may fluctuate significantly from quarter-to-quarter or year-to-year. To become and remain profitable, we must develop and eventually commercialize ACU193 or another drug with significant revenue.

We may never succeed in developing a commercial drug and, even if we succeed in commercializing one or more product candidates, we may never generate revenues that are large enough to achieve profitability. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown challenges. Because of these numerous risks and uncertainties, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to generate revenues or achieve profitability. If we do achieve

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profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis, and we will continue to incur substantial research and development costs and other expenditures to develop and market additional product candidates.

***We will require substantial additional funding to finance our operations, complete the development and commercialization of ACU193 for AD and evaluate future product candidates. If we are unable to raise this funding when needed, we may be forced to delay, reduce or eliminate our drug development programs or other operations.***

To date, we have used substantial amounts of cash to fund our operations, and we expect our expenses to increase substantially in the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development, conduct clinical trials of, and seek marketing approval for, ACU193. Developing ACU193 and conducting clinical trials for the treatment of AD and any other product candidates or indications that we may pursue in the future will require substantial amounts of capital. In addition, if we obtain marketing approval for ACU193 or any future product candidates, we expect to incur significant commercialization expenses related to the commercialization of the product, whether we are commercializing alone or with a collaborator. Furthermore, we expect to incur additional significant expenses associated with operating as a public company.

Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. As of December 31, 2021, we had \$122.2 million in cash and cash equivalents and \$103.7 million in marketable securities. Based on our current operating plan, we believe that our existing cash and cash equivalents and marketable securities will be sufficient to enable us to fund our operating expenses and capital expenditure requirements at least through 2025. However, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

The amount and timing of our future funding requirements will depend on many factors, some of which are outside of our control, including but not limited to:

- the progress, costs, timing and results of INTERCEPT-AD and other potential clinical trials of ACU193, including for potential additional indications that we may pursue beyond AD;
- the requirements of the U.S. Food and Drug Administration, or the FDA, and European Medicines Agency, or the EMA, for clinical trials and nonclinical studies and other work, for review and approval of ACU193 for AD;
- the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
- the number and characteristics of product candidates that we pursue;
- our ability to obtain sufficient quantities of our product candidates from our third-party manufacturers;
- our need to expand our research and development activities;
- the costs associated with securing and establishing commercialization capabilities if we were to elect to commercialize one or more products on our own;
- the economics and other terms, timing of and success of any collaboration, licensing or other arrangements into which we may enter for the commercialization of our products;
- the costs and other terms, timing and success, of acquiring, in-licensing or investing in businesses, product candidates and technologies;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;

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- our need and ability to retain management and hire scientific and clinical personnel;
- the effect of competing drugs and product candidates and other market developments; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

Additional funding may not be available to us on acceptable terms or at all. Any such funding may result in dilution to stockholders, imposition of debt covenants and repayment obligations or other restrictions that may affect our business. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us. Any funds we raise may not be sufficient to enable us to continue to implement our long-term business strategy. Further, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic and conflict with Russia and Ukraine. If we are unable to raise sufficient additional capital on a timely basis, we could be forced to curtail our planned operations and the pursuit of our business strategy, which would have a material adverse effect on the value of our common stock.

### **Risks Related to the Development of our Product Candidates**

*We are substantially dependent on the success of ACU193, our sole product candidate, which will require significant clinical testing before we can seek regulatory approval and potentially launch commercial sales, and which may not be successful in clinical trials, receive regulatory approval or be successfully commercialized, even if approved.*

We are early in our development efforts. To date, we have invested substantially all of our efforts and financial resources in the research and development of ACU193, which is currently our only product candidate. Before seeking marketing approval from regulatory authorities for the sale of ACU193, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the drug in humans. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA, or comparable foreign regulatory authorities, and we may never receive such regulatory approval. We cannot be certain that ACU193 will be successful in clinical trials. Further, ACU193 may not receive regulatory approval even if it is successful in clinical trials. If we do not receive regulatory approvals for ACU193, we may not be able to continue our operations. Our prospects, including our ability to finance our operations and generate revenue, will depend entirely on the successful development, regulatory approval and commercialization of ACU193 by us or by one or more of our partners. The clinical and commercial success of ACU193 will depend on a number of factors, including the following:

- successful patient enrollment in INTERCEPT-AD and other clinical trials of ACU193;
- sufficiency of our financial and other resources to complete the necessary clinical trials;
- the results from INTERCEPT-AD and future clinical trials of ACU193;
- the frequency and severity of adverse effects of ACU193;
- the ability of third-party manufacturers to manufacture supplies of ACU193 and to develop, validate and maintain a commercial-scale manufacturing process that is compliant with current good manufacturing practices, or cGMP;
- our ability to demonstrate ACU193's safety and efficacy to the satisfaction of the FDA and foreign regulatory authorities in order to receive necessary marketing approvals for ACU193;
- whether we are required by the FDA to conduct additional clinical trials prior to the approval to market ACU193 and whether the FDA may disagree with the number, design, size, conduct, implementation or other aspects of our clinical trials;

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- whether the FDA may require implementation of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or post-approval;
- our ability to successfully commercialize ACU193, if approved for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;
- our success in educating physicians and patients about the benefits, administration and use of ACU193;
- acceptance of ACU193 as safe and effective by patients and the medical community;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;
- achieving and maintaining compliance with all regulatory requirements applicable to ACU193, including any required post-marketing approval commitments;
- effectively competing with other AD therapies;
- the effectiveness of our own or any future collaborators' marketing, pricing, coverage and reimbursement, sales and distribution strategies and operations;
- our ability to maintain our existing patents and obtain newly issued patents that cover ACU193 and to enforce such patents and other intellectual property rights in and to ACU193;
- our ability to avoid third-party intellectual property claims;
- the availability of third-party coverage and adequate reimbursement for ACU193 and any other product candidates, once approved; and
- a continued acceptable safety, tolerability and efficacy profile of ACU193 following approval.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of ACU193. If we are not successful in commercializing ACU193, or are significantly delayed in doing so, our business will be materially harmed.

### ***We have concentrated our research and development efforts on the treatment of AD, a field that has to date seen very limited success in drug development.***

We have focused our research and development efforts solely on developing effective treatments for AD. Collectively, efforts by pharmaceutical companies in the field of AD have seen very limited successes in drug development. There are few approved products available for patients with AD.

Our future success is highly dependent on the successful development of ACU193 for treating AD. The development and, if approved, commercialization of ACU193 subjects us to a number of challenges, including ensuring that we select an effective dose of ACU193, executing appropriate clinical trials to test for safety and efficacy and obtaining regulatory approval from the FDA and other regulatory authorities. We cannot be sure that ACU193, or any other product candidate we develop, will ultimately prove to be safe and effective, scalable or profitable. Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to prescribe novel treatments.

### ***Our approach to the potential treatment of AD is based on a novel therapeutic approach, which exposes us to unforeseen risks.***

There is no current scientific or general consensus on the causation of AD or method of action to treat AD. We have discovered and are developing ACU193, a humanized monoclonal antibody that selectively targets amyloid-beta oligomers, or A $\beta$ Os, to treat AD. Our approach is based on research on A $\beta$ Os, globular assemblies

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of the amyloid-beta, or A $\beta$ , peptide that are distinct from other forms of amyloid. A $\beta$ Os have gained scientific acceptance as primary toxins involved in the initiation and propagation of AD pathology. Based on the results of our nonclinical studies to date, we believe ACU193 is different from current and prior clinical-stage anti-amyloid drugs and product candidates based on its selectivity for A $\beta$ Os. We believe that this is a novel mechanism which has the potential to provide more clinically meaningful benefits, with a possible improved safety profile, as compared to approved therapies and product candidates in development. However, we may ultimately discover that ACU193 does not possess properties required for therapeutic effectiveness. We have no evidence regarding the efficacy, safety or tolerability of ACU193 in humans. We may spend substantial funds attempting to develop ACU193 or other product candidates and never succeed in doing so.

The market for any products that we successfully develop, if any, will also depend on the cost of the product. We do not yet have sufficient information to reliably estimate what it would cost to commercially manufacture ACU193, and the actual cost to manufacture ACU193 or any drug we develop in the future could materially and adversely affect the commercial viability of the drug. We may also find that the manufacture of our product candidates is more difficult than anticipated, resulting in an inability to produce a sufficient amount of our product candidates for our clinical trials or, if approved, commercial supply. If we do not successfully develop ACU193 or any other drug we develop with drug product cannot be reliably and economically manufactured at scale, we will not become profitable, which would materially and adversely affect the value of our common stock.

***Nonclinical and clinical drug development involves a lengthy, expensive and uncertain process. The results of nonclinical studies and early clinical trials are not always predictive of future results. ACU193 or any other product candidate that we advance into clinical trials may not achieve favorable results in later clinical trials, if any, or receive marketing approval.***

The research and development of product candidates is extremely risky. Only a small percentage of product candidates that enter the development process ever receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete nonclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain.

The results of nonclinical studies and early clinical trials are not necessarily predictive of future results and ACU193, or any other product candidate that we may develop, may not be further developed or have favorable results in later studies or trials. Clinical trial failure may result from a multitude of factors including, but not limited to, flaws in study design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. A number of companies in the pharmaceutical industry have suffered setbacks in the advancement of their product candidates into later-stage clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding results in earlier nonclinical studies or clinical trials. We intend to enroll 62 patients with early AD in INTERCEPT-AD. Even if the results of INTERCEPT-AD are positive, it may not be predictive of the results of outcomes in our later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in AD, where failure rates historically are higher than in most other disease areas.

In the event of negative or inconclusive results, we may decide, or regulatory authorities may require us, to conduct additional clinical trials or nonclinical studies. In addition, data obtained from clinical trials and nonclinical studies is susceptible to varying interpretations, and regulatory authorities may not interpret our data

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as favorably as we do, which may further delay, limit or prevent development efforts, clinical trials or marketing approval. Furthermore, as more competing product candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change.

If we are unable to complete nonclinical studies or clinical trials of ACU193 or future product candidates, due to safety concerns or otherwise, or if the results of these trials are not sufficient to convince regulatory authorities of their safety or efficacy, we will not be able to obtain marketing approval for commercialization on a timely basis or at all. Even if we are able to obtain marketing approval for ACU193 or any future product candidates, those approvals may be for indications or dose levels that deviate from our desired approach or may contain other limitations that would adversely affect our ability to generate revenue from sales of those product candidates. Moreover, if we are not able to differentiate our product candidate against other approved product candidates within the same class of drugs, or if any of the other circumstances described above occur, our business would be harmed and our ability to generate revenue from that class of drugs would be severely impaired.

### ***Clinical failure can occur at any stage of clinical development and we have never completed a clinical trial or submitted a biologics license application, or BLA, or marketing authorization application, or MAA.***

We are early in our development efforts for ACU193, and will need to successfully complete our ongoing and planned clinical trials, including pivotal clinical trials, in order to obtain FDA approval to market ACU193 or any other product candidate we seek to develop. Carrying out clinical trials and the submission of a successful BLA is a complicated process. Although members of the Acumen team have significant experience in clinical development of drugs through regulatory approval, as an organization, Acumen recently began conducting its first clinical trial, has no experience in conducting any clinical trials, has limited experience in preparing regulatory submissions and has not previously submitted a BLA for any product candidate.

In addition, we have had limited interactions with the FDA and cannot be certain how many clinical trials of ACU193 will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to BLA submission and approval of ACU193 or any other product candidate. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing ACU193 or any future product candidates we may develop, and failure to successfully complete any of these activities in a timely manner could have a material adverse impact on our business and financial performance.

### ***We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.***

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulatory authorities, Institutional Review Boards, or IRBs, or Ethics Committees, or ECs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or we may fail to reach a consensus with regulatory authorities on trial design; for example, our initial submission of the IND for ACU193 was placed on clinical hold by the FDA until we were able to address the FDA's initial concerns regarding potential off-target binding of ACU193 with an additional nonclinical tissue cross reactivity study, after which the FDA permitted us to initiate the Phase 1 clinical trial of ACU193 in the second quarter of 2021;
- regulatory authorities in jurisdictions in which we seek to conduct clinical trials may differ from each other on our trial design, and it may be difficult or impossible to satisfy all such authorities with one approach;

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- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different contract research organizations, or CROs, and trial sites;
- we may be unable to add or be delayed in adding a sufficient number of clinical trial sites and obtaining IRB or independent EC approval at each clinical trial site;
- clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulatory authorities may require us, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- difficulties in having subjects complete a clinical trial or returning for post-treatment follow-up;
- changes to clinical trial protocols;
- our third-party contractors, including clinical investigators, contract manufacturers and vendors may fail to comply with applicable regulatory requirements, lose their licenses or permits, or otherwise fail, or lose the ability to, meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulatory authorities or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate, and we may lack adequate funding to continue one or more clinical trials;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- clinical trial sites may deviate from clinical trial protocol or drop out of a clinical trial; and
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies.

***Adverse side effects, properties or other safety risks associated with ACU193 or any future product candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon further development, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if any.***

As is the case with pharmaceuticals generally, it is possible that there may be side effects and adverse events associated with the use of ACU193 or any future product candidates we may develop. Results of INTERCEPT-AD, or future clinical trials, could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics as the clinical trials progress to greater exposures and a larger number of patients. Undesirable side effects caused by, or unexpected or unacceptable characteristics associated with, ACU193 or any future product candidates we may develop, could result in the delay, suspension or termination of clinical trials by us, the FDA or other regulatory authorities, or IRBs for a number of reasons. We may also elect to limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less

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severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for such product candidate if approved. If we elect or are required to further delay, suspend or terminate any clinical trial of any product candidates we may develop, the commercial prospects of such product candidates will be harmed and our ability to generate drug revenues from any such product candidates will be delayed or eliminated.

It is possible that, as we test ACU193 in INTERCEPT-AD or future trials, or as the use of ACU193 becomes more widespread if it receives regulatory approval, we may identify additional adverse events that were not identified or not considered significant in our earlier trials. If such side effects become later known in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly. If we or others later identify undesirable side effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approval of ACU193 or any future product candidates;
- we may be required to recall a drug or change the way such drug is administered to patients;
- regulatory authorities may require additional warnings or statements in the labeling, such as a boxed warning or a contraindication or issue safety alerts, press releases or other communications containing warnings or other safety information about the product candidate, for example, field alerts to physicians and pharmacies;
- regulatory authorities may require us to implement a REMS to ensure that the benefits of the drug outweigh its risks, which 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;
- we may be required to change the way a drug is distributed or administered, conduct additional clinical trials or be required to conduct additional post-marketing studies or surveillance;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such product candidates from the market;
- we could be sued and held liable for harm caused to patients;
- sales of the drug may decrease significantly or ACU193 or any future drug could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of ACU193 or any future product candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

***We have experienced and may continue to experience delays or difficulties in the enrollment and retention of patients in clinical trials, which could delay or prevent our receipt of necessary regulatory approvals.***

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population and competition for patients eligible for our clinical trials with competitors which may have ongoing clinical trials for product candidates that are under development to treat the same indications as one or more of our product candidates or approved products for the conditions for which we are developing our product candidates.

Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our product candidates if we are unable

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to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, EMA or foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. We have experienced delays in clinical site initiation and patient enrollment as a result of the COVID-19 pandemic. Subject enrollment is affected by other factors including:

- the severity and difficulty of diagnosing the disease under investigation;
- the eligibility and exclusion criteria for the trial in question;
- the size of the patient population and process for identifying patients;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the design of the trial protocol;
- the perceived risks and benefits of the product candidate in the trial, including relating to cell therapy approaches;
- the availability of competing commercially available therapies and other competing therapeutic candidates' clinical trials for the disease or condition under investigation;
- the willingness of patients to be enrolled in our clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- further disruptions caused by the ongoing COVID-19 pandemic, including further difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance. Additionally, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

***Interim, “topline” and preliminary results from our clinical trials that we announce or publish from time to time may change as more data become available and is subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publish interim, topline or preliminary results from our clinical trials. Interim results 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. Preliminary or topline results 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, interim and preliminary data should be viewed with caution until the final data are reported. Differences between preliminary, topline or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly. 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

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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.

Further, others, including regulatory agencies may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular development program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed meaningful by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our business prospects.

***We cannot be certain that ACU193 or any of our future product candidates will receive regulatory approval, and without regulatory approval we will not be able to market our product candidates.***

We currently have no product candidates approved for sale and we cannot guarantee that we will ever have marketable product candidates. ACU193 is our sole product candidate designed for the treatment of AD. Our ability to generate revenue related to sales of ACU193, if ever, will depend on the successful development and regulatory approval of ACU193 for the treatment of AD and, potentially, other indications.

The development of a product candidate and its approval and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to extensive regulation by the FDA, the EMA and regulatory authorities in other countries, with regulations differing from country to country. We are not permitted to market our product candidates in the United States, Europe or other countries until we receive approval of a BLA from the FDA or MAA from the EMA, respectively. We have not submitted any marketing applications for ACU193.

BLAs and MAAs must include extensive nonclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. BLAs and MAAs must also include significant information regarding the chemistry, manufacturing and controls for the drug. Obtaining approval of a BLA or a MAA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. The FDA and the EMA review processes can take years to complete and approval is never guaranteed. If we submit a BLA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA. Regulators of other jurisdictions, such as the EMA, have their own procedures for approval of product candidates.

Even if a drug is approved, the FDA or the EMA, as the case may be, may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of product candidates with which we must comply prior with marketing in those countries. Obtaining regulatory approval for marketing of a product candidate in one country does not ensure that we will be able to obtain regulatory approval in any other country. In addition, delays in approvals or rejections of marketing applications in the United States, Europe or other countries may be based upon many factors, including regulatory requests for additional analyses, reports, data, nonclinical studies and clinical trials, regulatory questions regarding different interpretations of data and results, changes in regulatory policy during the period of drug development and the emergence of new information regarding ACU193 or other product candidates we may develop in the future. Also, regulatory approval for any of our product candidates may be withdrawn.

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We are currently conducting the INTERCEPT-AD Phase 1 trial in patients with AD. Before we submit a BLA to the FDA or a MAA to the EMA for ACU193 for the treatment of patients with AD, we will be required to successfully complete our Phase 1 clinical trial and at least one additional late-stage clinical trial. The FDA generally requires two pivotal clinical trials to support approval. In addition, we must scale up manufacturing and complete other standard nonclinical and clinical studies. We cannot predict whether our current or future trials will be successful or whether regulators will agree with our conclusions regarding the nonclinical studies and the clinical trials we conduct.

***We may in the future conduct clinical trials for our product candidates outside the United States, and the FDA, EMA and other foreign regulatory authorities may not accept data from such trials.***

We may in the future choose to conduct one or more of our clinical trials outside the United States, including in Europe. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA or applicable foreign regulatory authorities may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to current good clinical practice, or CGCP, regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any other foreign regulatory authority will accept data from trials conducted outside of the United States or the 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.

***We may not be successful in our efforts to build a pipeline of additional product candidates.***

Our sole product candidate is ACU193. We may not be able to identify and successfully develop new product candidates in addition to ACU193. Even if we are successful in building our product pipeline, the potential product candidates that we identify may not be suitable for clinical development or, if deemed suitable for clinical development, successful in any clinical trials. For example, product candidates may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be successfully developed, much less receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates, we will not be able to obtain product revenue in future periods, which would result in significant harm to our financial position and adversely affect our stock price.

***If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed.***

From time to time, we may estimate the timing of the accomplishment of various scientific, clinical, regulatory, manufacturing and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of nonclinical studies and clinical trials and the submission of regulatory filings, including BLA submissions. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are, and will be, based on a variety of assumptions. The actual timing of these milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates.

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### ***Our business and operations have been and may continue to be adversely affected by the evolving and ongoing COVID-19 global pandemic.***

Our business and operations have been and may continue to be adversely affected by the effects of the evolving COVID-19 virus, which was declared a global pandemic by the World Health Organization in March 2020. The COVID-19 pandemic has resulted in travel and other restrictions in order to reduce the spread of the disease, including public health directives and orders in the United States and the European Union that, among other things and for various periods of time, directed individuals to shelter at their places of residence, directed businesses and governmental agencies to cease non-essential operations at physical locations, prohibited certain non-essential gatherings and events and ordered cessation of non-essential travel. Future remote work policies and similar government orders or other restrictions on the conduct of business operations related to the COVID-19 pandemic may negatively impact productivity and may disrupt our ongoing research and development activities and our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. Further, such orders also may impact the availability or cost of materials, which would disrupt our supply chain and manufacturing efforts and could affect our ability to conduct ongoing and planned clinical trials and preparatory activities.

Our Phase 1 clinical trial has been and will continue to be affected by the COVID-19 pandemic. We have experienced delays in clinical site activation and patient enrollment in INTERCEPT-AD, which we believe is a result of the COVID-19 pandemic, which has delayed the expected timeline of INTERCEPT-AD. We believe that the COVID-19 pandemic has negatively impacted our ability to activate clinical trial sites as planned as a result of trial sites, especially in certain geographies within the United States that have been experiencing relatively higher rates of COVID-19, requiring more time to implement site activation requirements and enrollment efforts being impeded by lower-than-expected willingness of potential patients to visit active sites for screening. We may experience further related disruptions in the future that could severely impact our clinical trials, including:

- interruptions in our ability to obtain drug supply for our clinical trials;
- interruptions in our ability to obtain clinical test kits for our clinical trials;
- delays in receiving authorizations from regulatory authorities to initiate our planned clinical trials;
- further delays, difficulties or a suspension in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- further delays or difficulties in enrolling and retaining patients in our 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;
- changes in local regulations as part of a response to the COVID-19 pandemic that may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs or to discontinue the clinical trials altogether;
- interruption of key clinical trial activities, such as clinical trial site monitoring, and the ability or willingness of subjects to travel to trial sites due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;

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- interruptions of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations, or CMOs, due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- 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; and
- refusal of the FDA to accept data from clinical trials in these affected geographies.

