PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

Our business and our industry are subject to significant risks. You should carefully consider all of the information set forth in this Annual Report, including the following risk factors. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. Additional risks not currently known to us or that we currently deem immaterial may also affect our business operations. Additional risks not currently known to us or that we currently deem immaterial may also affect our business operations.

Summary of Risk Factors Associated with Our Business

Our business and our industry are subject to numerous risks described in “Risk Factors” and elsewhere in this Annual Report. You should carefully consider these risks before making a decision to invest in our securities. Key risks include, but are not limited to, the following:

Risks Related to Our Therapeutics Business:

- Our operating history, which has focused primarily on research and development and advancing immunotherapy gene-editing clinical trials, makes it difficult to assess our future prospects.
- We have not generated significant revenues and have incurred significant operating losses since our inception. While the amount of our future net losses will depend, in part, on the amount of our future operating expenses and our ability to obtain funding, realize payments under our strategic licensing arrangements, and obtain reimbursements of research tax credit claims, we anticipate that we will continue to incur significant losses for the foreseeable future.
- We face substantial competition in our discovery, development and commercialization activities from competitors who may have significantly greater resources than we do.
- Because our product candidates all apply novel gene-editing technology, we are heavily dependent on the successful development of this technology.
- The extent to which the COVID-19 pandemic and resulting deterioration of worldwide economic conditions adversely impacts our business, financial condition, and operating results will depend on future developments, which are difficult to predict.
- We may need to raise additional funding, which may not be available on acceptable terms or at all, and our ability to raise additional share capital is limited by French corporate law.

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

- Our product candidates must undergo clinical trials that are time-consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure, and which are susceptible under a variety of circumstances to additional costs, delays, suspensions and terminations.
- Initial, interim and preliminary data from our clinical trials may change as more data becomes available, and subsequent data may not bear out promising early results.
- Because we anticipate that our product candidates will initially receive regulatory approval as treatments for advanced disease or rare diseases, the size of the initial market for our product candidates may be limited.
- Our manufacturing process, which is highly complex and heavily regulated, may be difficult to efficiently and effectively operate and scale to the level required for advanced clinical trials or commercialization.
- Our manufacturing facilities may not obtain or maintain the required regulatory authorizations to supply commercial products.
- Acceptance and adoption of gene-editing and enrollment in our trials may be adversely affected by undesirable side effects, negative perceptions among the public or the medical community, or the inadequacy of payor coverage.
- Our future profitability depends, in part, on our ability to penetrate global markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Risks Related to Our Reliance on Third Parties:

- We rely on third parties for certain aspects of our discovery, development, manufacturing and commercialization, if any, of our product candidates and issues relating to such third parties, or their activities, which could result in additional costs and delays and hinder our research, development and commercialization prospects.
- Strategic license relationships may not be successful, including as a result of failures by our strategic licensees to perform satisfactorily or to devote resources to advance product candidates under our arrangements with them.

Risks Related to Operational Compliance and Risk Management:

- We may encounter difficulties in managing our development and expansion, including challenges associated with recruiting additional employees, managing our internal development efforts and improving our operational, financial and management controls.
- The risk of product liability claims is inherent in the development and commercialization of therapeutic products, and product liability or other lawsuits could divert management and financial resources, result in substantial liabilities and reduce the commercial potential of our product candidates.
- The buy-out mechanism in our collaboration agreement with Servier may prevent or delay a takeover attempt.

Risks Related to Regulatory Approvals for Our Product Candidates:

- Our business is governed by a rigorous, complex and evolving regulatory framework, including premarketing regulatory requirements, pricing, reimbursement and cost-containment regulations, and rigorous ongoing regulation of approved products. This regulatory framework results in significant compliance costs, makes the development and approval of our product candidates time intensive and unpredictable, and may reduce the ultimate economic value and prospects for our product candidates.
- A Fast Track, Breakthrough Therapy or Regenerative Medicine Advanced Therapy designation by the U.S. Food and Drug Administration, or FDA, or a Priority Medicines designation by the European Medicines Agency, or EMA, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive regulatory approval.
- Any regulatory compliance failures could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Risks Related to Intellectual Property.

- Because our commercial success depends, in part, on obtaining and maintaining proprietary rights to our and our licensors' intellectual property, our ability to compete may decline if we fail to obtain protection for our products, product candidates, processes and technologies or do not adequately protect our intellectual property.
- Our competitive position may be adversely impacted as a result of a variety of factors, including potentially adverse determinations of complex legal and factual questions involved in patents and patent applications or insufficiently long patent lifespans in one or more jurisdictions where we obtain intellectual property protection.
- Because it is cost prohibitive to seek intellectual property protection on a global basis, our intellectual property protection in certain jurisdictions many not be as robust as in the United States, which may adversely impact our competitive position.
- Third parties may assert rights to inventions we develop or otherwise regard as our own.
- A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business.

Risks Related to Human Capital.

- Our business could be harmed if we lose key management personnel or cannot attract and retain other qualified personnel.

Risks Relating to Our Status as a Foreign Private Issuer and a French Company:

- The rights of shareholders in companies subject to French corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.
- Our By-laws and French corporate law contain provisions that may delay or discourage a takeover attempt.
- Our international operations may be exposed to foreign exchange risks, U.S. federal income tax risks, and additional risks, which may adversely affect our financial condition, results of operations and cash flows.
- If we are classified as a PFIC for 2022 or any future taxable year, there may be adverse U.S. federal income tax consequences to U.S. holders.
- As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and the Nasdaq's corporate governance standards. We expect to follow certain home country practices in relation to certain corporate governance matters, which may afford less protection than would be provided if we complied fully with the Nasdaq requirements.