For example, one clinical trial site was closed for one week in January 2022 due to staff infections with COVID-19. The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, the continued widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the COVID-19 pandemic impacts our business and operations, including our clinical development and regulatory efforts, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate geographic spread of the disease, the duration of the outbreak, the duration and effect of business disruptions and the short-term effects and ultimate effectiveness of the travel restrictions, quarantines, social distancing requirements and business closures in the United States and other countries to contain and treat the disease. Accordingly, we do not yet know the full extent of delays or impacts on our business, our clinical and regulatory activities, healthcare systems or the global economy as a whole. However, these impacts have adversely affected and continue to adversely affect our business, financial condition, results of operations and growth prospects.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this “Risk Factors” section.

### ***We may develop ACU193 and future product candidates for use in combination with other therapies, which could expose us to additional regulatory risks.***

We may develop ACU193 and future product candidates for use in combination with one or more other approved therapies for AD. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risk that the FDA, EMA or comparable foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially.

Further, we will not be able to market and sell any product candidate we develop in combination with an unapproved AD therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved AD therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

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

As product candidates proceed through nonclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing

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methods and formulation, are altered along the way in an effort to optimize processes and product characteristics. For example, through our CMOs we plan to implement a larger scale ACU193 manufacturing process with increased yields and at larger scale production levels. We are also developing a lyophilized drug product form and refrigeration-stable formulation prior to the initiation of Phase 2 human clinical studies.

Such changes carry the risk that they will not achieve our intended objectives. Any such changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. 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 commence sales and generate revenue. In addition, we may be required to make significant changes to our upstream and downstream processes across our pipeline, which could delay the development of our future product candidates.

### **Risks Related to the Commercialization of our Product Candidates**

***Even if ACU193 or any other product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.***

If ACU193 or any other product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the clinical indications for which our product candidates are licensed;
- the efficacy, safety and potential advantages compared to alternative treatments;
- our ability to demonstrate the advantages of our product candidates over other medicines;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- product labeling or product insert requirements of the FDA, EMA or other foreign regulatory authorities, including any limitations or warnings contained in a product's approved labeling, including any black box warning or REMS;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- our ability to commercialize the product either in collaboration with a third party or on our own;
- the timing of market introduction of our product candidates as well as competitive products;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for ACU193 and any other product candidates, once approved;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

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***If we are unable to enter into a commercial collaboration or, alternatively, establish internal sales, marketing and distribution capabilities, for ACU193 or any other product candidate that may receive regulatory approval, we may not be successful in commercializing those product candidates if and when they are approved.***

We do not have sales or marketing infrastructure. To achieve commercial success for ACU193 or any other product candidate for which we may obtain marketing approval, we will either need to establish a commercial collaboration with a pharmaceutical company that has a sales and marketing organization or we will be required to develop these capabilities internally. There are risks and limitations associated with entering into a commercial collaboration. For example, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. Even if we are able to enter into a collaboration, our revenue and profitability, if any, are likely to be significantly lower than if we were able to successfully commercialize a product ourselves. In addition, we likely would 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.

At the same time, there are significant risks associated with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This would be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to market our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians in order to educate physicians about our product candidates, once approved;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we do not establish sales, marketing and distribution capabilities successfully, either in collaboration with third parties or on our own, we will not be successful in commercializing our product candidates.

***The affected populations for ACU193 or any other product candidate we may develop may be smaller than we or third parties currently project, which may affect the addressable markets for our product candidates.***

Our projections of the number of people who have AD, as well as the subset of people with AD who have the potential to benefit from treatment with ACU193, are estimates based on our knowledge and understanding of the disease. These estimates may prove to be incorrect and new studies may further reduce the estimated incidence or prevalence of the disease or narrow the universe of patients who would be understood to potentially benefit for treatment with ACU193, if approved. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our product candidates or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects. Further, even if we obtain approval for ACU193, the FDA or other regulators may limit their approved indications to more narrow uses or subpopulations within the populations for which we are targeting development of ACU193.

The total addressable market opportunity for our product candidates will ultimately depend upon a number of factors including the diagnosis and treatment criteria included in the final label, if approved for sale in specified

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indications, acceptance by the medical community, patient access and product pricing and reimbursement. Incidence and prevalence estimates are frequently based on information and assumptions that are not exact and may not be appropriate, and the methodology is forward-looking and speculative.

The estimated incidence and prevalence ranges included herein have been derived from data from multiple sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Accordingly, the incidence and prevalence estimates included in this Annual Report on Form 10-K should be viewed with caution. Further, the data and statistical information used in this Annual Report on Form 10-K, including estimates derived from them, may differ from information and estimates made by our competitors or from current or future studies conducted by independent sources.

***Off-label use or misuse of our products may harm our reputation in the marketplace, result in injuries that lead to costly product liability suits, and subject us to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with any product.***

If ACU193 or any other product candidate we develop is approved by the FDA, we may only promote or market our product candidate for its specifically approved indications and consistent with its approved labeling. We or any third-party collaborator responsible for commercialization of our products will train the marketing and sales forces responsible for our products against promoting them for uses outside of their approved indications for use, known as “off-label uses.” However, neither we, nor any future commercial partner of ours will be able to prevent a physician from using our products off-label, when in the physician’s independent professional medical judgment, he or she deems it appropriate. Furthermore, the use of our products for indications other than those approved by the FDA may not effectively treat such conditions. Any such off-label use of our product candidates could harm our reputation in the marketplace among physicians and patients. There may also be an increased risk of injury to patients if physicians attempt to use our products for these uses for which they are not approved, which could lead to product liability suits that might require significant financial and management resources and that could harm our reputation.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the U.S. Federal Trade Commission, the Department of Justice, or DOJ, the Office of Inspector General of the U.S. Department of Health and Human Services, or HHS, state attorneys general, members of the U.S. Congress and the public. Additionally, advertising and promotion of any product candidate that obtains approval outside of the United States will be heavily scrutinized by comparable foreign entities and stakeholders. Violations, including actual or alleged promotion of our products for unapproved or off-label uses, are subject to enforcement or warning letters, mandates to issue corrective information to healthcare practitioners, inquiries, investigations, injunctions and civil and criminal sanctions by the FDA, DOJ or comparable foreign bodies. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and as enjoined several companies from engaging in an off-label promotion.

***We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more effective than ours.***

The development and commercialization of new drugs is highly competitive. Moreover, the AD field is characterized by strong competition and a strong emphasis on intellectual property. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

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If approved, ACU193 will compete with therapies currently approved for the treatment of AD, which have primarily been developed to treat the symptoms of AD rather than the underlying cause of the disease, such as memantine and cholinesterase inhibitors. ACU193 may also compete with one or more potentially disease-modifying therapeutics that target A $\beta$  or amyloid plaques, the most advanced of which is Biogen Inc.'s Aduhelm (aducanumab), which the FDA approved in June 2021 under the accelerated approval pathway, which allows for earlier approval of drugs that treat serious conditions, and that fill an unmet medical need based on a surrogate endpoint. Regulatory approval of aducanumab is pending in Europe and Japan. Eisai Co., Ltd. (lecanamab), Eli Lilly and Company (donenamab), and Roche Holding AG (gantenerumab), are anticipated to complete Phase 3 studies in 2022 and 2023 and may obtain FDA approval under the accelerated approval pathway or full approval.

Other companies known to be developing therapies with A $\beta$ -, A $\beta$ O- amyloid plaque-related targets include Alzheon, Inc., Alzinova AB, Chugai Pharmaceutical Co. Ltd., Cognition Therapeutics, Inc., Eisai Co., Ltd., Eli Lilly and Company, Grifols, S.A., KalGene Pharmaceuticals, Inc., Neurimmune AG, Novartis AG, ProMIS Neurosciences, Inc., Prothena Biosciences, Inc., Roche Holding AG (including Genentech, its wholly owned subsidiary) Vaxxinity, Inc., Vivoryon Therapeutics N.V. and Wren Therapeutics, Inc. Additionally, ACU193, if approved, may also compete with other potential therapies intended to address underlying causes of AD that are being developed by several companies, including AbbVie Inc., AC Immune SA, Alector, Inc., Anavex Life Sciences Corp., Anovis Bio, Inc., Athira Pharma, Inc., Biohaven Pharmaceuticals, Inc., Cassava Sciences, Inc., Cortexyme, Inc., Denali Therapeutics, Inc., Johnson & Johnson (including Janssen, its wholly-owned subsidiary) and Takeda Pharmaceutical Co. Ltd.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, nonclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved product candidates than we do. 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. 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. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any product candidates that we may develop. Furthermore, currently approved product candidates could be discovered to have application for treatment of AD, which could give such product candidates significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours from the FDA, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, product candidates or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

If our competitors market product candidates that are more effective, safer or less expensive than our product candidates, if approved, or that reach the market sooner than our product candidates, we may not achieve commercial success. In addition, the pharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or product candidates developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

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### ***Any product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.***

If we are successful in achieving regulatory approval to commercialize any biologic product candidate that we develop, it may face competition from biosimilar products. In the United States, ACU193 is, and we expect that any other product candidate we may seek to develop likely will be, regulated by the FDA as a biologic product subject to approval under the BLA pathway. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four (4) years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed by the FDA. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own nonclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

There is a risk that any of our product candidates approved as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing. If competitors are able to obtain marketing approval for biosimilars referencing our candidates, if approved, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences.

### ***The success of our product candidates will depend significantly on coverage and adequate reimbursement or the willingness of patients to pay for these therapies.***

We believe our success depends on obtaining and maintaining coverage and adequate reimbursement from third-party payors for ACU193 and any other product candidate we successfully develop, and the extent to which patients will be willing to pay out-of-pocket for such products, in the absence of reimbursement for all or part of the cost. In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (e.g., Medicare, Medicaid, TRICARE), managed care providers, private health insurers, health maintenance organizations, and other organizations is essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a payor-by-payor basis. One payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage, and adequate reimbursement. The principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the HHS. CMS decides whether and to what extent products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Third-party payors determine which products and procedures they will cover and establish reimbursement levels. Even if a third-party payor covers a particular product or procedure, the resulting reimbursement payment rates may not be adequate. Patients who are treated in-office for a medical condition generally rely on third-party payors to reimburse all or part of the costs associated with the procedure, including costs associated with products used during

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the procedure, and may be unwilling to undergo such procedures in the absence of such coverage and adequate reimbursement. Physicians may be unlikely to offer procedures for such treatment if they are not covered by insurance and may be unlikely to purchase and use our product candidates, if approved, for our stated indications unless coverage is provided and reimbursement is adequate. In addition, for products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs.

Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a procedure is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental nor investigational. Further, increasing efforts by third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Foreign governments also have their own healthcare reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to the treatments in which our products are used under any foreign reimbursement system.

There can be no assurance that ACU193 or any other product candidate, if approved for sale in the United States or in other countries, will be considered medically reasonable and necessary, that it will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available or that reimbursement policies and practices in the United States and in foreign countries where our products are sold will not adversely affect our ability to sell our product candidates profitably, if they are approved for sale.

### ***Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.***

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or drugs that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards paid to trial participants or patients;
- loss of revenue;

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- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

### ***We are subject to a variety of privacy and data security laws, and our failure to comply with them could harm our business.***

We maintain a large quantity of sensitive information, including confidential business and personal information in connection with the conduct of our clinical trials and related to our employees, and we are subject to laws and regulations governing the privacy and security of such information. In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect our business and is expected to increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations could apply to our operations or the operations of our partners, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations (e.g. Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and regulations promulgated thereunder. Depending on the facts and circumstances, we could be subject to significant penalties if we obtain, use or disclose individually identifiable health information in a manner that is not authorized or permitted by HIPAA.

In Europe, the General Data Protection Regulation, or GDPR, took effect in May 2018. The GDPR governs the collection, use, disclosure, transfer or other processing of personal data of individuals within the European Economic Area, or EEA, including clinical trial data. Among other things, the GDPR imposes requirements regarding the security of personal data and notification of data processing obligations to the competent national data processing authorities, requires having lawful bases on which personal data can be processed, requires changes to informed consent practices, and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR increases the scrutiny of transfers of personal data from the EEA to the United States and other jurisdictions that the European Commission does not recognize as having “adequate” data protection laws. In July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-U.S. Privacy Shield and imposing further restrictions on use of the standard contractual clauses, which could increase our costs and our ability to efficiently process personal data from the EEA. The GDPR imposes substantial fines for breaches and violations (up to the greater of €20 million or four percent (4%) of our consolidated annual worldwide gross revenue) and confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. Relatedly, following the United Kingdom's, or U.K., withdrawal from the EEA and the European Union, and the expiry of the transition period, which ended on January 1, 2021, companies have to comply with both the GDPR and the GDPR as incorporated into U.K. national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or four percent (4%) of global turnover. On January 1, 2021, the U.K. became a third country for the purposes of the GDPR.

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The relationship between the U.K. and the European Union in relation to certain aspects of data protection law remains unclear. For example, it is unclear how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk. Pursuant to the EU-U.K. Trade and Cooperation Agreement of December 24, 2020, transfers of personal data from the European Union to the U.K. may continue to take place without a need for additional safeguards during a further transition period, to expire on (1) the date on which an adequacy decision with respect to the U.K. is adopted by the EU Commission; or (2) the expiry of four (4) months, which shall be extended by a further two (2) months unless either the European Union or the U.K. objects. It remains unclear whether the EU Commission will adopt an adequacy decision with respect to the U.K. In the absence of such decision after the expiry of the additional transition period, we may need to put in place additional safeguards for transfers of personal data from the European Union to the U.K., such as standard contractual clauses approved by the EU Commission.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations.

Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly. In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements. For example, California enacted the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020, became enforceable by the California Attorney General on July 1, 2020, and has been dubbed the first “GDPR-like” law in the United States. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act, or CPRA, recently passed in California. The CPRA will impose additional data protection obligations on companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Although the CCPA currently exempts certain health-related information, including clinical trial data, the CCPA and the CPRA may increase our compliance costs and potential liability. Similar laws have been proposed in other states and at the federal level, and if passed, such laws may have potentially conflicting requirements that would make compliance challenging.

***If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could seriously harm 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. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste. We 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, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain

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environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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 carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could seriously harm our business.

### **Risks Related to Our Dependence on Third Parties**

*We currently rely on CMOs to supply components of and manufacture ACU193. The loss of any of these CMOs or the failure of any of them to meet their obligations to us could affect our ability to develop ACU193 in a timely manner.*

We do not own or operate manufacturing facilities and rely on a limited number of CMOs to manufacture our product candidates. We have entered into agreements with third-party CMOs to manufacture ACU193 and supply the Phase 1 clinical trial material, in compliance with applicable regulatory and quality standards. We intend to continue to rely on third-party CMOs to manufacture our clinical supply for the foreseeable future. Any replacement of a third-party CMO could require significant effort and expertise because there may be a limited number of qualified replacements. Any delays in obtaining adequate clinical supply that meets the necessary quality standards may delay our development or commercialization.

Our reliance on CMOs for manufacturing activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations. Under certain circumstances, these CMOs may be entitled to terminate their engagements with us. If a CMO terminates its engagement with us, or does not successfully carry out its contractual duties, meet expected deadlines or manufacture ACU193 or any other product candidate that we develop in accordance with regulatory requirements, or if there are disagreements between us and a CMO, we may not be able to complete, or may be delayed in completing, the nonclinical studies required to support clinical trials required for approval of ACU193 or any other product candidate. In such instance, we may need to enter into an appropriate replacement third-party relationship, which may not be readily available or available on acceptable terms, which would cause additional delay or increased expense prior to the approval of ACU193 or any future product candidate and would thereby have a negative impact on our business, financial condition, results of operations and prospects.

We may rely on additional third parties to manufacture ingredients of our product candidates in the future and to perform quality testing. Reliance on CMOs and other third-party service providers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- reduced control for certain aspects of manufacturing activities;
- termination or nonrenewal of the applicable manufacturing and service agreements in a manner or at a time that is costly or damaging to us;
- the possible breach by our third-party manufacturers and service providers of our agreements with them;

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- the failure of our third-party manufacturers and service providers to comply with applicable regulatory requirements;
- disruptions to the operations of our third-party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, impact our ability to successfully commercialize any of our product candidates or otherwise harm our business, financial condition, results of operations, stock price and prospects. Some of these events could be the basis for FDA or other regulatory authority action, including injunction, recall, seizure or total or partial suspension of product manufacture.

***We intend to rely on CROs and other third parties to conduct, supervise and monitor a significant portion of our research and nonclinical testing and clinical trials for ACU 193 or any future product candidates, and if those third parties do not successfully carry out their contractual duties, comply with regulatory requirements or otherwise perform satisfactorily, we may not be able to obtain regulatory approval or commercialize product candidates, or such approval or commercialization may be delayed, and our business may be substantially harmed.***

We intend to engage CROs and other third parties to conduct our planned nonclinical studies or clinical trials, including INTERCEPT-AD and future clinical trials of ACU193, and to monitor and manage data. We expect to continue to rely on third parties, including clinical data management organizations, medical institutions and clinical investigators, in the future. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. Further, the performance of our CROs and other third parties conducting our trials may also be interrupted by the ongoing COVID-19 pandemic, including due to travel or quarantine policies, heightened exposure of a CRO or clinical site or other vendor staff who are healthcare providers to COVID-19 or prioritization of resources toward the pandemic.

In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

We rely on these parties for execution of our nonclinical studies and clinical trials and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and

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protocols for the trial. Moreover, the FDA requires us to comply with GCPs, which are standards for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional 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 clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process, or may result in fines, adverse publicity and civil and criminal sanctions.

We also are required to register certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval for ACU193 or any other product candidate we develop.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue.

***If any of our third-party manufacturers encounter difficulties in production of ACU193 or any future product candidate we develop, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or, if approved, for commercial sale could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.***

The processes involved in manufacturing ACU193 and any other product candidate we may develop are highly regulated and subject to multiple risks. As product candidates are developed through nonclinical 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 our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. 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 potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our third-party manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business.

In order to conduct clinical trials of our product candidates, or supply commercial product candidates, if approved, we will need to manufacture them in both small and large quantities. We currently rely on third parties to manufacture ACU193 for clinical trial purposes, and our manufacturing partners will have to modify and scale-up the manufacturing process when we transition to commercialization of our product candidates. Our manufacturing partners may be unable to successfully modify or scale-up the manufacturing capacity for any of

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our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our manufacturing partners are unable to successfully scale-up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risks would apply to our internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner.

In addition, the manufacturing process for any product candidates that we may develop is subject to FDA, EMA and foreign regulatory requirements, and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA and foreign regulatory authority requirements, including complying cGMPs on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce product candidates in accordance with the requirements of the FDA, EMA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such product candidates. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our third-party contract manufacturers will be able to manufacture the approved product in accordance with the requirements of the FDA, EMA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. 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 trial 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. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

***We will likely seek collaborations with third parties for the development or commercialization of ACU193 or any future product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates, including ACU193.***

We will likely seek third-party collaborators for the commercialization of ACU193 and any of our future product candidates, in the United States and may enter into collaboration agreements for the development and commercialization of any of our product candidates outside the United States. In the United States, commercialization partners are likely to include large biotechnology or pharmaceutical companies. Our likely collaborators outside the United States would most likely include regional and national pharmaceutical companies and biotechnology companies. If we enter into such 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 revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;

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- 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 ours;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise 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. If any future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any 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 similar regulatory authorities outside the United States, 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 products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. 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.

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We may not be able to negotiate additional 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 such product candidate, reduce or delay its development program or one or more of our other development programs, delay its 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 revenue.

### ***We may be exposed to a variety of international risks that could materially adversely affect our business.***

We may enter into agreements with third parties for the development and commercialization of product candidates in international markets. International business relationships will subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- differing regulatory requirements for product approvals internationally;
- potentially reduced protection for intellectual property rights;
- potential third-party patent rights in countries outside of the United States;
- the potential for so-called “parallel importing,” which is what occurs when a local seller, faced with relatively high local prices, opts to import goods from another jurisdiction with relatively low prices, rather than buying them locally;
- pricing pressure and differing reimbursement regimes;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability, particularly in non-U.S. economies and markets, including several countries in Europe;
- compliance with tax, employment, immigration and labor laws for employees traveling abroad;
- taxes in other countries;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in 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, or natural disasters, including earthquakes, volcanoes, typhoons, pandemics, epidemics, floods, hurricanes and fires.

### ***If we engage in acquisitions, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.***

Although we currently have no plans to do so, we may attempt to acquire businesses, technologies or drug candidates that we believe are a strategic fit with our business. If we do undertake any acquisitions, the process of integrating an acquired business, technology or drug candidates into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management’s attention from our core business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders.

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Future acquisitions could also result in the incurrence of debt, contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits or synergies of any acquisition.

### **Risks Related to Our Intellectual Property**

*If we are unable to obtain and maintain sufficient intellectual property protection for our product candidate, and other proprietary technologies we develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidate, and other proprietary technologies if approved, may be adversely affected.*

Our commercial success will depend in part on our ability to obtain and maintain a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidate, and other proprietary technologies we develop. If we are unable to obtain or maintain patent protection with respect to our product candidate, and other proprietary technologies we may develop, our business, financial condition, results of operations, and prospects could be materially harmed.

The patent position of biotechnology and pharmaceutical companies is highly uncertain and involves complex legal, scientific, and factual questions and has been the subject of frequent litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our patent applications may not result in patents being issued that protect our product candidate and other proprietary technologies we may develop or that effectively prevent others from commercializing competitive technologies and products. Further, no consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in many jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in

the patents that may be issued from the applications we may own or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

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

- the United States Patent and Trademark Office, or 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;
- issued patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, or may otherwise 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 will limit, interfere with, or eliminate our ability to make, use and sell our product candidate;

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- other parties may have designed around our claims or developed technologies that may be related or competitive to ours, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications and/or patents, either by claiming the same composition of matter, methods or formulations or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any product candidate that we may develop;
- because 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 or our licensors were the first to file any patent application related to our product candidate and other proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of any application with an effective filing date before March 16, 2013;
- there may be significant pressure on the U.S. 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 U.S. courts, allowing foreign competitors a better opportunity to create, develop, and market competing product candidate in those countries.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, or maintain all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. 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, corporate collaborators, outside scientific collaborators, CROs, contract 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 for such output. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our product candidate and other proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations. For example:

- others may be able to make compounds that are similar to our product candidate but that are not covered by the claims of our patents;
- we might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents that we obtain may not provide us with any competitive advantages;

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- we may not develop additional proprietary technologies that are patentable;
- our competitors might conduct research and development activities in countries where we do not have patent rights or where patent protection is weak and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that we will be able to successfully commercialize our product candidate on a substantial scale, if approved, before the relevant patents that we own or license expire; or
- the patents of others may have an adverse effect on our business.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

We cannot be certain that claims in an issued patent covering our product candidate will be considered patentable by the USPTO, courts in the United States, or by patent offices and courts in foreign countries. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property internationally.

The strength of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and can be uncertain. Patent applications that we file or in-license may fail to result in issued patents with claims that cover our product candidate in the United States or in foreign countries. Even if such patents do successfully issue, third parties may challenge the ownership, validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to our patents could deprive us of exclusive rights necessary for the successful commercialization of our product candidate. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property, provide exclusivity for our product candidate or prevent others from designing around our claims. If the breadth or strength of protection provided by our patents with respect to our product candidate is threatened, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize, our product candidate.

For U.S. patent applications in which claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management and other employees.

For U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, or America Invents Act, was signed into law. The America Invents Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO is developing regulations and procedures to govern the administration of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and in particular, the “first to file” provisions, were enacted on March 16, 2013. This will require us to be cognizant going forward of the time from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. It remains unclear what impact the America Invents Act will have on the operation of our business.

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As such, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

### ***Patent terms may be inadequate to protect our competitive position on our product candidate for an adequate amount of time.***

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. When the terms of all patents covering our product candidate expire, our business may become subject to competition from competitive products, including biosimilar version of our products.

Our product candidate is protected by patents covering the composition of matter and methods of using ACU193. The patents in this portfolio are predicted to expire in 2031 without taking into account any possible extensions and assuming payment of all appropriate maintenance, renewal, annuity, or other governmental fees. We cannot be certain that we will file and, if filed, obtain patent protection for our product candidate beyond our rights in the current ACU193 patent portfolio. If we are unable to obtain additional patent protection on ACU193, our primary protection from biosimilar market entry will be limited to regulatory biologic exclusivity.

### ***If we do not obtain patent term extension for our product candidate our business may be materially harmed.***

Depending upon the timing, duration, and specifics of any FDA marketing approval of our product candidate, one or more of patents issuing from U.S. patent applications that we file or license may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term, or PTE, of up to five years as compensation for 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, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign jurisdictions, such as in Europe under Supplemental Protection Certificate, or SPC. If we encounter delays in our development efforts, including our future clinical trials, the period of time during which we could market our product candidate under patent protection would be reduced. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced.

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

Licensing of intellectual property rights is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property rights 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 rights of the licensor that are not subject to the license agreement;

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- our right to sublicense intellectual property rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidate, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms and/or to secure our rights to the licensed intellectual property, our business, results of operations, financial condition, and prospects may be adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer adverse consequences.

We were a party to a collaboration agreement with Merck to research, discover and develop certain technology related to amyloid beta-derived diffusible ligands, or ADDLs. This collaboration was initiated in 2003 and was later terminated by Merck in 2011. During the collaboration, ACU193, an ADDL-binding antibody, was developed and intellectual property was filed by Merck. Under the surviving provisions of the collaboration agreement, Merck exclusively licensed Merck's interest in patent rights claiming ADDL antibodies, ADDL antigens and/or products to Acumen. If a dispute were to arise in the future as to our rights to the intellectual property under the agreement, our ability to commercialize ACU193 may be jeopardized.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on any issued patents and/or applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ outside counsel to pay these fees due to foreign patent agencies. While an inadvertent lapse may sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, 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. In such an event, our competitors might be able to enter the market with similar or identical products or technology earlier than should otherwise have been the case, which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidate.***

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents. Our patent rights may be affected by developments or uncertainty in U.S. or foreign patent statutes, patent case law, USPTO rules and regulations or the rules and regulations of foreign patent offices. Obtaining and enforcing patents in the biotechnology and pharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States may, at any time, enact changes to U.S. patent law and regulations, including by legislation, by regulatory rule-making, or by judicial precedent, that adversely affect the scope of patent protection available and weaken the rights of patent owners to obtain patents, enforce patent infringement and obtain injunctions and/or damages. For example, the scope of patentable subject matter under 35 U.S.C. 101 has evolved significantly over the past several years as the Court of Appeals for the Federal

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Circuit and the Supreme Court issued various opinions, and the USPTO modified its guidance for practitioners on multiple occasions. Other countries may likewise enact changes to their patent laws in ways that adversely diminish the scope of patent protection and weaken the rights of patent owners to obtain patents, enforce patent infringement, and obtain injunctions and/or damages.

Further, the United States and other governments may, at any time, enact changes to law and regulation that create new avenues for challenging the validity of issued patents. For example, the America Invents Act created new administrative post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings that allow third parties to challenge the validity of issued patents. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. 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. 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 U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Patents are of national or regional effect. Filing, prosecuting, and defending patents on our product candidate, and other proprietary technologies we develop in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights in the same manner and to the same extent as 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. Competitors may use our technologies in jurisdictions where we 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 of such patent protection is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The requirements for patentability may differ in certain countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of claimed drug. In India, unlike the United States, there is no link between regulatory approval for a drug and its patent status. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors.

In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities.

Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology or pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally.

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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 at risk of being invalidated or interpreted narrowly, 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.

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

We may be subject to claims that former employees (including former employees of our licensors), collaborators or other third parties have an interest in our patents rights, trade secrets, or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. For example, we may have inventorship disputes arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidate or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business, financial condition, results of operations and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

### ***We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through in-licenses.***

Presently we have intellectual property rights to our product candidate, through a license from Merck. We also have an intellectual property license through a license with Northwestern University and, if this agreement remains in place, we could be required to pay low single digit royalties to Northwestern in the future. Because our program may require the use of additional proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidate may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license, on reasonable terms, proprietary rights related to any compositions, formulations, methods of use, processes or other intellectual property rights from third parties that we identify as being necessary for our product candidate. Even if we are able to obtain a license to such proprietary rights, 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 develop or license replacement technology.

Where we obtain licenses from or collaborate with third parties, we may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. 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 candidate, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidate may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to the date upon which we assumed control over

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patent prosecution. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business, or in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such application.

Moreover, we will likely have obligations under our current or future licenses, including making royalty and milestone payments, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business. Our business would suffer if any such licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical or similar to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

The licensing and acquisition of third-party proprietary rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party proprietary rights that we may consider necessary or attractive in order to commercialize our product candidate. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we have collaborated and may in the future collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate an exclusive license to any of the institution's proprietary rights in technology resulting from the collaboration. Regardless of such option to negotiate a license, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer, on an exclusive basis, their proprietary rights to other parties, potentially blocking our ability to pursue our program. In addition, disputes may arise under our existing or future license agreements with these institutions or with other counterparties which may, among other things, lead to the termination or renegotiation of these agreements, or otherwise require us to incur significant financial obligations.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us, either on reasonable terms, or at all. We also may 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 obtain rights to required third-party intellectual property rights on commercially reasonable terms, our ability to commercialize our products, and our business, financial condition, and prospects for growth, could suffer.

### ***Third-party claims alleging intellectual property infringement may prevent or delay our drug discovery and development efforts.***

Our success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including inter partes review, interference and reexamination proceedings

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before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. The America Invents Act introduced new procedures including inter partes review and post grant review. The implementation of these procedures brings uncertainty to the possibility of challenges to our patents in the future and the outcome of such challenges. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidate. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to our product candidate may give rise to claims of infringement of the patent rights of others.

The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. We cannot assure you that any of our current or future product candidate will not infringe existing or future patents. We may not be aware of patents that have already issued that a third party might assert are infringed by one of our current or future product candidate.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents of which we are currently unaware with claims to materials, compositions, formulations, methods of manufacture or methods for treatment related to our product candidate, or the use or manufacture of our product candidate. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be currently pending third-party patent applications which may later result in issued patents that our product candidate, and other proprietary technologies may infringe, or which such third parties claim are infringed by the use of our technologies. Parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidate. Defense of these claims, regardless of their merit, could involve substantial expenses and could be a substantial diversion of management and other employee resources from our business.

If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties.

Any claims of patent infringement asserted by third parties would be time-consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing our product candidate until the asserted patent expires or is finally held invalid, unenforceable, 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;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be willfully infringing; and/or
- require us to enter into royalty or license agreements, which may not be available on commercially reasonable terms, or at all.

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If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do either. Proving invalidity or unenforceability is difficult. For example, in the United States, proving invalidity before federal courts requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity or enforceability of the patents in court. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid or unenforceable, we may incur substantial monetary damages, encounter significant delays in bringing our product candidate to market and be precluded from developing, manufacturing or selling our product candidate.

We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. We cannot be certain that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidate in any jurisdiction, because:

- some patent applications in the United States may be maintained in secrecy until the patents are issued;
- patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived;
- pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidate or their uses;
- 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;
- patent applications in the United States are typically not published until 18 months after the priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies or product candidate are not covered by a third party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or internationally that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our products or product candidate.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours, and others may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidate or future products or impair our competitive position. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidate. 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

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candidate. Any such patent application may have priority over one of our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications and may be entitled to priority over our applications in such jurisdictions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

If a third party prevails in a patent infringement lawsuit against us, we may have to stop making and selling the infringing product, pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidate. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidate, which could harm our business significantly. Even if we were able to obtain a license, the rights may be nonexclusive, which may give our competitors access to the same intellectual property.

***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 biotechnology and pharmaceutical industries, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidate, and other proprietary technologies. 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 our competitors or 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.

***We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court, and we may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.***

Third parties including competitors may infringe, misappropriate or otherwise violate our patents, patents that may issue to us in the future, or the patents of our licensors that are licensed to us. To counter infringement or unauthorized use, we may need to or choose to file infringement claims, which can be expensive and time-consuming. We may not be able to prevent, alone or with our licensors, infringement, misappropriation, or other

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violation of our intellectual property, particularly in countries where the laws may not protect those rights as fully as in the United States, or if we require, but do not receive, the consent or cooperation of our licensors to enforce such intellectual property.

If we choose to go to court to stop another party from using the inventions claimed in our patents, that individual or company has the right to ask the court to rule that such patents are invalid, unenforceable, or should not be enforced against that third party for any number of reasons. 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 for patentability, including lack of novelty, obviousness, lack of written description, indefiniteness, or non-enablement. 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, i.e., committed inequitable conduct. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent offices and courts and may result in the revocation, cancellation, or amendment of any foreign patents we or our licensors hold now or in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference or 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 it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference 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 litigation could have a material adverse effect on our ability to raise the funds necessary to conduct our future 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 candidate to market.

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

Our ability to enforce our patent rights depends on our ability to establish standing in a court of competent jurisdiction. Whether a patent holder or licensee of a patent has standing can be uncertain and the considerations complex. However, if a licensor is required to be joined, and they are unwilling to do so, we may be unable to proceed with an infringement action.

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Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

***Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.***

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent or patents that may issue from patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and/or other advisors, and inventions agreements with employees, consultants, and advisors, to protect our trade secrets and other proprietary information. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer, or third party with authorized access. Our security measures may not prevent an employee, consultant or customer from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

Enforcing a claim that a party illegally disclosed 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. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel

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skilled in the art from company to company or academic to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors, and/or consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. 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.

***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.***

Our trademarks or trade names, once registered, 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 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. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, 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.

Moreover, any names we may propose to use with our product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. Similar requirements exist in Europe. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties 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. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

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***Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our future products.***

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our products or may elect not to continue or renew development or commercialization programs based on trial or test results, changes in their strategic focus due to the acquisition of competitive products, availability of funding, or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidate;
- a collaborator with marketing, manufacturing, and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development, or commercialization of our current or future products or that results 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 current or future products;
- collaborators may own or co-own intellectual property covering our products that results from our 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.

***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 U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.***

Some of our patents may have been generated through the use of U.S. government funding, and we may acquire or license in the future intellectual property rights that have been generated through the use of U.S. government funding or grants. Pursuant to the Bayh-Dole Act of 1980, the U.S. government has certain rights in inventions developed with government funding. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. 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

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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 (also referred to as “march-in rights”). If the U.S. government exercised its march-in rights in our existing or future intellectual property rights that are generated through the use of U.S. government funding or grants, we could be forced to license or sublicense intellectual property developed by us or that we license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U.S. government for the exercise of such rights. The U.S. 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 U.S. 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 U.S. 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 U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

### **Risks Related to Legal and Regulatory Compliance Matters**

*Our relationships with customers, healthcare providers, including physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.*

Healthcare providers, including physicians, and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third- party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations promulgated under such laws. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs, and other interactions with healthcare professionals. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct or may conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind in return for, or to induce, either the referral of an individual, or the purchase, lease, order or arrangement for or recommendation of the purchase, lease, order or arrangement for any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term “remuneration” has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;

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- the federal civil and criminal false claims laws, including, without limitation, the federal False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes “any request or demand” for money or property presented to the U.S. federal government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of products for unapproved, and thus non-reimbursable, uses. 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;
- HIPAA which created additional federal criminal statutes which prohibit, among other things, a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. 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 and their implementing regulations, also imposes obligations, including mandatory contractual terms, on “covered entities,” including certain healthcare providers, health plans, healthcare clearinghouses, and their respective “business associates,” that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, as well as analogous state and foreign laws that 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;
- the federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the State Children’s Health Insurance Program, with specific exceptions, to report annually to CMS, information related to: (i) payments or other “transfers of value” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, and (ii) ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or that otherwise restrict payments that may be made to healthcare providers; and state and local laws that require the registration of pharmaceutical sales representatives.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply

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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, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, 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. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

***Even if we obtain regulatory approval for ACU193 or any future product candidates, they will remain subject to ongoing regulatory oversight, which may result in significant additional expense.***

Even if we obtain any regulatory approval for ACU193 or any future product candidates, such product candidates will be subject to ongoing regulatory requirements applicable to research, development, testing, manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submission of safety and other post-market information, among other things. Any regulatory approvals that we receive for ACU193 or any future product candidates may also be subject to REMS, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval or requirements that we conduct potentially costly post-marketing testing and surveillance studies, including Phase 4 trials and surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will further be required to immediately report any serious and unexpected adverse events and certain quality or production problems with our products to regulatory authorities along with other periodic reports. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. 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 marketing approval that we may have obtained and we may not achieve or sustain profitability.

In addition, drug manufacturers are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

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If we fail to comply with applicable regulatory requirements following approval of ACU193 or any future product candidates, a regulatory authority may:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- issue a safety alert, Dear Healthcare Provider letter, press release or other communication containing warnings or safety information about the product;
- mandate corrections to promotional materials and labeling or issuance of corrective information;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending marketing application or supplement to an approved application or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of products or product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize ACU193 or any future product candidates and harm our business, financial condition, results of operations and prospects.

***Even if we obtain FDA or EMA approval any of our product candidates in the United States or European Union, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential.***

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy.

Approval by the FDA in the United States or the EMA in the European Union does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. 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.

Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional nonclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

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### ***Healthcare legislative or regulatory reform measures may have a negative impact on our business and results of operations.***

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (i) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (ii) expanded the entities eligible for discounts under the 340B drug pricing program; (iii) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (iv) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new eligibility categories for individuals with income at or below 133% (as calculated, it constitutes 138%) of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (v) addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected; (vi) introduced a new Medicare Part D coverage gap discount program in which manufacturers must now agree to offer 70% 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 (increased from 50%, effective January 1, 2019, pursuant to the Bipartisan Budget Act of 2018); (vii) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (viii) established the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 (the Tax Act) included a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is also unclear how such challenges and the healthcare reform measures of the Biden administration will impact the ACA or our business.

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Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the Bipartisan Budget Act of 2018 and the Infrastructure Investment and Jobs Act, will remain in effect through 2031, with the exception of a temporary suspension 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, further reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent 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 products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA concurrently released a final rule and guidance in September 2020 providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. Further, in November 2020, CMS issued an interim final rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021 and ending December 31, 2027. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinds the Most Favored Nation model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of other reform initiatives. It is unclear whether these or similar policy initiatives will be implemented in the future.

We expect that these and 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 drug. 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

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reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

In addition, FDA regulations and guidance may be revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. For example, the results of the 2020 U.S. Presidential election may impact our business and industry. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for ACU193 or any other product candidate we may develop. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recalls, replacements, or discontinuance of one or more of our products; and
- additional recordkeeping.

Such changes would likely require substantial time and impose significant costs, or could reduce the potential commercial value of ACU193 or other product candidates, and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any other products would harm our business, financial condition and results of operations.

### ***Our business activities may be subject to the U.S. Foreign Corrupt Practices Act of 1977, or FCPA, and similar anti-bribery and anti-corruption laws.***

Our business activities may be subject to the FCPA, U.S. domestic bribery statutes, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we may operate, including the U.K. Bribery Act of 2010. The FCPA generally prohibits 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 would be considered foreign officials under the FCPA. There is no certainty that all of our employees, agents, 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, the closing down of our facilities, implementation of compliance programs and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our product candidates in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results and financial condition.

### ***Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.***

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with health care fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing

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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, customer incentive programs and other business arrangements. Employee misconduct 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. It is not always possible to identify and deter employee misconduct, 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, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

### ***Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.***

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of ACU193 or any other product candidate. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

### **Risks Related to Employee Matters and Managing our Growth**

#### ***We will need to expand our operations and increase the size of our company, and we may experience difficulties in managing growth.***

As we advance ACU193 through clinical development, and potentially expand the number of our drug development programs, we will need to increase our drug development, scientific and administrative headcount to manage these programs. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and various projects requires that we:

- successfully attract and recruit new employees or consultants with the expertise and experience we will require;
- manage our clinical programs effectively, which we anticipate being conducted at numerous clinical sites;
- develop a marketing and sales infrastructure; and
- continue to improve our operational, financial and management controls, reporting systems and procedures.

If we are unable to successfully manage this growth and increased complexity of operations, our business may be adversely affected.

#### ***We may not be able to manage our business effectively if we are unable to attract and retain key personnel and consultants.***

We may not be able to attract or retain qualified management, finance, scientific and clinical personnel and consultants due to the intense competition for qualified personnel and consultants among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel and consultants

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to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the research and development, clinical, regulatory and business development expertise of Daniel O'Connell, President and Chief Executive Officer, Matthew Zuga, our Chief Financial Officer and Chief Business Officer, Eric Siemers, M.D., our Chief Medical Officer and Russell Barton, our Chief Operating Officer. If we lose the services of any of these individuals, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or key employees or consultants may terminate their employment at any time. Replacing executive officers, key employees and consultants may be difficult and may take an extended period because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel and consultants. Our failure to retain key personnel or consultants could materially harm our business.

We have scientific and clinical advisors and consultants who assist us in formulating our research, development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. Non-compete agreements are not permissible or are limited by law in certain jurisdictions and, even where they are permitted, these individuals 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. In addition, our advisors may have arrangements with other companies to assist those companies in developing product candidates or technologies that may compete with ours.

### ***If we fail to build our finance infrastructure and improve our accounting systems and controls, we may be unable to comply with the financial reporting and internal controls requirements for publicly traded companies.***

We are subject to the reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the rules and regulations of Nasdaq Global Select Market, or Nasdaq. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. Commencing with our fiscal year ending December 31, 2022, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. Prior to our initial public offering, we have never been required to test our internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner. In connection with the preparation and audit of our financial statements as of December 31, 2020 and for the year then ended, a material weakness was identified in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. As of December 31, 2021, this material weakness has been remediated, see "Item 9A—Remediation of Material Weakness." Although we were able to remediate this material weakness, there is no guarantee that we will not experience additional material weaknesses in the future or that we will be able to remediate any such material weakness in a timely manner or at all. In addition, we have in the past identified other material weaknesses in our internal controls over financial accounting, which have since been remediated.

We anticipate that the process of building our accounting and financial functions and infrastructure will require significant additional professional fees, internal costs and management efforts. We expect that we will need to

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implement a new internal system to combine and streamline the management of our financial, accounting, human resources and other functions. However, such a system would likely require us to complete many processes and procedures for the effective use of the system or to run our business using the system, which may result in substantial costs. Any disruptions or difficulties in implementing or using such a system could adversely affect our controls and harm our business. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention. In addition, we may discover additional weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

We cannot be certain that the measures we have taken to date, and actions we may take in the future, will prevent or avoid potential future material weaknesses. If we are unable to successfully remediate any future material weaknesses in our internal control over financial reporting, if we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements and we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed, investors could lose confidence in our reported financial information and our stock price could decline as a result, and we could be subject to sanctions or investigations by Nasdaq, the Commission or other regulatory authorities.

### **Risks Related to Ownership of our Common Stock and our Status as a Public Company**

#### ***An active trading market for our common stock may not continue to be developed or sustained.***

Prior to our initial public offering, there was no public market for our common stock. Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares of our common stock at an attractive price or at all.

#### ***The trading price of the shares of our common stock may be volatile, and purchasers of our common stock could incur substantial losses.***

Our stock price may be volatile. From July 1, 2021, the date our stock began trading on Nasdaq, through March 1, 2022 our stock price fluctuated from a low of \$4.60 to a high of \$26.98. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the commencement, enrollment or results of our clinical trials, including INTERCEPT-AD and any future clinical trials we may conduct, or changes in the development status of our product candidates;
- any delay in our regulatory filings for ACU193 or any other product candidate we may develop, and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- delays in, or termination of, clinical trials;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;

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- unanticipated serious safety concerns related to the use of ACU193 or any other product candidate we develop;
- changes in financial estimates by us or by any equity research analysts who might cover our stock;
- conditions or trends in our industry;
- changes in the market valuations of similar companies;
- announcements by our competitors of new product candidates or technologies, or the results of clinical trials or regulatory decisions;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- our relationships with our collaborators;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

The stock market in general, Nasdaq and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including very recently in connection with the ongoing COVID-19 pandemic and conflict with Russia and Ukraine, which have resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to the ongoing COVID-19 pandemic, especially as more infectious variants of the virus emerge, and conflict with Russia and Ukraine may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this section, could have a significant and material adverse impact on the market price of our common stock.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

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**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 equity research analysts publish about us and our business. As a newly public company, we have only limited research coverage by equity research analysts. 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 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 our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

***Future sales of our common stock in the public market could cause our share price to fall.***

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. As of March 25, 2022, we had 40,473,270 shares of common stock outstanding. All of the shares of common stock sold during the initial public offering are currently freely tradable, except for any shares held by our affiliates as defined in Rule 144 under the Securities Act of 1933.

Additionally, the holders of approximately 26.9 million shares of common stock, or their transferees, have rights, subject to some conditions, with respect to registration of such shares under the Securities Act pursuant to an investor rights agreement between such holders and us. If such holders, by exercising their registration rights, sell a large number of shares, they could adversely affect the market price for our common stock. If we file a registration statement for the purpose of selling additional shares to raise capital, we may be required to offer these holders the right to participate in the offering and, if we are required to include shares held by these holders pursuant to the exercise of their registration rights, our ability to raise capital may be impaired.

We have filed a registration statement on Form S-8 under the Securities Act registering approximately 7,406,178 shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans and plan to file additional registration statements on Form S-8 for additional shares of common stock issuable under our equity incentive plans. Shares registered under these registration statements on Form S-8 can be freely sold in the public market upon issuance, subject to the vesting of the equity awards, other restrictions provided under the terms of the applicable plan or equity award, the lock-up agreements described above, and the restrictions of Rule 144 in the case of our affiliates.

***Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.***

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors will be elected each year;

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- stockholders will not be entitled to remove directors other than by a 66 2/3% vote and only for cause;
- stockholders will not be permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

### ***Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.***

Our directors, executive officers and beneficial owners of greater than 5% of our outstanding stock and their respective affiliates beneficially own, in the aggregate, a majority of our outstanding common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the public offering price and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

### ***We are an “emerging growth company” and a “smaller reporting company” and, as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors.***

We are an “emerging growth company” as defined in the JOBS Act and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these

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reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of the last day of the fiscal year (i) following the fifth anniversary of the closing of our initial public offering, or July 6, 2026, (ii) in which we have total annual gross revenue of at least \$1.07 billion, or (iii) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the extended transition period to comply with new or revised accounting standards and to adopt certain of the reduced disclosure requirements available to emerging growth companies. As a result of the accounting standards election, we will not be subject to the same implementation timing for new or revised accounting standards as other public companies that are not emerging growth companies, which may make comparison of our financials to those of other public companies more difficult. As a result of these elections, the information that we provide in this Annual Report on Form 10-K may be different than the information you may receive from other public companies in which you hold equity interests. In addition, it is possible that some investors will find our common stock less attractive as a result of these elections, which may result in a less active trading market for our common stock and higher volatility in our share price.

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than \$250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than \$100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than \$700 million measured on the last business day of our second fiscal quarter.

***Our management team may use our cash and cash equivalents, including the net proceeds from our initial public offering, in ways in which you may not agree or in ways which may not yield a return.***

Our management has broad discretion over the use of our cash and cash equivalents, including the net proceeds from our recent public offering. You will not have the opportunity to influence our decisions on how to use our cash and cash equivalents and will need to rely on our judgment with respect to the use of our cash and cash equivalents. The failure by our management to apply our cash and cash equivalents effectively could adversely affect our ability to continue maintaining and expanding our business.

***We have never paid dividends on our capital stock and we do not intend to pay dividends for the foreseeable future. Consequently, any gains from an investment in our common stock will likely depend on whether the price of our common stock increases.***

We have never declared or paid any dividends on our common stock and do not intend to pay any dividends in the foreseeable future. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our board of directors. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investments.

***Our failure to meet Nasdaq's continued listing requirements could result in a delisting of our common stock.***

If we fail to satisfy Nasdaq's continued listing requirements, such as the corporate governance requirements or the minimum closing bid price requirement. Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that

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any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq's listing requirements.

***Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the U.S. federal district courts will be the exclusive forums 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 employees.***

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative claim or cause of action brought on our behalf;
- any claim or cause of action asserting a breach of fiduciary duty;
- any claim or cause of action against us arising under DGCL;
- any claim or cause of action arising under or seeking to interpret our amended and restated certificate of incorporation or our amended and restated bylaws; and
- any claim or cause of action against us that is governed by the internal affairs doctrine.

Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions.

Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation will further provide that the U.S. federal district courts will be the exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act, including all causes of action asserted against any defendant to such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering.

While the Delaware courts have determined that such choice of forum provisions are facially valid and several state trial courts have enforced such provisions and required that suits asserting Securities Act claims be filed in federal court, there is no guarantee that courts of appeal will affirm the enforceability of such provisions and, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions. If a court were to find either exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with litigating Securities Act claims in state court, or both state and federal court, which could seriously harm our business, financial condition, results of operations, and prospects.

These exclusive forum provisions 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 lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

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***Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.***

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the DGCL, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we are not obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;
- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

## **General Risk Factors**

***We incur increased costs and demands upon management as a result of being a public company.***

As a public company listed in the United States, we incur significant additional legal, accounting and other costs. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and Nasdaq, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies.

We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

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### ***Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.***

We have incurred NOLs during our history, we expect to continue to incur significant NOLs for the foreseeable future, and we may not achieve profitability prior to the time that certain of our NOLs expire. As of December 31, 2021, we had federal and state NOL carryforwards of \$40.9 million and \$49.5 million, respectively, that will begin expiring in the year 2028 for both federal and state NOLs if not utilized. We also have \$34.5 million of federal net operating loss carryforwards as of December 31, 2021, that do not expire as a result of recent tax law changes. Our NOL carryforwards are subject to review and possible adjustment by U.S. and state tax authorities. Our NOL carryforwards could expire unused or be unavailable to offset future income tax liabilities because of their limited duration or because of restrictions under U.S. tax law. Federal NOLs generated in tax years ending on or prior to December 31, 2017 are only permitted to be carried forward for 20 taxable years under applicable U.S. federal tax law. Under the Tax Act, as modified by the Coronavirus Aid, Relief, and Economic Security Act (the “CARES Act”) signed into law on March 27, 2020, federal NOLs arising in tax years beginning after December 31, 2017, and before January 1, 2021 may be carried back to each of the five tax years preceding the tax year of such loss, and federal NOLs arising in tax years beginning after December 31, 2020 may not be carried back. Moreover, under the Tax Act as modified by the CARES Act, federal NOLs generated in tax years ending after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs may be limited to 80% of current year taxable income for tax years beginning after December 31, 2020. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California recently imposed limits on the usability of California state NOL carryforwards to offset taxable income in taxable years beginning after 2019 and before 2023. It is generally uncertain if and to what extent various states will conform to the Tax Act or the CARES Act.

Additionally, we continue to generate business tax credits, including research and development tax credits, which generally may be carried forward to offset a portion of future taxable income, if any, subject to expiration of such credit carryforwards.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an “ownership change” (generally defined as a cumulative change in our ownership by “5-percent shareholders” 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 (such as research and development tax credits) to offset its post-change income and taxes may be limited. Similar rules may apply under state tax laws. The completion of our recent initial public offering, together with private placements and other transactions that have occurred since our inception, may trigger such an ownership change pursuant to Section 382. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside our control. We have not conducted any studies to determine annual limitations, if any, that could result from such changes in the ownership. Our ability to utilize those NOLs 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 an adverse effect on our cash flows and results of operations.

### ***Comprehensive tax reform legislation could adversely affect our business and financial condition.***

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Act enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. Furthermore, the CARES Act modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Act or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets, could

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result in significant one-time charges, and could increase our future U.S. tax expense. Among the changes made by the Tax Act was a reduction of the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as “orphan drugs.” We continue to examine the impact this tax reform legislation may have on our business. It is possible that U.S. tax law will be further modified by the Biden administration and Congress by making tax law changes included in proposed legislation (which has not yet been enacted) that could have an adverse effect on our operations, cash flows and results of operations and contribute to overall market volatility. We urge investors to consult with their legal and tax advisers regarding the implications of the Tax Act and potential changes in U.S. tax laws on an investment in our common stock.

***Our business and operations would suffer in the event of computer system failures, cyberattacks or a deficiency in our cybersecurity or a natural disaster.***

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyberattacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability and damage to our reputation, and the further development of our product candidates could be delayed.

***Disruptions at the FDA, the Commission and other government agencies caused by funding shortages or global health concerns 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 Commission 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 drugs or biologics to be reviewed and approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including most recently from December 22, 2018 to January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government 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.

FDA and regulatory authorities outside the United States may adopt policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. In response to the COVID-19 pandemic, the FDA postponed most inspections for a period and has since been utilizing a rating system to assist

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in determining when and where it is safest to conduct inspections based on data about the virus' trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments. Additionally, 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.

If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting business as usual or conducting inspections, reviews or other regulatory activities, 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.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Portions of our future clinical trials may be conducted outside of the United States and unfavorable economic conditions resulting in the weakening of the U.S. dollar would make those clinical trials more costly to operate. Furthermore, a severe or prolonged economic downturn, including a recession or depression resulting from the ongoing COVID-19 pandemic or political disruption such as the pending conflict with Russia and Ukraine could result in a variety of risks to our business, including weakened demand for our product candidates or any future product candidates, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption, including any international trade disputes, could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our potential products. Any of the foregoing could seriously harm our business, and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could seriously harm our business.

### **Item 1B. Unresolved Staff Comments.**

None.

### **Item 2. Properties.**

Our corporate headquarters are currently located in Charlottesville, Virginia, where we lease office space pursuant to a lease agreement that expires in December 2022. We also lease 8,573 square feet of office space in Carmel, Indiana pursuant to a lease agreement that expires in August 2023. We believe that these facilities will be adequate for our near-term needs. If required, we believe that suitable additional or alternative space would be available in the future on commercially reasonable terms.

### **Item 3. Legal Proceedings.**

We are not subject to any material legal proceedings. From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation 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.

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[\*\*Table of Contents\*\*](#)**PART II****Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.****Market Information for Common Stock**

Our common stock is listed on The Nasdaq Global Select Market under the symbol “ABOS.”

**Holders of Record**

As of March 25, 2022, we had 90 holders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

**Dividend Policy**

We have never paid cash dividends on any of our capital stock and currently intend to retain our future earnings, if any, to fund the development and growth of our business.

**Unregistered Sales of Equity Securities**

None.

**Use of Proceeds from Initial Public Offering**

On June 30, 2021, our Registration Statement on Form S-1, as amended (File No. 333-256945), was declared effective in connection with our initial public offering, pursuant to which we sold an aggregate of 11,499,998 shares of our common stock, including the full exercise of the underwriters' option to purchase additional shares, at a price to the public of \$16.00 per share. BofA Securities, Inc, Credit Suisse Securities (USA) LLC, and Stifel, Nicolaus & Company, Incorporated acted as joint lead book-running managers and UBS Securities LLC also acted as a book-running manager for the offering.

The initial public offering closed on July 6, 2021 with respect to 9,999,999 shares of common stock. On July 8, 2021, the offering closed with respect to an additional 1,499,999 shares purchased by the underwriters pursuant to the underwriters' option to purchase additional shares. The aggregate net proceeds from our initial public offering, after underwriting discounts and commissions, and other offering expenses of \$15.4 million, were \$168.6 million. In connection with our initial public offering, no payments were made by us to directors, officers or persons owning ten percent or more of our common stock or to their associates or to our affiliates. There has been no material change in the planned use of proceeds from our initial public offering as described in our prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on July 2, 2021.

**Issuer Purchases of Equity Securities**

None.

**Item 6. [Reserved]**

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

*The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our audited financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion, particularly information with respect to our future results of operations or financial condition, business strategy, plans and objectives of management for future operations and the potential impact that the ongoing COVID-19 pandemic may have on our business, includes forward-looking statements that involve risks and uncertainties as described under the heading “Special Note Regarding Forward-Looking Statements” in this Annual Report on Form 10-K. You should review the disclosure under the heading “Risk Factors” in this Annual Report on Form 10-K for a discussion of important factors that could cause our actual results to differ materially from those anticipated in these forward-looking statements.*

#### **Overview**

We are a clinical-stage biopharmaceutical company developing a novel disease-modifying approach to target what we believe to be a key underlying cause of AD. Alzheimer’s disease is a progressive neurodegenerative disease of the brain that leads to loss of memory and cognitive functions and ultimately results in death. Our scientific founders pioneered research on soluble A $\beta$ Os, which are globular assemblies of the A $\beta$  peptide that are distinct from A $\beta$  monomers and amyloid plaques. We are currently focused on advancing a targeted immunotherapy drug candidate, ACU193, through clinical proof of mechanism trials in early AD patients. We initiated a Phase 1 clinical trial of ACU193 in the second quarter of 2021, which we named “INTERCEPT-AD.” This trial is enrolling patients with mild dementia or MCI due to AD, conditions referred to as “early AD.” INTERCEPT-AD is a U.S.-based, multi-center, randomized, double-blind, placebo-controlled clinical trial with overlapping SAD and MAD cohorts involving a total of approximately 62 patients with early AD. The overall objective of the trial is to evaluate the safety and tolerability and establish clinical proof of mechanism of ACU193 administered intravenously. The primary trial endpoints are focused on safety and immunogenicity. An important safety measure will be the use of MRI to assess the presence or absence of ARIA. Secondary endpoints include pharmacokinetics in plasma and CSF and target engagement as evidenced by detection of ACU193 bound to A $\beta$ Os in CSF. Clinical scales typically used in AD trials as well as computerized cognitive testing are included as exploratory measures. In October 2021, we announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients. Due to delays in clinical trial site activation and patient enrollment that we believe are principally related to the effects of the COVID-19 pandemic, we are expanding the anticipated number of trial sites to support our enrollment objectives and anticipated timelines. Clinical trial site activation and patient recruitment and enrollment is ongoing. At present, INTERCEPT-AD is in the SAD portion of the trial. Based on current site activations and enrollment rates, we anticipate reporting our topline data from this trial in the first half of 2023.

We were incorporated in 1996 and were party to an exclusive license and research collaboration with Merck in 2003. Although we acquired the exclusive rights to ACU193 from Merck in 2011 following Merck’s strategic decision to focus its AD development efforts on a different product candidate, we did not recommence meaningful operations until we completed our first institutional fundraising in 2018. Since 2018, we have devoted substantially all of our efforts to organizing and staffing our company, business planning, raising capital, conducting discovery, research and development activities, and providing general and administrative support for these operations. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through the sale of our convertible preferred stock and common stock, the issuance of notes, grant revenue and during our collaboration with Merck, certain payments received under our collaboration agreement.

Prior to our IPO, which closed on July 6, 2021, we raised an aggregate of \$99.4 million of gross proceeds through the issuance of convertible preferred stock, as well as sales of common stock and issuance of notes that were converted to preferred stock, with the vast majority of this capital being raised since our Series A-1 convertible preferred stock, or Series A-1, financing in 2018. In 2020, we conducted a Series B convertible preferred stock, or Series B, financing, with the funding to occur in two tranches. We closed the first tranche of the Series B financing

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in November 2020, selling 11,862,043 shares of Series B at \$3.80 per share for gross proceeds of \$45.1 million. On June 9, 2021, our board of directors and the holders of more than 67% of the outstanding shares of Series B preferred stock elected to waive the achievement of the milestone event. On June 17, 2021, we closed the second tranche of our Series B preferred stock financing, pursuant to which certain of our investors funded an additional \$30.0 million in exchange for 7,908,027 shares of Series B preferred stock.

On July 6, 2021, we issued 9,999,999 shares of our common stock in the IPO, and on July 8, 2021, we issued an additional 1,499,999 shares of our common stock that were purchased by the underwriters pursuant to the underwriters' option to purchase additional shares at the public offering price less underwriting discounts and commissions. The price to the public for each share was \$16.00. The aggregate net proceeds from the IPO, after underwriting discounts and commissions and other offering expenses of \$15.4 million, were \$168.6 million.

We have incurred net losses and negative cash flows from operations since our inception. Our net losses were \$100.6 million and \$7.3 million for the years ended December 31, 2021 and 2020, respectively. Approximately \$81.2 million, or 81%, of the net loss for the year ended December 31, 2021 was due to increases in the fair value of the Series B tranche liability and the Series A-1 warrant liability of \$76.2 million and \$5.0 million, respectively. As of December 31, 2021, we had an accumulated deficit of \$127.6 million. Our net losses and cash flows from operations may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of nonclinical studies, clinical trials and our expenditures on other research and development activities. We expect our expenses and operating losses will increase substantially for the foreseeable future as we advance ACU193 in clinical trials, seek to expand our product candidate portfolio through developing additional product candidates, grow our clinical, regulatory and quality capabilities, and incur additional costs associated with operating as a public company. It is likely that we will seek third-party collaborators for the future commercialization of ACU193 or any other product candidate that is approved for marketing. However, we may seek to commercialize our products at our own expense, which would require us to incur significant additional expenses for marketing, sales, manufacturing and distribution.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates. In addition, if we obtain regulatory approval for our product candidates and do not enter into a third-party commercialization partnership, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing, manufacturing and distribution activities.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity offerings and debt financings or other sources, such as potential collaboration agreements, strategic alliances and licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on acceptable terms, or at all. Our failure to raise capital or enter into such agreements as, and when needed, could have a material adverse effect on our business, results of operations and financial condition.

As of December 31, 2021, we had cash and cash equivalents of \$122.2 million and \$103.7 million in marketable securities. Based on our current operating plan, we expect that our existing cash and cash equivalents and marketable securities will be sufficient to enable us to fund our operating expenses and capital expenditure requirements at least through 2025. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See “—Liquidity and Capital Resources.”

### **COVID-19 Business Update**

In March 2020, the World Health Organization declared COVID-19 a global pandemic and the United States declared a national emergency with respect to COVID-19. In response to the COVID-19 pandemic, a number of governmental orders and other public health guidance measures have been implemented across much of the United States, including in the locations of our office, clinical trial sites and third parties on whom we rely. We implemented a work-from-home policy allowing employees and consultants who can work from home to do so.

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Business travel has been limited, and online video and teleconference technology is used to meet virtually rather than in person. We have taken measures to secure our research and development activities, while work in laboratories by our partners has been organized to reduce risk of COVID-19 transmission.

In October 2021, we announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients. Due to delays in clinical trial site activation and patient enrollment that we believe are principally related to effects of the COVID-19 pandemic, we are expanding the anticipated number of trial sites to support our enrollment objectives and anticipated timelines. However, we cannot assure that we will not experience additional delays in site activation or enrollment. Clinical trial site activation and patient recruitment and enrollment is ongoing. At present, INTERCEPT-AD is in the SAD portion of the trial. Based on current site activations and enrollment rates, we anticipate reporting our topline data from this trial in the first half of 2023.

The ultimate impact of the COVID-19 pandemic on our business, results of operations, financial position and cash flows will depend on future developments, including the duration and spread of the outbreak and related advisories and restrictions. These developments and the impact of the COVID-19 pandemic on the financial markets and the overall economy are highly uncertain and cannot be predicted. If the financial markets and/or the overall economy are impacted for an extended period, our business, results of operations, financial position and cash flows may be materially adversely affected.

## **Components of Results of Operations**

### ***Grants and Other Revenue***

To date, we have not generated any revenues from the commercial sale of any products, and we do not expect to generate revenues from the commercial sale of any products for the foreseeable future, if ever. For the year ended December 31, 2020, we derived revenue from a grant awarded by the National Institutes of Health, or the NIH, in September 2017 and renewed annually in 2018 through 2020. The grant provided us with funding to support the completion of preclinical chemistry, manufacturing and control studies, toxicology and pharmacokinetic studies, submit an IND dossier to the FDA, and then conduct first in human clinical safety trials for ACU193. We recognized revenue from this grant when the related costs were incurred and the right to payment was realized. The full \$3.9 million awarded to us was fully recognized as of December 31, 2020, as the final \$1.4 million under the grant was recorded as revenue during the year ended December 31, 2020.

### ***Operating Expenses***

Our operating expenses consist of research and development expenses and general and administrative expenses.

#### ***Research and Development Expenses***

Research and development costs primarily consist of direct costs associated with consultants and materials, biologic storage, third party, contract research organization costs and contract development and manufacturing expenses, salaries and other personnel-related expenses. Research and development costs are expensed as incurred. More specifically, these costs include:

- costs of funding research performed by third parties that conduct research and development and nonclinical and clinical activities on our behalf;
- costs of manufacturing drug supply and drug product;
- costs of conducting nonclinical studies and clinical trials of our product candidates;
- consulting and professional fees related to research and development activities, including equity-based compensation to non-employees;

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- costs related to compliance with clinical regulatory requirements; and
- employee-related expenses, including salaries, benefits and stock-based compensation expense for our research and development personnel.

As we currently only have one product candidate, ACU193, in development, we do not separately track expenses by program. Further, as we have historically relied exclusively on consultants for research and development activities, we did not have any material internal research and development costs for the years ended December 31, 2021 and 2020. We expect that our research and development expenses will increase substantially in connection with our clinical development activities for our ACU193 program.

### ***General and Administrative Expenses***

General and administrative expenses consist primarily of management and business consultants and other related costs, including stock-based compensation. General and administrative expenses also include insurance, professional fees for legal, consulting, accounting, auditing, tax and patent services, investor and public relations, board of directors' expenses, franchise taxes and rent.

We expect that our general and administrative expenses will increase as our organization and headcount needed in the future grows to support continued research and development activities and potential commercialization of our product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, attorneys and accountants, among other expenses. Additionally, we expect to incur increased expenses associated with being a public company, including costs of additional personnel, accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs, and investor and public relations costs.

### ***Other Income (Expense)***

Other income (expense) primarily includes changes in fair value of the Series A-1 warrant liability and the Series B tranche rights, interest income, net and other expense, net.

The Series A-1 warrant liability and the Series B tranche rights were initially recorded at fair value as liabilities on our balance sheet. Each was subsequently re-measured at fair value at the end of each reporting period and also upon the exercise of the warrant on June 22, 2021 and upon settlement of the tranche rights with the milestone closing for the Series B on June 17, 2021. Changes in the fair value were recognized as a component of other income (expense).

Following our IPO, we made investments in marketable securities and the interest income earned, as well as the amortization and accretion of premiums and discounts are recorded in interest income, net.

Other income (expense), net generally consists of sublease income offset by fees incurred on our investments in marketable securities.

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### Results of Operations

#### **Comparison of the Years Ended December 31, 2021 and 2020**

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,		
	2021	2020	Change
Grant and other revenue	\$ —	\$ 1,436	\$ (1,436)
Costs and operating expenses			
Research and development	12,305	7,997	4,308
General and administrative	7,279	1,351	5,928
Total operating expenses	<u>19,584</u>	<u>9,348</u>	<u>10,236</u>
Loss from operations	(19,584)	(7,912)	(11,672)
Other income (expense)			
Change in fair value of preferred stock tranche rights liability and preferred stock warrant liability	(81,157)	586	(81,743)
Interest income, net	84	1	83
Other income, net	51	—	51
Total other income (expense)	<u>(81,022)</u>	<u>587</u>	<u>(81,609)</u>
Net loss	<u>(100,606)</u>	<u>(7,325)</u>	<u>(93,281)</u>
Other comprehensive loss			
Unrealized loss on marketable securities	(231)	—	(231)
Comprehensive loss	<u><u>\$100,837</u></u>	<u><u>\$(7,325)</u></u>	<u><u>\$(93,512)</u></u>

#### *Grant and Other Revenue*

Revenue related to our NIH grant was nil and \$1.4 million for the years ended December 31, 2021 and 2020, respectively. Revenue under the NIH grant was recognized when the related costs were incurred and the right to payment was realized.

#### *Research and Development Expenses*

Research and development expenses were \$12.3 million and \$8.0 million for the years ended December 31, 2021 and 2020, respectively. The \$4.3 million increase was primarily due to increases in expenses of \$2.3 million for personnel-related expenses, \$2.3 million for materials and \$2.1 million for contract research organization services, which were partially offset by decreases in expenses of \$1.6 million for drug safety testing, \$0.6 million for consulting and \$0.2 million for contract manufacturing. The net increase in research and development expenses in 2021 from 2020 was primarily due to increased costs related to initiating our clinical trial in 2021.

#### *General and Administrative Expenses*

General and administrative expenses were \$7.3 million and \$1.4 million for the years ended December 31, 2021 and 2020, respectively. The \$5.9 million increase was primarily due to increases of \$2.2 million for personnel expenses, including stock compensation costs, \$1.5 million for insurance expenses, \$0.8 million for accounting and audit expenses, \$0.5 million for legal expenses, \$0.3 million for investor relations, as well as \$0.1 million each for marketing/public relations, board of directors' fees, rent, travel, other general and administrative costs and the write-off of the remaining NIH grant receivable which was not submitted in a timely enough manner to

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collect these funds from the NIH. Following the IPO, we have added a number of new personnel and a large portion of the other increases are a direct result of our transition from a private to a public company.

### *Other Income (Expense)*

Increases in the fair value of the Series B tranche liability and the Series A-1 warrant liability of \$76.2 million and \$5.0 million, respectively, were primarily responsible for total other expense for the year ended December 30, 2021. Additionally, these expenses were offset by interest income earned on our investments in marketable securities, net of amortization and accretion of premium and discount which are recorded in interest income, net and sublease income. Other income (expense) for the year ended December 31, 2020 was related to decreases in the fair value of the Series B tranche liability and the Series A-1 warrant liability of \$0.4 million and \$0.2 million, respectively.

### **Liquidity and Capital Resources**

Since our inception up until the time of our IPO in July 2021, we had funded our operations primarily through the sale of our convertible preferred stock and common stock, the issuance of notes, grant revenue and, during our collaboration with Merck, certain payments received under our collaboration agreement. We do not have any products approved for sale and have not generated any revenue from product sales. Prior to our IPO, we had raised an aggregate of \$99.4 million of gross proceeds through the issuance of convertible preferred stock, as well as sales of common stock and issuance of notes that were converted to preferred stock, with the vast majority of this capital being raised since our Series A-1 financing in 2018. In 2020, we conducted a Series B financing, with the funding to occur in two tranches. We closed the first tranche of the Series B financing in November 2020 for gross proceeds of \$45.1 million and the second tranche closed on June 17, 2021 for gross proceeds of \$30.0 million following the election of our board of directors and a majority of the Series B investors to waive the requirement for a certain milestone event for ACU193 to be achieved prior to funding the second tranche on June 9, 2021.

On July 6, 2021, we issued 9,999,999 shares of common stock in our IPO, and on July 8, 2021, we issued an additional 1,499,999 shares of common stock that were purchased by the underwriters pursuant to the underwriters' option to purchase additional shares at the public offering price less underwriting discounts and commissions. The price to the public for each share was \$16.00. The aggregate net proceeds from our IPO, after underwriting discounts and commissions and other offering expenses of \$15.4 million, were \$168.6 million.

As of December 31, 2021, our cash and cash equivalents totaled \$122.2 million. Additionally, we had \$103.7 million of available-for-sale marketable securities as of December 31, 2021, which mature over the next one to two years. We enter into contracts in the normal course of business with contract research organizations, or CROs, and contract manufacturing organizations, or CMOs, for clinical trials, nonclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts do not contain any minimum purchase commitments and are generally cancelable by us upon prior notice of 30 days. Payments due upon cancellation consist only of payments for services provided and expenses incurred up to the date of cancellation.

Future minimum lease payments under our lease agreements for our leases in Carmel, Indiana and Charlottesville, Virginia total less than \$0.3 million.

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### **Cash Flows**

The following table summarizes our sources and uses of cash (in thousands):

	<u>Year Ended December 31,</u>	
	2021	2020
Net cash used in operating activities	\$ (17,961)	\$ (7,450)
Net cash used in investing activities	(104,120)	—
Net cash provided by financing activities	200,466	44,675
Net change in cash and cash equivalents	<u>\$ 78,385</u>	<u>\$ 37,225</u>

#### *Operating Activities*

Net cash used in operating activities was \$18.0 million and \$7.5 million for the years ended December 31, 2021 and 2020, respectively. Net cash used in operating activities during the year ended December 31, 2021 primarily consisted of our net loss of \$100.6 million, which includes \$81.2 million of non-cash expense related to the change in the fair values of the Series B tranche liability and the Series A-1 warrant liability and \$0.9 million for stock compensation costs, plus \$3.9 million of cash used for prepaid expenses mainly associated with research and development activities and insurance; partially offset by cash provided of \$3.6 million from accrued expenses and other current liabilities mainly related to research and development expenses and employee-related accruals, and \$0.6 million of cash provided by accounts payable. Cash used in operating activities during the year ended December 31, 2021, was the result of ongoing research and development activities as we commenced our clinical trial, as well as costs associated with the transition from a private to a public company. Net cash used in operating activities during the year ended December 31, 2020 primarily consisted of our net loss of \$7.3 million, which includes \$0.6 million of non-cash expense related to the change in the fair values of the Series B tranche liability and the Series A-1 warrant liability and \$0.2 million for stock compensation costs, partially offset by \$0.3 million of cash provided by changes in our operating assets and liabilities.

#### *Investing Activities*

Cash used in investing activities for the year ended December 31, 2021 was \$104.1 million and was predominantly related to the purchase of marketable securities, but also included less than \$0.1 million for purchases of computer hardware. Cash used in investing activities for the year ended December 31, 2020 was nil.

#### *Financing Activities*

Net cash provided by financing activities was \$200.5 million and \$44.7 million for the year ended December 31, 2021 and 2020, respectively. Net cash provided by financing activities during the year ended December 31, 2021 was primarily due to our IPO for net proceeds of \$168.6 million, the closing of the second tranche of our Series B convertible preferred stock for gross proceeds of \$30.0 million, plus a total of \$1.9 million received from the exercise of a Series A-1 preferred warrant, as well as exercises of common stock warrants. Net cash provided by financing activities during the year ended December 31, 2020 was primarily due to the closing of the first tranche of the Series B financing for net proceeds of \$44.7 million.

### **Funding Requirements**

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue our research and development, conduct clinical trials, and seek marketing approval for our current and any of our future product candidates. Furthermore, we have and expect to incur additional costs associated with operating as a public company following our July 2021 IPO. It is likely that we will seek third-party collaborators for the future commercialization of ACU193 or any other product candidate that is approved for marketing. However, we may seek to commercialize our products at our own expense, which would require us to incur significant

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additional expenses for marketing, sales, manufacturing and distribution., which costs we may seek to offset through entry into collaboration agreements with third parties. As a result, we expect that we will need to obtain substantial additional funding in connection with our future operations. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Based on our current operating plan, we expect that our existing cash and cash equivalents and our marketable securities will be sufficient to enable us to fund our operating expenses and capital expenditure requirements at least through 2025. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of discovery, nonclinical development, laboratory testing and clinical trials for other potential product candidates we may develop, if any;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we might have at such time;
- the costs and timing of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our longer-term cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interests may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect your rights as a common stockholder. Any debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

### **Critical Accounting Policies, Significant Judgments and Use of Estimates**

Our financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that

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affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates and assumptions are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources.

Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

While our significant accounting policies are described in the notes to our financial statements included elsewhere in this Annual Report for Form 10-K, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

### **Stock-Based Compensation Expense**

We recognize stock-based compensation expense for all stock-based awards. Stock-based compensation costs are estimated at the grant date based on the fair value of the equity and recognized as expense, net of actual forfeitures when they occur, on a straight-line basis over the requisite service period.

We calculate the fair value of options using the Black-Scholes option-pricing model, which requires the use of various highly subjective assumptions as follows:

- *Fair Value of Common Stock*—See the subsection titled “*Common Stock Valuations*” below.
- *Expected Term*—We have opted to use the “simplified method” for estimating the expected term of options, whereby the expected term equals the arithmetic average of the mid-point between the vesting date and the end of contractual term of the option (generally ten years).
- *Expected Volatility*—Due to our limited operating history and a lack of sufficient company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of industry peers that are publicly traded. We will continue to utilize a group of publicly traded peers to estimate volatility until a sufficient amount of historical information regarding the volatility of our own stock becomes available.
- *Risk-Free Interest Rate*—The risk-free rate assumption is based on the U.S. Treasury yield in effect at the time of the grant with maturities consistent with the expected term of our options.
- *Expected Dividend Yield*—We have not issued any dividends in our history and do not expect to pay dividends on our common stock over the life of the options and therefore have estimated the dividend yield to be zero.

We will continue to use judgment in evaluating the expected volatility, expected terms and interest rates utilized for our stock-based compensation expense calculations on a prospective basis.

For the years ended December 31, 2021 and 2020, stock-based compensation expense was \$0.9 million and \$0.2 million, respectively. As of December 31, 2021, we had approximately \$4.7 million of total unrecognized stock-based compensation costs, which we expect to recognize over an estimated weighted-average period of 3.0 years. We expect to continue to grant options and other stock-based awards in the future, and to the extent that we do, our stock-based compensation expense recognized in future periods will likely increase.

### **Common Stock Valuations**

Given the absence of a public trading market of our common stock prior to the IPO, and in accordance with the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately Held Company Equity*

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*Securities Issued as Compensation*, the Practice Aid, our board of directors exercised reasonable judgment and considered numerous and subjective factors to determine the best estimate of fair value of our common stock prior to the IPO, including, but not limited to:

- relevant precedent transactions involving our capital stock;
- contemporaneous valuations of our common stock performed by third-party specialists;
- rights, preferences, and privileges of our redeemable convertible preferred stock relative to those of our common stock;
- our business, financial condition and results of operations, including related industry trends affecting our operations;
- likelihood of achieving a liquidity event, such as an initial public offering or a sale of our business;
- the lack of marketability of our common stock, and the illiquidity of stock-based awards involving securities in a private company;
- market multiples of comparable publicly-traded companies; and
- U.S. and global capital and macroeconomic conditions.

The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, we considered the following methods:

- *Option Pricing Method, or OPM.* Under the OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options. This method is appropriate to use when the range of possible future outcomes is so difficult to predict that estimates would be highly speculative, and dissolution or liquidation is not imminent.
- *Probability-Weighted Expected Return Method, or PWERM.* The PWERM is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

For valuations performed during fiscal years 2018 through 2020 we used the OPM. For valuations performed beginning in 2021, prior to the IPO, in accordance with the Practice Aid, we used a hybrid approach of the OPM and the PWERM methods to determine the estimated fair value of our common stock as a result of the increasing likelihood of the occurrence of certain discrete events, such as a potential IPO, improving market conditions and receptivity of the market to initial public offerings. The enterprise value determined under the OPM and PWERM methods was weighted according to our board of directors' estimate of the probability of the occurrence of a certain discrete event as of the valuation date. The resulting equity value for the common stock was then divided by the number of shares of common stock outstanding at the date of the valuation to derive a per share value on a non-marketable basis. In order to determine the fair value of our common stock on a marketable basis, we then applied a discount for lack of marketability which we derived based on inputs including a company-specific volatility rate, a term equal to the expected time to a future liquidity event and a risk-free rate equal to the yield on treasuries of similar duration.

Application of these approaches involves the use of estimates, judgment and assumptions that are highly complex and subjective, such as those regarding our expected future revenue, expenses, cash flows, discount rates, market multiples, the selection of comparable companies and the probability of future events. Changes in any or all of these estimates and assumptions, or the relationships between those assumptions, impact our valuations as of each valuation date and may have a material impact on the valuation of common stock. The assumptions underlying these valuations represent our management's best estimate, which involve inherent uncertainties and

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the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different.

Following the closing of the initial public offering, the fair value of our common stock has been determined based on the quoted market price of our common stock.

### ***Accrued Research and Development Expenses***

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced. Since our inception, we have not experienced any material differences between accrued or prepaid costs and actual costs.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Accrued research and development expenses increased to \$2.6 million as of December 31, 2021, compared with \$0.1 million as of December 31, 2020, and prepaid research and development expenses increased to \$2.6 million as of December 31, 2021, compared with \$0.4 million as of December 31, 2020. The increases in both accrued and prepaid research and development are due to commencement of our clinical trial.

### ***Emerging Growth Company and Smaller Reporting Company Status***

In April 2012, the Jumpstart Our Business Startups Act of 2012, or JOBS Act, was enacted. 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 of 1933, as amended, 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 elected the extended transition period for complying with new or revised accounting standards, which delays the adoption of these accounting standards until they would apply to private companies.

In addition, as an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- an exception from compliance with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure about our executive compensation arrangements in our periodic reports, proxy statements and registration statements;

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- exemptions from the requirements of holding non-binding advisory votes on executive compensation or golden parachute arrangements; and
- an exemption from compliance with the requirements of the Public Company Accounting Oversight Board regarding the communication of critical audit matters in the auditor’s report on financial statements.

We may take advantage of these provisions until we no longer qualify as an emerging growth company. We will cease to qualify as an emerging growth company on the date that is the earliest of: (i) December 31, 2025, (ii) the last day of the fiscal year in which we have more than \$1.07 billion in total annual gross revenues, (iii) the date on which we are deemed to be a “large accelerated filer” under the rules of the SEC, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, or (iv) the date on which we have issued more than \$1.0 billion of non-convertible debt over the prior three-year period. We may choose to take advantage of some but not all of these reduced reporting burdens. We have taken advantage of certain reduced reporting requirements in this Annual Report on Form 10-K and our other filings with the SEC. Accordingly, the information contained herein may be different than you might obtain from other public companies in which you hold equity interests.

We are also a “smaller reporting company,” meaning that the market value of our shares held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our shares held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

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

As a “smaller reporting company” as defined by Item 10 of Regulation S-K, the Company is not required to provide the information required by this item.

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**Item 8. Financial Statements and Supplementary Data.**

**ACUMEN PHARMACEUTICALS, INC.  
INDEX TO FINANCIAL STATEMENTS**

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To the Shareholders and the Board of Directors of Acumen Pharmaceuticals, Inc.

**Opinion on the Financial Statements**

We have audited the accompanying balance sheets of Acumen Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, the related statements of operations, changes in convertible preferred stock and stockholders' deficit and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the 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 U.S. generally accepted accounting principles.

**Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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 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 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditors since 2021.

Tysons, Virginia  
March 28, 2022

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**ACUMEN PHARMACEUTICALS, INC.**  
**BALANCE SHEETS**  
(in thousands, except share and per share data)

	December 31,	
	2021	2020
<b>ASSETS</b>		
Current assets		
Cash and cash equivalents	\$ 122,162	\$ 43,777
Marketable securities, short-term	72,075	—
Grant receivable	—	109
Prepaid expenses and other current assets	4,424	543
Total current assets	198,661	44,429
Marketable securities, long-term	31,619	—
Property and equipment, net	36	—
Other assets	14	—
Total assets	\$ 230,330	\$ 44,429
<b>LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)</b>		
Current liabilities		
Accounts payable	\$ 1,088	\$ 531
Accrued expenses and other current liabilities	4,059	423
Preferred stock tranche rights liability	—	5,033
Preferred stock warrant liability	—	380
Total liabilities	5,147	6,367
Series A convertible preferred stock, \$0.0001 par value; no shares authorized, issued and outstanding as of December 31, 2021; 711,203 shares authorized and 477,297 shares issued and outstanding as of December 31, 2020; liquidation preference of \$1,067 as of December 31, 2020	—	1,067
Series A-1 convertible preferred stock, \$0.0001 par value; no shares authorized, issued and outstanding as of December 31, 2021; 11,898,177 shares authorized and 7,537,879 shares issued and outstanding as of December 31, 2020; liquidation preference of \$16,847 as of December 31, 2020	—	16,333
Series B convertible preferred stock, \$0.0001 par value; no shares authorized, issued and outstanding as of December 31, 2021; 29,457,450 shares authorized and 11,862,043 shares issued and outstanding as of December 31, 2020; liquidation preference of \$45,070 as of December 31, 2020	—	39,253
Stockholders' equity (deficit)		
Preferred stock, \$0.0001 par value; 10,000,000 shares authorized and no shares issued and outstanding as of December 31, 2021; no shares authorized, issued and outstanding as of December 31, 2020	—	—
Common stock, \$0.0001 par value; 300,000,000 shares authorized and 40,473,270 shares issued and outstanding as of December 31, 2021; 50,500,000 shares authorized and 419,124 shares issued and outstanding as of December 31, 2020	4	—
Additional paid-in capital	352,981	8,374
Accumulated deficit	(127,571)	(26,965)
Accumulated other comprehensive loss	(231)	—
Total stockholders' equity (deficit)	225,183	(18,591)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	\$ 230,330	\$ 44,429

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

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**ACUMEN PHARMACEUTICALS, INC.**  
**STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
(in thousands, except share and per share data)

	Year Ended December 31,	
	2021	2020
<b>Grant and other revenue</b>	\$ —	\$ 1,436
<b>Operating expenses</b>		
Research and development	12,305	7,997
General and administrative	7,279	1,351
Total operating expenses	<u>19,584</u>	<u>9,348</u>
<b>Loss from operations</b>	(19,584)	(7,912)
<b>Other income (expense)</b>		
Change in fair value of preferred stock tranche rights liability and preferred stock warrant liability	(81,157)	586
Interest income, net	84	1
Other income, net	51	—
Total other income (expense)	<u>(81,022)</u>	<u>587</u>
<b>Net loss</b>	<u>(100,606)</u>	<u>(7,325)</u>
<b>Other comprehensive loss</b>		
Unrealized loss on marketable securities	(231)	—
<b>Comprehensive loss</b>	<u>\$ (100,837)</u>	<u>\$ (7,325)</u>
Net loss per common share, basic and diluted	<u>\$ (5.02)</u>	<u>\$ (17.48)</u>
Weighted-average shares outstanding, basic and diluted	<u>20,057,534</u>	<u>419,124</u>

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

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**ACUMEN PHARMACEUTICALS, INC.**  
**STATEMENTS OF CHANGES IN CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)**  
(in thousands, except share data)

	Series A Convertible Preferred Stock			Series A-1 Convertible Preferred Stock			Series B Convertible Preferred Stock							
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)			
Balance as of December 31, 2019	477,297	\$ 1,067	7,537,879	\$ 16,333	—	\$ —	419,124	\$ —	\$ 8,220	\$ (19,640)	\$ —	\$ —	(11,420)	
Issuance of Series B convertible preferred stock for cash, net of issuance costs of \$395	—	—	—	—	11,862,043	39,253	—	—	—	—	—	—	—	
Share-based compensation	—	—	—	—	—	—	—	—	154	—	—	—	154	
Net loss	—	—	—	—	—	—	—	—	(7,325)	—	—	—	(7,325)	
Balance as of December 31, 2020	477,297	1,067	7,537,879	16,333	11,862,043	39,253	419,124	—	8,374	(26,965)	—	—	(18,591)	
Issuance of milestone shares for cash, net of issuance costs of \$16	—	—	—	—	7,908,027	30,031	—	—	—	—	—	—	—	
Exercise of preferred stock warrant	—	—	447,426	1,250	—	—	—	—	—	—	—	—	—	
Reclassification of preferred stock tranche rights liability upon issuance of milestone shares	—	—	—	—	—	81,190	—	—	—	—	—	—	—	
Reclassification of warrant liability upon exercise of preferred stock warrant	—	—	—	5,380	—	—	—	—	—	—	—	—	—	
Exercise of common stock warrants	—	—	—	—	—	—	137,446	—	614	—	—	—	614	
Conversion of convertible preferred stock into common stock upon initial public offering	(477,297)	(1,067)	(7,985,305)	(22,963)	(19,770,070)	(150,474)	28,232,672	3	174,501	—	—	—	174,504	
Issuance of common stock for cash, net of issuance costs of \$15,445	—	—	—	—	—	—	11,499,998	1	168,555	—	—	—	168,556	
Cashless exercise of common stock warrants	—	—	—	—	—	—	178,847	—	—	—	—	—	—	
Stock options exercised	—	—	—	—	—	—	5,183	—	15	—	—	—	15	
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	(231)	—	—	(231)	
Share-based compensation	—	—	—	—	—	—	—	—	922	—	—	—	922	
Net loss	—	—	—	—	—	—	—	—	(100,606)	—	—	—	(100,606)	
Balance as of December 31, 2021	—	\$ —	—	\$ —	—	\$ —	40,473,270	\$ 4	\$ 352,981	\$ (127,571)	\$ (231)	\$ —	\$ 225,183	

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

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**ACUMEN PHARMACEUTICALS, INC.**  
**STATEMENTS OF CASH FLOWS**  
(in thousands)

	Year Ended December 31,	
	2021	2020
<b>Cash flows from operating activities</b>		
Net loss	\$(100,606)	\$(7,325)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	4	—
Change in fair value of preferred stock tranche rights liability and preferred stock warrant liability	81,157	(586)
Stock-based compensation expense	922	154
Amortization of premiums and accretion of discounts on marketable securities, net	155	—
Other non-cash expense	109	—
Changes in operating assets and liabilities:		
Grant receivable	—	(79)
Prepaid expenses and other current assets	(3,881)	53
Other assets	(14)	144
Accounts payable	557	308
Accrued expenses and other current liabilities	3,636	(119)
Net cash used in operating activities	(17,961)	(7,450)
<b>Cash flows from investing activities</b>		
Purchases of available-for-sale marketable securities	(104,080)	—
Purchases of property and equipment	(40)	—
Net cash used in investing activities	(104,120)	—
<b>Cash flows from financing activities</b>		
Proceeds from issuance of Series B milestone shares, net of issuance costs	30,031	—
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	44,675
Proceeds from exercise of Series A-1 warrant	1,250	—
Proceeds from exercise of common stock warrants	614	—
Proceeds from issuance of common stock upon initial public offering, net of issuance costs	168,556	—
Proceeds from stock option exercises	15	—
Net cash provided by financing activities	200,466	44,675
Net change in cash and cash equivalents	78,385	37,225
Cash and cash equivalents at the beginning of the period	43,777	6,552
Cash and cash equivalents at the end of the period	\$ 122,162	\$43,777
<b>Supplemental disclosure of cash flow information</b>		
Cash paid for income taxes	\$ —	\$ —
Cash paid for interest	\$ —	\$ —
<b>Supplemental disclosure of noncash financing activities</b>		
Reclassification of preferred stock tranche rights liability upon share issuance	\$ 81,190	\$ —
Reclassification of warrant liability upon exercise of preferred stock warrant	\$ 5,380	\$ —
Conversion of convertible preferred stock into common stock upon IPO	\$ 174,504	\$ —

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

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**ACUMEN PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

**NOTE 1. DESCRIPTION OF ORGANIZATION AND BUSINESS OPERATIONS**

Acumen Pharmaceuticals, Inc. (“Acumen” or the “Company”) was incorporated in 1996 in the state of Delaware. Acumen discovers and develops targeted therapies for the treatment of Alzheimer’s disease (“AD”). Acumen’s sole drug candidate, ACU193, is a humanized monoclonal antibody which selectively targets amyloid-beta oligomers (“A $\beta$ Os”). Acumen and Merck & Co., Inc. discovered and developed ACU193 through an eight-year research collaboration. Acumen currently holds exclusive rights to the program. The Company submitted an Investigational New Drug Application for ACU193 to the Food and Drug Administration in the fourth quarter of 2020. The Company initiated a Phase 1 clinical trial of ACU193 in the second quarter of 2021, which the Company named “INTERCEPT-AD.” Approximately 62 individuals with early AD (mild cognitive impairment or mild dementia due to AD) are expected to be randomized into this double-blind, placebo-controlled, first-in-human study of ACU193. INTERCEPT-AD consists of single-ascending-dose and multiple-ascending-dose cohorts and the overall objective of the trial is to evaluate the safety and tolerability and establish clinical proof of mechanism of ACU193 administered intravenously. In October 2021, the Company announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients. Clinical trial site activation and patient recruitment and enrollment is ongoing. At present, INTERCEPT-AD is in the single-ascending-dose portion of the trial. Based on current site activations and enrollment rates, the Company anticipates reporting its topline data from this trial in the first half of 2023.

The Company is subject to the uncertainty of whether the Company’s intellectual property will develop into successful commercial products.

***November 2020 Reverse Stock Split***

On November 20, 2020, the Company effected a 1-for-30 reverse stock split of its authorized, issued and outstanding shares of common stock and convertible preferred stock. Accordingly, all share and per share amounts for the periods presented in the accompanying financial statements and these notes have been adjusted retroactively, where applicable, to reflect this reverse stock split. On November 20, 2020, the Company also increased the number of shares of preferred stock and common stock authorized for issuance (see Note 6).

***June 2021 Reverse Stock Split***

The Company’s Board of Directors (“Board”) approved a reverse split of shares of the Company’s common stock and convertible preferred stock on a 1-for-1.49 basis (the “June 2021 Reverse Stock Split”), which was effected on June 23, 2021. The par value and the number of authorized shares of the convertible preferred stock and common stock were not adjusted in connection with the June 2021 Reverse Stock Split. All references to common stock, convertible preferred stock, warrants to purchase common stock, warrants to purchase convertible preferred stock, options to purchase common stock, share data, per share data and related information contained in the financial statements have been retrospectively adjusted to reflect the effect of the June 2021 Reverse Stock Split for all periods presented. No fractional shares of the Company’s common stock were issued in connection with the June 2021 Reverse Stock Split. Any fractional share resulting from the June 2021 Reverse Stock Split was rounded down to the nearest whole share, and any stockholder entitled to a fractional share as a result of the June 2021 Reverse Stock Split received a cash payment in lieu of receiving fractional shares.

***Initial Public Offering***

On July 6, 2021, the Company issued 9,999,999 shares of common stock in an initial public offering (“IPO”), and on July 8, 2021, the Company issued an additional 1,499,999 shares of common stock that were purchased by the underwriters pursuant to the underwriters’ option to purchase additional shares at the public offering price

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**ACUMEN PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

less underwriting discounts and commissions. The price to the public for each share was \$16.00. The aggregate net proceeds from the Company's IPO, after underwriting discounts and commissions and other offering expenses of \$15.4 million, were \$168.6 million.

On July 6, 2021, in connection with the closing of the IPO, 477,297 shares of Series A, 7,985,305 shares of Series A-1, and 19,770,070 shares of Series B convertible preferred stock, respectively, automatically converted into an equal number of shares of common stock. Warrants to purchase shares of common stock were automatically net exercised for the purchase of an aggregate of 178,847 shares of common stock.

As a result of the IPO, the underwriters' exercise of their option, the conversions of the Series A, A-1 and B convertible preferred stock, and the exercise of the warrants, the Company's total number of outstanding common shares increased by 39,911,517 immediately following the closing of the IPO.

***Liquidity and Capital Resources***

The Company has incurred operating losses since inception and expects to continue to incur significant operating losses for the foreseeable future and may never become profitable. As of December 31, 2021 and 2020, the Company had an accumulated deficit of \$127.6 million and \$27.0 million, respectively, and working capital of \$193.5 million and \$38.1 million, respectively. Prior to the IPO, the Company historically relied on raising capital from venture capital firms and private investors and funding from a government grant to finance its operations.

On June 9, 2021, the Board and the holders of more than 67% of the then outstanding shares of Series B convertible preferred stock held by the Series B purchasers (the "Requisite Investors") elected to waive the achievement of the milestone subject to the terms and conditions of the Series B Preferred Stock Purchase Agreement (the "Series B Agreement") and consummate the subsequent closing (the "Milestone Closing") (see Note 5). On June 17, 2021, the Milestone Closing for the Series B convertible preferred stock occurred, resulting in the sale of 7,908,027 shares of Series B convertible preferred stock at \$3.80 per share for gross proceeds of \$30.0 million.

As a result of the Milestone Closing and the closing of the Company's IPO on July 6, 2021, management believes that its existing cash and cash equivalents and marketable securities will be sufficient to enable the Company to fund its operating expenses and capital expenditure requirements at least through 2025. Future capital requirements will depend upon many factors, including the timing and extent of spending on research and development and market acceptance of the Company's products. The Company may need to obtain additional financing to complete clinical trials and launch and commercialize any product candidates for which it receives regulatory approval. Until such time, if ever, the Company can generate revenue sufficient to achieve profitability, the Company expects to finance its operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. There can be no assurance that such financing will be available on terms acceptable to the Company, or at all. To the extent that the Company raises additional capital through the sale of equity or convertible debt securities, the ownership interest of its stockholders will be diluted, and the terms of these securities may include liquidation of other preferences that adversely affect the rights of common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting the Company's ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. If the Company is unable to maintain sufficient financial resources, its business, financial condition and results of operations will be materially and adversely affected. The Company may be required to delay, limit, reduce or terminate its product discovery and development activities or future commercialization efforts.

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[\*\*Table of Contents\*\*](#)**ACUMEN PHARMACEUTICALS, INC.  
NOTES TO FINANCIAL STATEMENTS**

In October 2021, the Company announced the initial dosing of the first patient in the INTERCEPT-AD trial and the subsequent successful sentinel safety review of the first two patients. Due to delays in clinical trial site activation and patient enrollment that the Company believes are principally related to effects of the coronavirus (“COVID-19”) pandemic, the Company is expanding the anticipated number of trial sites to support its enrollment objectives and anticipated timelines. Clinical trial site activation and patient recruitment and enrollment is ongoing. At present, INTERCEPT-AD is in the single-ascending-dose portion of the trial. Based on current site activations and enrollment rates, the Company anticipates reporting its topline data from this trial in the first half of 2023. The ultimate impact of the COVID-19 pandemic on the Company’s business, results of operations, financial position and cash flows will depend on future developments, including the duration and spread of the outbreak and related advisories and restrictions. These developments and the impact of the COVID-19 pandemic on the financial markets and the overall economy are highly uncertain and cannot be predicted. If the financial markets and/or the overall economy are impacted for an extended period, the Company’s business, results of operations, financial position and cash flows may be materially adversely affected.

**NOTE 2. BASIS OF PRESENTATION, SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES AND RECENT ACCOUNTING PRONOUNCEMENTS*****Basis of Presentation***

The accompanying financial statements of the Company have been prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”) and pursuant to the rules and regulations of the U.S. Securities and Exchange Commission (“SEC”). In the opinion of management, all adjustments (consisting of normal recurring adjustments) have been made that are necessary to present fairly the Company’s financial position, and the results of its operations and its cash flows.

***Emerging Growth Company***

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (“FASB”), or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on the Company’s financial statements upon adoption. Under the Jumpstart Our Business Startups Act of 2012, as amended, the Company meets the definition of an emerging growth company and has elected the extended transition period for complying with new or revised accounting standards, which delays the adoption of these accounting standards until they would apply to private companies.

***Use of Estimates***

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of expenses during the reporting periods. These estimates and assumptions are based on our historical experience, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources.

Actual results may differ from these estimates under different assumptions or conditions. To the extent there are material differences between the estimates and actual results, the Company’s future results of operations will be affected.

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### **ACUMEN PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS**

#### **Cash and Cash Equivalents**

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. The Company's cash equivalents consist of funds held in several money market accounts. The Company had \$121.2 million and \$36.8 million in cash equivalents as of December 31, 2021 and 2020, respectively.

#### **Marketable Securities**

The Company's marketable securities portfolio consists primarily of investments in money market funds, commercial paper, asset-backed securities, U.S. treasury securities and short-term highly liquid, high credit quality corporate debt securities. The Company considers its marketable securities to be available-for-sale. Available-for-sale securities are classified as cash equivalents, or as short-term or long-term marketable securities based on the maturity date at time of purchase and their availability to meet current operating requirements. Available-for-sale securities that mature in three months or less from the date of purchase are classified as cash equivalents. Available-for-sale securities, excluding cash equivalents, that mature in one year or less are classified as short-term marketable securities and those that mature in more than one year are classified as long-term.

Securities that are classified as available-for-sale are measured at fair value; see "*Fair Value of Financial Instruments*" below. Any premium arising at purchase is amortized to the earliest call date and any discount arising at purchase is accreted to maturity. Amortization and accretion of premiums and discounts are recorded along with interest income on investments in interest income, net in the statements of operations and comprehensive loss. Unrealized gains and losses are excluded from earnings and are reported as a component of other comprehensive income. The Company periodically evaluates whether declines in fair values of its available-for-sale securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss, as well as the Company's ability and intent to hold the available-for-sale security until a forecasted recovery occurs. The Company does not generally intend to sell its available-for-sale securities; however, the Company assesses whether it is more likely than not that it will be required to sell any security before recovery of its amortized cost basis. Realized gains and losses and declines in fair value judged to be other-than-temporary on available-for-sale securities will be included in other expense, net. The cost of investments sold will be calculated using the specific-identification method. The Company did not record any other-than-temporary impairments related to available-for-sale securities for the year ended December 31, 2021. The Company did not own any marketable securities during the year ended December 31, 2020.

#### **Concentrations of Credit Risk**

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash, cash equivalents and marketable securities. The Company may maintain deposits in financial institutions in excess of government insured limits. Management believes that the Company is not exposed to significant credit risk as the Company's cash and cash equivalents are held at financial institutions that management believes to be of high credit quality. The Company has not experienced any losses due to credit risk on such accounts during any of the periods presented.

#### **Fair Value of Financial Instruments**

The Company's financial assets and liabilities are accounted for in accordance with Accounting Standards Codification ("ASC") 820, *Fair Value Measurements and Disclosures*, which defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most

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**ACUMEN PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The fair value hierarchy requires an entity to maximize the use of observable inputs when measuring fair value and classifies those inputs into three levels:

- Level 1 — Observable inputs, such as quoted prices in active markets for identical assets or liabilities.
- Level 2 — Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the instrument's anticipated life.
- Level 3 — Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair values requires more judgement. Accordingly, the degree of judgement exercised by management in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying values reported in the Company's balance sheets for cash (excluding cash equivalents which are recorded at fair value on a recurring basis), accounts payable and accrued expenses are reasonable estimates of their fair values due to the short-term nature of these items.

The following tables present the Company's fair value hierarchy for its money market securities, available-for-sale marketable securities, preferred stock tranche rights liability and preferred stock warrant liability measured at fair value on a recurring basis (in thousands):

	Fair value measurements at reporting date using			Fair Value at December 31, 2021
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	
<b>Assets included in:</b>				
Cash and cash equivalents				
Money market securities	\$ 121,162	\$ —	\$ —	\$ 121,162
Marketable securities				
Commercial paper	—	47,939	—	47,939
Corporate debt securities	—	24,694	—	24,694
Asset-backed securities	—	19,143	—	19,143
U.S. treasury securities	—	11,918	—	11,918
Total fair value	<u>\$ 121,162</u>	<u>\$ 103,694</u>	<u>\$ —</u>	<u>\$ 224,856</u>

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**ACUMEN PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

	Fair value measurements at reporting date using			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Fair Value at December 31, 2020
<b>Assets included in:</b>				
Cash and cash equivalents				
Money market securities	\$ 36,758	\$ —	\$ —	\$ 36,758
Total fair value	<u><u>\$ 36,758</u></u>	<u><u>\$ —</u></u>	<u><u>\$ —</u></u>	<u><u>\$ 36,758</u></u>
<b>Liabilities included in:</b>				
Preferred stock tranche rights liability	\$ —	\$ —	\$ 5,033	\$ 5,033
Preferred stock warrant liability	—	—	380	380
Total fair value	<u><u>\$ —</u></u>	<u><u>\$ —</u></u>	<u><u>\$ 5,413</u></u>	<u><u>\$ 5,413</u></u>

The fair value of the Company's money market funds is determined using quoted market prices in active markets for identical assets.

The fair value for the available-for-sale marketable securities is determined based on valuation models using inputs that are observable either directly or indirectly (Level 2 inputs), such as quoted prices for similar assets or liabilities, yield curve, volatility factors, credit spreads, default rates, loss severity, current market and contractual prices for the underlying instruments or debt, broker and dealer quotes, as well as other relevant economic measures.

Refer to Note 5 for further information about the Level 3 rollforward of activity and Level 3 inputs.

**Grant Receivable**

Grant receivable consists of research expenses reimbursable under a grant from the National Institute of Health ("NIH"). The Company carried its grant receivable at the unreimbursed amount. Management determined that the remainder of the unreimbursed amount under the grant receivable could no longer be collected from the NIH and the Company recorded a loss of \$0.1 million in general and administrative expense on the statement of operations and comprehensive loss during the year ended December 31, 2021. Management determined that no allowance was necessary for this receivable as of December 31, 2020.

**Property and Equipment**

Property and equipment consists primarily of computer equipment and is stated at cost and depreciated using the straight-line method over the estimated useful lives of the assets, which is generally three years for computer-related assets.

**Convertible Preferred Stock**

The Company recorded shares of convertible preferred stock at their respective fair values on the dates of issuance, net of issuance costs. The Company applied the guidance in ASC 480-10-S99-3A, *SEC Staff Announcement: Classification and Measurement of Redeemable Securities*, and therefore classified the Series A, Series A-1 and Series B convertible preferred stock as mezzanine equity. The convertible preferred stock was recorded outside of stockholders' deficit because, in the event of certain deemed liquidation events considered

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# **ACUMEN PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS**

not solely within the Company's control, such as a merger, acquisition and sale of all or substantially all of the Company's assets, the convertible preferred stock would have become redeemable at the option of the holders. In the event of a change of control of the Company, proceeds received from the sale of such shares would have been distributed in accordance with the corresponding liquidation preferences. The Company did not adjust the carrying values of the convertible preferred stock to the deemed liquidation values of such shares since a liquidation event was not probable at any of the reporting dates.

As mentioned above in Note 1, in connection with the closing of the IPO, all of the outstanding shares of Series A, Series A-1 and Series B convertible preferred stock automatically converted into an equal number of shares of common stock on July 6, 2021.

### ***Preferred Stock Tranche Rights Liability***

The Company determined that its obligation to issue, and the Company's investors' right to purchase, additional shares of Series B convertible preferred stock pursuant to the Milestone Closing (see Note 1 and Note 5) represented a freestanding financial instrument (the "tranche liability"). The tranche liability was initially recorded at fair value. The proceeds from the sale of the convertible preferred stock were first allocated to the fair value of the tranche liability with the remaining proceeds from the sale of the convertible preferred stock allocated to the Series B convertible preferred stock. The tranche liability was remeasured at each reporting period and upon the exercise of the obligation, with gains and losses arising from subsequent changes in its fair value recognized in other income and expense in the statements of operations and comprehensive loss. As discussed above in Note 1, the Milestone Closing occurred on June 17, 2021, and as a result, the remaining value of the tranche liability was reclassified to convertible preferred stock on the balance sheet.

### ***Preferred Stock Warrant Liability***

The Company accounted for the warrant to purchase Series A-1 convertible preferred stock as a liability as this warrant was a freestanding financial instrument that required the Company to transfer assets upon exercise. The warrant liability was initially recorded at fair value. The warrant liability was remeasured at each reporting period and upon the exercise of the applicable warrant, with gains and losses arising from subsequent changes in its fair value recognized in other income and expense in the statements of operations and comprehensive loss. The warrant was exercised on June 22, 2021, and the remaining value of the warrant liability was reclassified to convertible preferred stock on the balance sheet. There were no preferred stock warrants outstanding as of December 31, 2021.

### ***Common Stock Warrants***

The Company assesses whether warrants issued require accounting as derivatives. The Company determined that its common stock warrants were (1) indexed to the Company's own stock and (2) classified in stockholders' equity in accordance with FASB ASC Topic 815, *Derivatives and Hedging*. As such, the Company concluded the warrants met the scope exception for determining whether the instruments require accounting as derivatives and should be classified in stockholders' equity. In June 2021, several holders of warrants to purchase the Company's common stock exercised their warrants and purchased a total of 137,446 shares of common stock at an exercise price of \$4.47. On July 6, 2021, in connection with the closing of the Company's IPO, the Company issued 178,847 shares of common stock in exchange for the 248,247 outstanding common stock warrants at an exercise price of \$4.47. There were no common stock warrants outstanding as of December 31, 2021.

### ***Grant and Other Revenue Recognition***

The Company's NIH grant is not within the scope of ASC 606, *Revenue from Contracts with Customers* ("ASC 606"), as the grant does not meet the definition of a contract with a customer. The Company has concluded that

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# **ACUMEN PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS**

the grant meets the definition of a contribution and is a non-reciprocal transaction, and management has also concluded that Subtopic 958-605, *Not-for-Profit-Entities-Revenue Recognition* does not apply, as Acumen is a business entity and the grant is with a governmental agency.

In the absence of applicable guidance under U.S. GAAP, the Company's policy is to recognize grant revenue when the related costs are incurred and the right to payment is realized. Costs incurred are recorded in research and development and general and administrative expenses on the statements of operations and comprehensive loss.

The Company believes the recognition of revenue as costs are incurred and amounts become realizable is analogous to the concept of transfer of control of a service over time under ASC 606.

### ***Research and Development Expenses***

Research and development expenses primarily consist of consultants and materials, biologic storage, salaries and other personnel-related expenses related to research and development activities and are expensed as incurred. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected on the balance sheets as prepaid or accrued expenses. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies, including the phase or completion of events, invoices received and contracted costs.

### ***Stock-based Compensation***

The Company expenses stock-based compensation to employees, non-employees and board members over the requisite service period based on the estimated grant date fair value of the awards and actual forfeitures. The Company estimates the fair value of stock option grants using the Black-Scholes option pricing model, which requires the use of a number of complex assumptions including the fair value of the common stock, expected volatility, risk-free interest rate, expected dividends, and the expected term of the option. The assumptions used in calculating the fair value of stock-based awards represent management's best estimates and involve inherent uncertainties and the application of management's judgment. Stock-based awards with graded-vesting schedules are recognized on a straight-line basis over the requisite service period for each separately vesting portion of the award. All stock-based compensation costs are recorded in research and development expense or general and administrative expense in the statements of operations and comprehensive loss based upon the respective employee's or non-employee's roles within the Company. Forfeitures are recorded as they occur. See also Note 7 below.

### ***Income Taxes***

Income taxes are recorded in accordance with ASC 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse, and net operating loss ("NOL") carryforwards and research and development ("R&D") tax credit carryforwards. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has recorded a full valuation allowance to reduce its net deferred income tax assets to zero. In the event the Company were to determine that it would be able to realize some or all of its deferred income tax assets in the future, an adjustment

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# **ACUMEN PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS**

to the deferred income tax asset valuation allowance would increase income in the period such determination was made.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit would more likely than not be realized assuming examination by the taxing authority. 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 has not recorded any accruals related to uncertain tax positions as of December 31, 2021 and 2020. The Company's policy is to record interest and penalties, if any, as part of income tax benefit. No interest or penalties were recorded during the years ended December 31, 2021 and 2020.

### ***Net Loss Per Share of Common Stock***

Basic net loss per share of common stock is calculated using the two-class method under which earnings are allocated to both common shares and participating securities based on their participation rights. Net loss attributable to common stockholders was not allocated to the convertible preferred stock as the holders of the convertible preferred stock did not have a contractual obligation to share in any losses. Basic net loss per share is calculated by dividing the net loss attributable to common shares by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share of common stock is computed by dividing the net loss using the weighted-average number of common shares and, if dilutive, potential common shares outstanding during the period. Potential common shares consist of stock options and warrants to purchase common stock (using the treasury stock method), and the conversion of convertible preferred stock and the preferred warrant (using the if-converted method). See Note 10 below.

### ***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 segment.

### ***Recently Issued Accounting Pronouncements***

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, as amended, with guidance regarding the accounting for and disclosure of leases. This update requires lessees to recognize the liabilities related to all leases, including operating leases, with a term greater than 12 months on the balance sheet. This update also requires lessees and lessors to disclose key information about their leasing transactions. Topic 842 became effective on January 1, 2022. The Company will adopt this guidance using the modified retrospective method and will elect the package of practical expedients upon transition, which will retain the lease classification for leases that existed prior to the adoption of this guidance. Additionally, in calculating the right-of-use asset and lease liability, the Company will elect to combine lease and non-lease components as permitted under the guidance and to exclude short-term leases having initial terms of 12 months or less as an accounting policy election and recognize rent expense on a straight-line basis over the lease term for short-term leases. Upon adoption, the Company will record both a right-of-use asset and a lease liability of approximately \$0.2 million on its balance sheet.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which was codified with its subsequent amendments as ASC 326. ASC 326 changes how entities account for credit losses on financial assets and other instruments that are not measured.

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**ACUMEN PHARMACEUTICALS, INC.**  
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at fair value through net income, including available-for-sale securities. The amendments require an entity to replace the incurred loss impairment methodology in current U.S. GAAP with a methodology that reflects current expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. The updated guidance is effective for the Company on January 1, 2023, with early adoption permitted. The Company is currently evaluating the impact of this new guidance on its financial statements and related disclosures.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* (“ASU 2019-12”), which is intended to simplify various aspects related to accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in ASC 740 and also clarifies and amends existing guidance to improve consistent application. This guidance is effective for the Company for annual reporting periods beginning January 1, 2022, and interim periods within fiscal years beginning on January 1, 2023, with early adoption permitted. The Company is currently evaluating the impact of this standard on its financial statements.

### **NOTE 3. MARKETABLE SECURITIES**

Marketable securities consisted of the following as of December 31, 2021 (in thousands):

	<u>Amortized Cost</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	<u>Fair Value</u>
Available-for-sale securities, short-term				
Commercial paper	\$ 47,939	\$ —	\$ —	\$ 47,939
Corporate debt securities	7,992	—	(11)	7,981
Asset-backed securities	<u>16,177</u>	<u>—</u>	<u>(22)</u>	<u>16,155</u>
Total available-for-sale securities, short-term	72,108	—	(33)	72,075
Available-for-sale securities, long-term				
Corporate debt securities	16,816	—	(103)	16,713
Asset-backed securities	3,013	—	(25)	2,988
U.S. treasury securities	<u>11,988</u>	<u>—</u>	<u>(70)</u>	<u>11,918</u>
Total available-for-sale securities, long-term	31,817	—	(198)	31,619
Total available-for-sale securities	<u>\$103,925</u>	<u>\$ —</u>	<u>\$ (231)</u>	<u>\$103,694</u>

As of December 31, 2021, the Company’s available-for-sale securities classified as short-term mature in one year or less and the Company’s available-for-sale securities classified as long-term mature within two years. Fourteen of the available-for-sale marketable securities were in an unrealized loss position as of December 31, 2021, all of which were in a loss position for less than twelve months. Unrealized losses on available-for-sale securities as of December 31, 2021 were not significant and were primarily due to changes in interest rates, including market credit spreads, and not due to increased credit risks associated with specific securities. Accordingly, no other-than-temporary impairment was recorded for the year ended December 31, 2021. There were no realized gains or losses for the year ended December 31, 2021.

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**NOTE 4. SUPPLEMENTAL FINANCIAL INFORMATION**

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2021	2020
Research and development service agreements	\$2,591	\$432
Prepaid insurance	1,514	5
Dues and subscriptions	96	—
Prepaid raw materials	83	91
Other	140	15
Total prepaid expenses and other current assets	<u>\$4,424</u>	<u>\$543</u>

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2021	2020
Research and development	\$2,623	\$133
Bonuses and other employee liabilities	1,102	—
Legal	130	—
Professional fees	—	200
Other	204	90
Total accrued expenses and other current liabilities	<u>\$4,059</u>	<u>\$423</u>

**NOTE 5. CONVERTIBLE PREFERRED STOCK, TRANCHE LIABILITY AND WARRANT LIABILITY**

***Convertible Preferred Stock***

On November 20, 2020, the Company entered into the Series B Agreement for a private placement of up to 19,770,070 shares of Series B convertible preferred stock, \$0.0001 par value per share, at an original issuance price of \$3.80 per share, subject to separate closings, including: (1) 11,862,043 shares at the Initial Closing on November 20, 2020, and (2) 7,908,027 shares at a subsequent closing that would be triggered by the achievement of a specific clinical milestone. The Series B Agreement obligated the Company to issue and sell and the Series B purchasers to purchase up to a total of 7,908,027 additional shares of Series B convertible preferred stock (the “Milestone Shares”) at the same price per share upon the achievement of a certain defined clinical milestone. The determination as to whether the milestone event has been met was subject to certification by the Board and the Requisite Investors. Each Series B convertible preferred stock investor had the right, but not the obligation, to purchase all or any portion of the Milestone Shares at any time in its sole option and in its sole and absolute discretion, whether or not the Company achieved the applicable clinical milestone. See “*Series B Convertible Preferred Stock Tranche Rights Liability*” below.

As discussed above in Note 1, on June 9, 2021, the Board and the Requisite Investors elected to waive the achievement of the milestone subject to the terms and conditions of the Series B Agreement and consummate the Milestone Closing and, on June 17, 2021, the Milestone Closing occurred, resulting in the sale of 7,908,027 shares of Series B convertible preferred stock at \$3.80 per share for gross proceeds of \$30.0 million, bringing the total number of Series B convertible preferred shares outstanding to 19,770,070.

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On June 22, 2021, a warrant to purchase 447,426 shares of Series A-1 convertible preferred stock at an exercise price of \$2.794 per share was exercised (see “*Series A-1 Convertible Preferred Stock Warrant Liability*” below), bringing the total number of Series A-1 convertible preferred shares outstanding to 7,985,305.

Additionally, on July 6, 2021, in connection with the closing of the IPO, 477,297 shares of Series A, 7,985,305 shares of Series A-1, and 19,770,070 shares of Series B convertible preferred stock, respectively, automatically converted into an equal number of shares of common stock. There were no shares of convertible preferred stock outstanding as of December 31, 2021.

Convertible preferred stock consisted of the following as of December 31, 2020 (in thousands, except share and per share data):

	<u>Shares Authorized</u>	<u>Shares Issued and Outstanding</u>	<u>Weighted Average Issuance Price per Share</u>	<u>Carrying Value</u>	<u>Liquidation Preference</u>
Series A	711,203	477,297	\$ 2.24	\$ 1,067	\$ 1,067
Series A-1	11,898,177	7,537,879	2.24	16,333	16,847
Series B	29,457,450	11,862,043	3.80	39,253	45,070
Total	<u>42,066,830</u>	<u>19,877,219</u>		<u>\$56,653</u>	<u>\$ 62,984</u>

*Dividends*

The holders of Series B, Series A-1 and Series A convertible preferred stock were entitled to receive dividends ahead of, or simultaneously with, common stockholders in an amount equal to the product of (A) the dividend payable on each share of the class or series of convertible preferred stock determined, if applicable, as if all shares of such class or series of convertible preferred stock had been converted into common stock and (B) the number of shares of common stock issuable upon conversion of a share of preferred stock. No dividends have been declared since inception.

*Liquidation preference*

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, holders of Series B convertible preferred stock were entitled to receive, prior and in preference to, holders of Series A-1 convertible preferred stock, Series A convertible preferred stock, and holders of common stock, in the amount of the original issue price plus any declared but unpaid dividends thereon. If upon occurrence of such an event, the assets and funds to be distributed among the holders of Series B convertible preferred stock were insufficient to permit full payment to such holders, the entire assets and funds of the Company legally available for distribution would have been distributed ratably among the holders of the Series B convertible preferred stock.

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, holders of Series A-1 convertible preferred stock were entitled to receive, prior and in preference to, holders of Series A convertible preferred stock and holders of common stock, in the amount of the original issue price plus any declared but unpaid dividends thereon. If upon occurrence of such an event, the assets and funds to be distributed among the holders of Series A-1 convertible preferred stock were insufficient to permit full payment to such holders, the entire assets and funds of the Company legally available for distribution would have been distributed ratably among the holders of the Series A-1 convertible preferred stock.

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, holders of Series A convertible preferred stock were entitled to receive, prior and in preference to, holders of common

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stock, in the amount of the original issue price plus any declared but unpaid dividends thereon. If upon occurrence of such an event, the assets and funds to be distributed among the holders of Series A convertible preferred stock were insufficient to permit full payment to such holders, the entire assets and funds of the Company legally available for distribution would have been distributed ratably among the holders of the Series A convertible preferred stock.

***Conversion rights***

Shares of all series of convertible preferred stock were convertible into such number of fully paid and non-assessable shares of common stock as determined by dividing the original issuance price for such series by the applicable conversion price for such series then in effect. The initial conversion price per share for each series of convertible preferred stock was the original issue price applicable to such series as shown in the table above, subject to adjustment in the event of certain dilutive issuances. The convertible preferred stock original issuance price and conversion price were each subject to adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the convertible preferred stock.

Each share of convertible preferred stock was convertible at any time at the option of the holder at the conversion ratio then in effect. In addition, each share of convertible preferred stock was to be automatically converted into common stock at the conversion ratio then in effect upon either (a) the closing of an underwritten public offering resulting in gross proceeds to the Company of at least \$75 million and at a price per share equal to at least two times the Series B original issuance price, or \$7.60 (subject to adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B convertible preferred stock), or (b) the date and time, or the occurrence of an event, specified in such vote or written consent of at least 67% of the holders of the then outstanding shares of Series B convertible preferred stock.

If any Series B purchaser failed to purchase its respective portion of the Milestone Shares upon occurrence of the Milestone Closing, each existing share of Series B convertible preferred stock held by such stockholder would have automatically converted into one share of common stock two days after the Milestone Closing.

On July 6, 2021, in connection with the closing of the IPO, each outstanding share of Series A, Series A-1 and Series B convertible preferred stock converted into one share of common stock.

***Voting rights***

Holders of convertible preferred stock were entitled to vote as a single class together with the holders of common stock and had one vote for each share of common stock into which the convertible preferred stock was convertible.

The holders of Series B convertible preferred stock were entitled to elect two directors to the Board, and the holders of Series A and Series A-1 convertible preferred stock, voting together as a single class, were also entitled to elect two directors to the Board. The holders of common stock, exclusively and as a separate class, are entitled to elect two directors to the Board. The final director to the Board was designated by the holders of a majority of the shares of the preferred stock and common stock, voting together as a single class.

A majority of the outstanding shares of convertible preferred stock was necessary for approving certain matters, including the ability to either increase or decrease the authorized number of directors constituting the Board, pursuant to protective provisions in the Company's amended and restated certificate of incorporation.

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# ACUMEN PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS

### **Series B Convertible Preferred Stock Tranche Rights Liability**

The Company concluded that the tranche liability met the definition of a freestanding financial instrument, as it was legally detachable and separately exercisable from the initial closing of the Series B convertible preferred stock. The fair value for the tranche liability was estimated as a forward contract using a valuation model, calibrated at issuance. The valuation model at issuance estimated the implied value of the Series B stock as of the expected milestone date utilizing the probability of milestone achievement, expected timing of milestone achievement, and risk-free rate. The model was calibrated such that the value of the initial tranche and the forward contract were equal to the initial tranche proceeds at issuance. Subsequently, the fair value of the liability was discounted to the valuation date and adjusted for probability of the achievement of the milestone event. The calibrated valuation model was updated as of December 31, 2020, March 31, 2021 and in the Stay Private scenario utilized in the hybrid methodology as of June 17, 2021 (the date of the Milestone Closing). Significant estimates and assumptions impacting fair value include the discount rate, expected time to the Milestone Closing, and probability of the Milestone Closing. The discount rate was equal to the risk-free rate commensurate with the estimated timing of the Milestone Closing.

The following assumptions were used in the estimation of the fair value of the tranche liability as a forward contract as of each of the dates indicated:

	<u>June 17, 2021</u>	<u>December 31, 2020</u>
Risk-free interest rate	0.07%	0.12%
Expected time to Milestone Closing (in years)	0.8	1.3
Probability of achievement of Milestone Closing	100%	65%

For the other portion of the hybrid method used as of June 17, 2021, the fair value for the tranche liability was estimated based upon an allocation of the underlying equity value, which was determined using an IPO value as estimated through analysis of IPOs for comparable guideline companies, to arrive at a value per share in the IPO scenario. The estimated fair value of the tranche liability was \$81,190,000 and \$5,033,000 as of the Milestone Closing on June 17, 2021 and December 31, 2020, respectively. The significant increase in the June 17, 2021 valuation stems from both a shift in methodology from an option pricing method (“OPM”) to a Hybrid Model where the concluded value of the forward tranche is derived by the sum of the probability weighted present value of the forward tranche in the Stay Private and IPO scenarios (with the former including all other potential exit scenarios other than an imminent IPO), as well as the increase in the probability of achievement of the Milestone Closing. The resulting difference in estimated fair value was recognized as a change in fair value within other income in the accompanying statements of operations.

The tranche liability was revalued each reporting period with the change in fair value recorded in the accompanying statements of operations through the issuance of the Milestone Shares on June 17, 2021. Following the Milestone Closing, the remaining tranche liability was reclassified to convertible preferred stock on the balance sheet.

### **Series A-1 Convertible Preferred Stock Warrant Liability**

On October 19, 2018, the Company issued a ten-year warrant (the “Series A-1 Warrant”) to purchase up to an aggregate of 447,426 shares of Series A-1 convertible preferred stock at an exercise price of \$2.794 on or before October 18, 2028.

The warrant liability met the definition of a freestanding financial instrument, as it was legally detachable and separately exercisable from the initial closing of the Series A-1 convertible preferred stock. As such, it was

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revalued each reporting period with the change in fair value recorded in the accompanying statements of operations until the warrant was exercised on June 22, 2021.

The fair value of the warrant liability was estimated using the OPM backsolve method as of December 31, 2020 and using a hybrid method, which included an OPM backsolve in the Stay Private scenario as of June 22, 2021. The following assumptions were used in the estimation of the fair value of the warrant liability using the OPM backsolve method as of each of the dates indicated:

	June 22, 2021	December 31, 2020
Risk-free interest rate	0.25%	0.13%
Expected term (in years)	2.0	2.0
Expected volatility	90%	90%
Expected dividend yield	0%	0%

The hybrid method used to value the warrant liability at June 22, 2021 considered both the underlying equity value determined using the OPM backsolve method in a Stay Private scenario, as well as the underlying equity value that was determined using an expected IPO value as estimated through analysis of IPOs for comparable guideline companies, to arrive at a value per share in the IPO scenario. The underlying equity values from each approach were probability weighted based upon the expected likelihood of each scenario. The fair value of the warrant liability was estimated to be \$12.02 and \$0.85 as of June 22, 2021 and December 31, 2020, respectively.

The following table provides a reconciliation of the tranche liability and warrant liability measured at fair value using Level 3 significant unobservable inputs (in thousands):

	Series A-1 Preferred Stock Warrant	Series B Tranche Rights	Total
Balance, December 31, 2019	\$ 577	\$ —	\$ 577
Fair value at issuance of Series B convertible preferred stock (November 2020)	—	5,422	5,422
Change in fair value	(197)	(389)	(586)
Balance, December 31, 2020	380	5,033	5,413
Change in fair value	5,000	76,157	81,157
Settlement of tranche liability due to issuance of Milestone Shares	—	(81,190)	(81,190)
Settlement of warrant liability upon exercise of warrant	(5,380)	—	(5,380)
Balance, December 31, 2021	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

#### **NOTE 6. STOCKHOLDERS' EQUITY (DEFICIT)**

##### **Authorized Shares**

On July 6, 2021, the Company issued 9,999,999 shares of common stock in an IPO, and on July 8, 2021, the Company issued an additional 1,499,999 shares of common stock that were purchased by the underwriters pursuant to the underwriters' option to purchase additional shares at the public offering price less underwriting discounts and commissions. The price to the public for each share was \$16.00. The aggregate net proceeds from the Company's IPO, after underwriting discounts and commissions and other offering expenses of \$15.4 million, were \$168.6 million.

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### **ACUMEN PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS**

Effective upon the closing of the IPO on July 6, 2021, the Company amended its certificate of incorporation such that the total number of shares of all classes of capital stock authorized to be issued was increased to 310,000,000, with 10,000,000 shares designated as preferred stock with a par value of \$0.0001, and 300,000,000 shares designated as common stock with a par value of \$0.0001.

The Company amended its certificate of incorporation on November 20, 2020, such that the total number of shares of common stock authorized to be issued was increased to 50,500,000, and the total number of shares of preferred stock authorized to be issued was increased to 42,066,830, of which 711,203 were designated Series A convertible preferred stock, 11,898,177 were designated as Series A-1 convertible preferred stock and 29,457,450 were designated as Series B convertible preferred stock. The certificate of incorporation was also amended for the reverse stock splits that became effective on June 23, 2021 and November 20, 2020, but there were no changes to the authorized shares as a result of the reverse stock split that became effective on June 23, 2021 (see Note 1).

#### **Common Stock**

As of December 31, 2021, the Company's Amended and Restated Certificate of Incorporation authorized the issuance of 300,000,000 shares of common stock, \$0.0001 par value per share. Each share of common stock is entitled to one voting right.

#### **Common Stock Warrants**

In accordance with ASC 815, the common stock warrants issued in 2014 through 2017 did not meet the definition of a derivative and were classified in stockholders' deficit in the consolidated balance sheets.

In June 2021, several holders of warrants to purchase the Company's common stock exercised their warrants and purchased a total of 137,446 shares of common stock at an exercise price of \$4.47. On July 6, 2021, the Company issued 178,847 shares of common stock in exchange for the remaining 248,247 outstanding common stock warrants at an exercise price of \$4.47. As of December 31, 2021, there were no common stock warrants outstanding.

As of December 31, 2020, the outstanding warrants to purchase the Company's common stock were comprised of the following:

	<b>Equity Upon Exercise</b>	<b>Exercise Price</b>	<b>Expiration Dates</b>	<b>Number of Warrants</b>
Warrants issued in 2014	Common Stock	\$ 4.47	3/21/2024 – 6/30/2025	83,726
Warrants issued in 2015	Common Stock	\$ 4.47	6/30/2025	209,690
Warrants issued in 2016	Common Stock	\$ 4.47	6/30/2025	34,396
Warrants issued in 2017	Common Stock	\$ 4.47	6/30/2025	57,881
<b>Total Warrants</b>				<b>385,693</b>

## **NOTE 7. STOCK-BASED COMPENSATION**

### **2021 Equity Incentive Plan**

The 2021 Equity Incentive Plan (the "2021 Plan"), which provides for the grant of incentive stock options to employees, and the grant of nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance awards and other forms of stock awards to employees, directors and

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### ACUMEN PHARMACEUTICALS, INC. NOTES TO FINANCIAL STATEMENTS

consultants, became effective on June 30, 2021. Initially, the maximum number of shares of the Company's common stock that may be issued under the 2021 Plan was 7,698,282 shares, which is the sum of (1) 3,550,000 new shares, plus (2) 667,104 shares that remained available for issuance under the Company's Amended and Restated Stock Performance Plan that was adopted by the Board and stockholders on April 8, 2013 (as amended from time to time, most recently on November 20, 2020, the "2013 Plan") at the time the 2021 Plan became effective, plus (3) any shares subject to outstanding stock options or other stock awards that were granted under the 2013 Plan that, on or after the 2021 Plan became effective, terminate or expire prior to exercise or settlement, are settled in cash, are forfeited or repurchased because of the failure to vest, or are reacquired or withheld to satisfy a tax withholding obligation or the purchase or exercise price in accordance with the terms of the 2013 Plan. In addition, the number of shares of the Company's common stock reserved for issuance under the 2021 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2022 through January 1, 2031, in an amount equal to 5% of the total number of shares of the Company's common stock outstanding on December 31 of the fiscal year before the date of each automatic increase, or a lesser number of shares determined by the Board prior to the applicable January 1. The maximum number of shares of the Company's common stock that may be issued upon the exercise of incentive stock options under the 2021 Plan is 12,000,000. As of December 31, 2021, 4,217,104 shares were authorized for issuance under the 2021 Plan and 3,857,481 shares remained available for issuance under the 2021 Plan. The 2013 Plan provided for the grant of incentive stock options, nonstatutory stock options, issuance of shares of restricted stock and other equity awards to the Company's employees, officers, directors, consultants and advisors. All outstanding awards issued under the 2013 Plan remain subject to the terms of the 2013 Plan. As of December 31, 2021, there were 3,475,995 options outstanding under the 2013 Plan.

#### **Stock Options**

The Black-Scholes option-pricing model was used to estimate the fair value of stock options granted during the year ended December 31, 2021 with the following weighted average assumptions:

Risk-free interest rate	0.4% – 1.3%
Expected term (in years)	5.3 – 6.1
Expected volatility	90%
Expected dividend yield	0%

The weighted average grant date fair value of options granted during the year ended December 31, 2021, was \$1.93 per share. The Company did not grant any options during the year ended December 31, 2020.

Prior to its IPO, the fair value of the Company's common stock underlying the stock options has historically been determined by the Board with assistance from management and, occasionally with input from an independent third-party valuation firm. For the year ended December 31, 2020, management engaged an independent third-party valuation firm to provide an estimate of the fair value of its common stock. The fair value of common stock was determined considering a number of objective and subjective factors, including valuations of comparable companies, sales of convertible preferred stock, operating and financial performance, the lack of liquidity of the Company's common stock and the general and industry-specific economic outlook.

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As of December 31, 2020, management, with the assistance of an independent third-party valuation firm, estimated the fair value of a share of common stock to be \$0.83 utilizing the following assumptions:

Risk-free interest rate	0.13%
Expected time to liquidity event (in years)	2.0
Expected volatility	90%
Expected dividend yield	0%

The stock options granted after December 31, 2017 vest monthly over 24 or 36 months and have a ten-year contractual term. Stock options granted prior to December 31, 2017 were either fully vested upon grant or generally vested monthly over a range of three to 24 months and have a ten-year term. The Company became publicly traded in July 2021 and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies. Due to the lack of historical exercise history, the expected term of the Company's stock options has been determined using the "simplified" method for awards. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is zero based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The following table reflects summarized stock option activity:

	<u>Stock Options</u>	<u>Weighted Average Exercise Price</u>	<u>Weighted Average Remaining Contractual Life (in years)</u>	<u>Aggregate Intrinsic Value (in thousands)</u>
Outstanding at December 31, 2020	1,001,517	\$ 1.13		
Granted	2,839,284	2.99		
Exercised	<u>(5,183)</u>	2.85		
Outstanding at December 31, 2021	<u>3,835,618</u>	<u>\$ 2.51</u>	<u>8.5</u>	<u>\$ 19,458</u>
Vested and exercisable at December 31, 2021	<u>1,004,510</u>	<u>\$ 1.56</u>	<u>6.9</u>	<u>\$ 5,523</u>

The intrinsic value of stock options exercised during the year ended December 31, 2021 was approximately \$54,000. No options were exercised during the year ended December 31, 2020. As of December 31, 2021, total unrecognized compensation costs related to unvested stock option awards granted was approximately \$4.7 million, which the Company expects to recognize over a weighted-average period of approximately 3.0 years.

The Company recorded stock-based compensation expense related to stock options in the following expense categories of its statements of operations for the periods shown (in thousands):

	Year Ended December 31,	
	2021	2020
General and administrative	\$690	\$103
Research and development	232	51
Total stock-based compensation	<u>\$922</u>	<u>\$154</u>

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**Employee Stock Purchase Plan**

The 2021 Employee Stock Purchase Plan (the “ESPP”), which permits employees to purchase shares of the Company’s common stock, became effective on June 30, 2021. A total of 375,000 shares of the Company’s common stock were initially reserved for sale under the ESPP. The number of shares of the Company’s common stock reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2022 through January 1, 2031, by the lesser of (1) 1% of the total number of shares of the Company’s common stock outstanding on the last day of the fiscal year before the date of the automatic increase, and (2) 800,000 shares; provided that before the date of any such increase, the Board may determine that such increase will be less than the amount set forth in clauses (1) and (2). As of December 31, 2021, there have been no purchases of shares under the ESPP.

**NOTE 8. INCOME TAXES**

The Company has not recorded any tax provision or benefit for federal income taxes for the years ended December 31, 2021 and 2020. Current income taxes are based upon the year’s income taxable for federal and state tax reporting purposes. Deferred income taxes (benefits) are provided for certain income and expenses, which are recognized in different periods for tax and financial reporting purposes. Deferred tax assets and liabilities are computed for differences between the financial statements and tax bases of assets and liabilities that will result in taxable or deductible amounts in the future based on enacted tax laws and rates applicable to the period in which the differences are expected to affect taxable income, and NOL and R&D tax credit carryforwards.

A reconciliation of the expected tax computed at the U.S. statutory federal income tax rate to the total benefit for income taxes for the years ended December 31, 2021 and 2020 is as follows:

	For the Year Ended December 31,	
	2021	2020
Statutory federal income tax rate	21.0%	21.0%
State tax, net of federal benefit	0.7	5.1
Change in fair value of tranche and warrant liabilities	(16.9)	1.7
Non-deductible expense	(0.1)	—
R&D credit	(0.3)	4.1
Rate change	(0.2)	—
Other	0.1	—
Change in valuation allowance	(4.3)	(31.9)
Income tax provision (benefit)	<u>0.0%</u>	<u>0.0%</u>

Significant components of the Company’s deferred tax assets as of December 31, 2021 and 2020 were as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss	\$ 10,819	\$ 6,354
R&D credit	1,381	1,681
Stock compensation	263	85
Accruals and other temporary differences	58	—
Gross deferred tax assets	12,521	8,120
Depreciation	(1)	—
Valuation allowance	<u>(12,520)</u>	<u>(8,120)</u>
Deferred tax assets, net of allowance	<u>\$ —</u>	<u>\$ —</u>

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**ACUMEN PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

In assessing the realizability of deferred tax assets as of December 31, 2021 and 2020, management considered whether it is more likely than not that some portion or all of the deferred tax assets will be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible or the NOL carryforwards and R&D tax credit carryforwards will be used. The Company has determined that it is not more likely than not that its deferred tax assets will be realized. Accordingly, a valuation allowance for the full amount of the net deferred tax assets has been recorded as of December 31, 2021 and 2020. The change in the valuation allowance as of December 31, 2021 from December 31, 2020 is due to the pretax loss incurred for the year ended December 31, 2021.

As of December 31, 2021, the Company had approximately \$40.9 million of NOL carryforwards available for federal tax purposes which begin to expire on December 31, 2028. As a result of the Tax Act of 2017, for U.S. income tax purposes, NOLs generated prior to December 31, 2017 can still be carried forward for up to 20 years, but NOLs generated after December 31, 2017 carryforward indefinitely, but are limited to 80% utilization against taxable income. Of the total federal NOL of \$40.9 million, \$6.4 million will begin to expire in 2028 and \$34.5 million will not expire but will only offset 80% of future taxable income.

As of December 31, 2021, the Company also had approximately \$49.5 million of state NOL carryforwards. The state NOLs begin to expire on December 31, 2028.

As of December 31, 2021, the Company had approximately \$1.4 million of R&D credit carryforwards available for federal tax purposes, which begin to expire on December 31, 2023.

NOL carryforwards and R&D carryforwards may be subject to a substantial annual limitation due to ownership change limitations that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the “Code”), as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be used annually to offset future taxable income and tax, respectively. In general, an “ownership change” as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50% of the outstanding stock of a company by certain stockholders. The Company has not completed a study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since the Company’s formation due to the complexity and cost associated with such study, and the fact that there may be additional such ownership changes in the future.

The Company conducts intensive research and experimentation activities, generating R&D tax credits for federal and state purposes under section 41 of the Code. The Company has not performed a formal study validating these credits claimed in the tax returns. Once a study is prepared, the amount of R&D tax credits available could vary from what was originally claimed on the tax returns.

The Company is subject to U.S. federal and various state taxes. Generally, the tax years remain open for examination by the federal statute under a three-year statute of limitation; however, states generally keep their statutes open for four years. However, the Company’s tax years from 2003 and after are subject to examination by the United States and state taxing authorities due to the carry forward of unused NOLs and R&D credits.

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**ACUMEN PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

**NOTE 9. COMMITMENTS AND CONTINGENCIES**

The Company is not a party to any material legal proceedings and is not aware of any pending or threatened claims. From time to time, the Company may be subject to various legal proceedings and claims that arise in the ordinary course of its business activities.

**Leases**

The Company has been subleasing space in Indiana since March 1, 2020, under a lease that initially expired on December 31, 2020. The Company executed a new sublease for this space that was effective February 1, 2021. The term of the sublease is for 31 months, expiring on August 30, 2023. The Company pays monthly rent of \$12,719 and is allowing others to sublease a portion of the space from the Company for less than a one-year period. As of December 31, 2021, the remaining aggregate minimum rent obligation over the remaining term was approximately \$255,000.

As of December 31, 2021, future minimum lease payments under this lease agreement associated with the Company's operations were as follows (in thousands):

Year ended December 31, 2022	\$153
Year ended December 31, 2023	102
Total	<u>\$255</u>

**NOTE 10. NET LOSS PER SHARE**

The Company computes loss per common share using the two-class method required for participating securities. Basic and diluted loss per share was the same for each period presented as the inclusion of all potential common stock outstanding would have been anti-dilutive.

The table below provides potentially dilutive securities not included in the calculation of the diluted net loss per common share because to do so would be anti-dilutive:

	<b>Year Ended December 31,</b>	
	<b>2021</b>	<b>2020</b>
Shares issuable upon exercise of stock options	3,835,618	1,001,517
Shares issuable upon conversion of Series A Preferred Stock	—	477,297
Shares issuable upon conversion of Series A-1 Preferred Stock	—	7,537,879
Shares issuable upon conversion of Series B Preferred Stock	—	11,862,043
Shares issuable upon exercise of common stock warrants	—	385,693
Shares issuable upon exercise of preferred stock warrant	—	447,426
Total	3,835,618	21,711,855

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### **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,” as defined in Rule 13a-15(e) and Rule 15d-15(e) under the Exchange Act that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of December 31, 2021. Based on the evaluation of our disclosure controls and procedures, our management concluded that, as of December 31, 2021, our disclosure controls and procedures were effective to provide reasonable assurance that the information required to be disclosed by us in this Annual Report on Form 10-K was (a) reported within the time periods specified by SEC rules and regulations, and (b) communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding any required disclosure.

##### ***Management’s Report on Internal Control Over Financial Reporting***

This Annual Report on Form 10-K does not include a report of management’s assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm as allowed by the SEC during the transition period for newly public companies.

##### ***Remediation of Material Weakness***

Our board of directors and management take internal control over financial reporting and the integrity of our financial statements seriously. In the second half of 2021, we remediated the previously disclosed material weakness in our controls addressing segregation of duties related to roles and responsibilities in our accounting department by hiring additional accounting staff and upgrading our accounting systems.

##### ***Changes in Internal Control Over Financial Reporting***

Except for the changes noted above regarding the remediation of a material weakness that existed as of September 30, 2021, there have been no other changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Securities Exchange Act of 1934, as amended, that occurred during the fiscal quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

##### ***Inherent Limitations on Effectiveness of Internal Controls***

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, not absolute, assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in

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evaluating the benefits of possible controls and procedures relative to their costs. Our management, including our Chief Executive Officer and Chief Financial Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud.

### **Item 9B. Other Information.**

Because this Annual Report on Form 10-K is being filed within four business days from the date of the reportable events, we have elected to make the following disclosures in this Annual Report on Form 10-K instead of in a Current Report on Form 8-K under Item 5.02. Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers:

#### *Approval of Amendment to Non-Employee Director Compensation Policy*

On March 24, 2022, our board of directors approved an amendment to the Company's non-employee director compensation policy, or the Policy, effective immediately. The Policy applies to each non-employee who serves on the board of directors. The amendment increases the Initial Grant, as defined in the Policy, from 34,000 shares of the Company's common stock to 50,000 shares of the Company's common stock and increases the Annual Grant, as defined in the Policy, from 17,000 to 25,000 shares of Common Stock. The full text of the Policy is included as Exhibit 10.3 to this Annual Report on Form 10-K and is incorporated herein by reference.

#### *Election of Kim C. Drapkin to Board of Directors*

On March 24, 2022, upon the recommendation of its nominating and corporate governance committee, our board of directors voted to increase the size of the board to seven directors from six directors and to appoint Kim C. Drapkin to fill the vacancy created by the expansion, effective April 1, 2022. Ms. Drapkin will join the board as a Class I director, to serve the remainder of the full term of such Class I directorship until the Company's 2022 annual meeting of stockholders and until her successor has been duly elected and qualified. The board of directors also appointed Ms. Drapkin to serve as chair of the audit committee of the board of directors, effective April 1, 2022.

Ms. Drapkin serves as the chief financial officer and treasurer of Jounce Therapeutics, Inc., a publicly traded clinical-stage immunotherapy company, roles she has held since August 2015 and February 2013, respectively. Ms. Drapkin serves on the board of directors of Yumanity Therapeutics, Inc., a publicly traded clinical-stage biopharmaceutical company, a role she has had since its merger with Proteostasis Therapeutics, Inc., in December 2020. From February 2019 through this merger, Ms. Drapkin served as a member of the board of directors of Proteostasis Therapeutics, Inc., a clinical-stage biopharmaceutical company. Ms. Drapkin began her career at PricewaterhouseCoopers LLP, is a certified public accountant and holds a B.S. in accounting from Babson College. Our board of directors believes Ms. Drapkin is qualified to serve as a director based on her extensive financial expertise within the pharmaceutical industry.

In accordance with the Policy, as amended on March 24, 2022 and filed as Exhibit 10.3 to this Annual Report on Form 10-K, Ms. Drapkin's compensation for her services as a non-employee director will be consistent with that of the Company's other non-employee directors. In accordance with the Policy, on April 1, 2022, Ms. Drapkin will be granted an initial stock option to purchase 50,000 shares of the Company's common stock with an exercise price equal to the closing price of the Company's common stock on the date of grant. The option will have a ten-year term, and will vest in equal monthly installments over a three-year period, such that the option will be fully vested on the third anniversary of the date of grant, subject to Ms. Drapkin's continuous service through each such vesting date.

The Company also expects to enter into its standard indemnification agreement for directors with Ms. Drapkin.

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Ms. Drapkin was not selected as a director pursuant to any arrangements or understandings with the Company or with any other person, and there are no related party transactions between the Company and Ms. Drapkin that would require disclosure under Item 404(a) of Regulation S-K.

### **Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.**

Not applicable.

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[\*\*Table of Contents\*\*](#)**PART III****Item 10. Directors, Executive Officers and Corporate Governance.**

The information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with our 2022 annual meeting of stockholders, or the Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2021, under the captions “Information Regarding the Board of Directors and Corporate Governance,” “Election of Directors” and “Executive Officers” and is incorporated in this report by reference.

**Item 11. Executive Compensation.**

The information required by this item will be set forth in the Proxy Statement under the captions “Executive Compensation” and “Non-Employee Director Compensation” 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 will be set forth in the Proxy Statement under the captions “Security Ownership of Certain Beneficial Owners and Management” and “Securities Authorized for Issuance under Equity Compensation Plans” and is incorporated herein by reference.

**Item 13. Certain Relationships and Related Transactions, and Director Independence.**

The information required by this item will be set forth in the Proxy Statement under the captions “Transactions with Related Persons” and “Independence of the Board of Directors” and is incorporated herein by reference.

**Item 14. Principal Accountant Fees and Services.**

The information required by this item will be set forth in the Proxy Statement under the caption “Ratification of Selection of Independent Registered Public Accounting Firm” and is incorporated herein by reference.

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## PART IV

### **Item 15. Exhibit and Financial Statement Schedules.**

#### **(a)(1) Financial Statements**

The financial statements are included in Item 8. “Financial Statements and Supplementary Data.”

#### **(a)(2) Financial Statement Schedules**

All schedules are omitted as information required is inapplicable or the information is presented in the financial statements and the related notes.

#### **(a)(3) Exhibits**

Exhibit Number	Description of Exhibit
3.1	<a href="#">Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company’s Current Report on Form 8-K (File No. 001-40551), filed with the Securities and Exchange Commission on July 7, 2021).</a>
3.2	<a href="#">Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company’s Current Report on Form 8-K (File No. 001-40551), filed with the Securities and Exchange Commission on July 7, 2021).</a>
4.1	<a href="#">Amended and Restated Investors’ Rights Agreement, by and among the Registrant and certain of its stockholders, dated November 20, 2020 (incorporated by reference to Exhibit 4.1 to the Company’s Registration Statement on Form S-1 (File No. 333-256945), filed with the Securities and Exchange Commission on June 9, 2021)</a>
4.2*	<a href="#">Description of the Company’s Common Stock</a>
10.1†	<a href="#">Collaboration Agreement, by and between the Registrant and Merck &amp; Co., Inc., dated December 22, 2003, as amended and restated as of October 18, 2006 (incorporated by reference to Exhibit 10.1 to the Company’s Registration Statement on Form S-1 (File No. 333-256945), filed with the Securities and Exchange Commission on June 24, 2021)</a>
10.2+	<a href="#">2021 Equity Incentive Plan and Forms of Option Grant Notice and Agreement, Exercise Notice, Early Exercise Notice and Restricted Stock Award Notice (incorporated by reference to Exhibit 10.2 to the Company’s Registration Statement on Form S-1 (File No. 333-256945), filed with the Securities and Exchange Commission on June 24, 2021).</a>
10.3*+	<a href="#">Non-Employee Director Compensation Policy</a>
10.4+	<a href="#">2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.4 to the Company’s Registration Statement on Form S-1 (File No. 333-256945), filed with the Securities and Exchange Commission on June 24, 2021)</a>
10.5+	<a href="#">2013 Amended and Restated Stock Performance Plan (as amended through November 20, 2020) (incorporated by reference to Exhibit 10.5 to the Company’s Registration Statement on Form S-1 (File No. 333-256945), filed with the Securities and Exchange Commission on June 9, 2021)</a>
10.6+	<a href="#">Form of Indemnification Agreement with Executive Officers and Directors (incorporated by reference to Exhibit 10.6 to the Company’s Registration Statement on Form S-1 (File No. 333-256945), filed with the Securities and Exchange Commission on June 24, 2021)</a>
10.7*+	<a href="#">Executive Employment Agreement, by and between the Registrant and Daniel O’Connell</a>
10.8*+	<a href="#">Executive Employment Agreement, by and between the Registrant and Matthew Zuga</a>

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Exhibit Number	Description of Exhibit
10.9*+	<a href="#">Employment Agreement by and between the Registrant and Eric Siemers, M.D.</a>
10.10*+	<a href="#">Employment Agreement by and between the Registrant and Russell Barton</a>
23.1*	<a href="#">Consent of Ernst &amp; Young LLP, independent registered accounting firm</a>
24.1*	<a href="#">Power of Attorney (included on signature page)</a>
31.1*	<a href="#">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.</a>
31.2*	<a href="#">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.</a>
32.1#	<a href="#">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.</a>
32.2#	<a href="#">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.</a>
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

\* Filed herewith.

† Pursuant to Item 601(b)(10) of Regulation S-K, certain confidential portions of this exhibit have been omitted by means of marking such portions with asterisks [\*\*\*] as the identified confidential portions (i) are not material and (ii) the Registrant customarily and actually treats that information as private or confidential.

+ Indicates management contract or compensatory plan.

# These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

## **Item 16. Form 10-K Summary.**

None.

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**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**ACUMEN PHARMACEUTICALS, INC.**

Date: March 28, 2022

By: /s/ Daniel O'Connell  
Daniel O'Connell  
President and Chief Executive Officer

**POWER OF ATTORNEY**

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Daniel O'Connell and William Matthew Zuga, and each of them, as his or her true and lawful agents, proxies and attorneys-in-fact, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities to sign this Annual Report on Form 10-K of Acumen Pharmaceuticals, Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Daniel O'Connell</u> Daniel O'Connell	Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 28, 2022
<u>/s/ William Matthew Zuga</u> William Matthew Zuga	Chief Financial Officer and Chief Business Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	March 28, 2022
<u>/s/ Nathan B. Fountain</u> Nathan B. Fountain, M.D.	Director	March 28, 2022
<u>/s/ Jeffrey L. Ives</u> Jeffrey L. Ives, PhD	Director	March 28, 2022
<u>/s/ Sean Stalfort</u> Sean Stalfort	Director	March 28, 2022
<u>/s/ Laura Stoppel</u> Laura Stoppel, PhD	Director	March 28, 2022
<u>/s/ Jeffrey Sevigny</u> Jeffrey Sevigny, M.D.	Director	March 28, 2022