Risks Related to Ownership of Our ADSs:

- Holders of our ADSs do not directly hold our ordinary shares and may be subject to limitations on the transfer of their ADSs and certain voting and withdrawal rights of the underlying ordinary shares as well as limitations on their ability to exercise preferential subscription rights or receive share dividends.
- Share ownership is concentrated in the hands of our principal shareholders and management, who will continue to be able to exercise substantial influence.

Risks Related to Our Majority-owned Subsidiary Calyxt:

- Calyxt's ability to continue as a going concern will depend on its ability to obtain additional financing, which may not be available on acceptable terms or at all, and failure to obtain such financing may force Calyxt to delay, limit or terminate its operations. If financing is obtained through future equity offerings by Calyxt, we may experience substantial additional dilution and, in connection with our ownership level falling below 50%, we will lose certain rights under our stockholders agreement with Calyxt.
- Calyxt's success depends on its ability to successfully deliver synthetic biology solutions, which will require significant resources in a highly competitive industry. Calyxt has limited operating history in this industry, and will faces challenges associated with allocating limited resources, raising capital. gaining customers and competing with companies with greater resources.
- For Calyxt to be successful, it must secure customer collaborations, efficiently price its offerings, and demonstrate its technical capabilities and ability for commercial scale production, which involves risks of failure inherent in the deployment of innovative and complex emerging technologies.
- As a result of our ownership level in Calyxt, we are exposed to the various other risks to which Calyxt is subject, including (i) additional business and operational risks associated with developing an emerging technology, Calyxt's reliance on third parties for production and services, reliance on customers and licensees for development and commercialization efforts, and risks associated with outdoor agriculture; (ii) regulatory risks, including the navigation of ethical, legal and social concerns relating to genetically modified or edited plant cells, the complex and evolving regulatory framework, including uncertainty regarding foreign regulation, increasing regulation of hemp development activities, regulatory and compliance burdens under environmental, health and safety laws, (iii) intellectual property risks, including the corresponding risks described with respect to our intellectual property, and (iv) risk associated with attracting and maintaining key management personnel and protecting its data from cybersecurity attacks.

Risks Related to Our Therapeutics Business

We have a limited operating history, which makes it difficult to evaluate our current business and future prospects and may increase the risk of your investment.

We are a clinical-stage biopharmaceutical company with a limited operating history. Investment in biopharmaceutical development is a highly speculative endeavor. Biopharmaceutical product development entails substantial upfront capital expenditures, and there is significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, to gain required regulatory approvals or to become commercially viable. While there have been significant advances in cell-based immunotherapy, our gene-editing platform and T-cell and CAR technologies are new and unproven, our most advanced product candidates remain in clinical development, and we have not yet generated any revenue from biopharmaceutical product sales to date.

Our limited operating history may make it difficult to evaluate our current business and our future prospects. We have encountered, and will continue to encounter, risks and difficulties frequently experienced by growing companies in rapidly evolving industries, such as the biopharmaceutical industry. Consequently, the ability to predict our future operating results or business prospects is more limited than if we had a portfolio of approved products on the market.

We may not be able to fully implement or execute on our commercial strategy or realize, in whole or in part or within our expected time frames, the anticipated benefits of our strategies. You should consider our business and prospects in light of the risks and difficulties we face as an early-stage company focused on developing products in the field of immunotherapy gene editing and advancing clinical trials.

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We devote most of our financial resources to research and development relating to our CAR T-cell immunotherapy product candidates, including the advancement of our clinical trials. We finance our current immuno-oncology operations primarily through payments pursuant to strategic licensing relationships with pharmaceutical companies, including Servier and Allogene, as well as through the sale of equity securities and by obtaining public funding in support of innovation, reimbursements of research tax credit claims, and royalties on our licensed technology.

For the year ended December 31, 2021, we received $12.0 million in payments pursuant to our strategic licensing agreements, and our research and development expenses were $129.0 million.

We currently have no commercial biopharmaceutical products. Notwithstanding the commencement of several clinical studies, it will be several years, if ever, before we obtain regulatory approval for, and are ready for commercialization of, a biopharmaceutical product candidate. Even if we or our strategic licensees successfully commence and complete clinical studies and obtain regulatory approval to market a product candidate, any future revenues will depend upon the size of any markets in which the product candidates are approved for sale as well as the market share captured by such product candidates, market acceptance of such product candidates and levels of reimbursement from third-party payors.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. We expect our losses and our cash utilization to increase in the near term as we conduct our clinical studies, file IND and/or foreign equivalent filings for additional product candidates, conduct research and development for product candidates, invest in deploying and scaling our manufacturing capabilities, seek regulatory and marketing approvals, and establish necessary infrastructure for the commercialization of any products for which we obtain marketing approval.

The net losses we incur may fluctuate significantly from year to year and quarter to quarter, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular period or periods, our operating result could be below the expectations of securities analysts or investors which could cause the price of our ADSs to decline.

We face substantial competition from companies many of which have considerably more resources and experience than we have.

The biopharmaceutical industry, and the immuno-oncology industry in particular, is characterized by intense competition and rapid innovation. We face competition from new and established biotechnology and pharmaceutical companies, academic research institutions, government agencies and public and private research institutions. Many of our competitors, either alone or with strategic partners, have substantially greater financial, technical and other resources, such as larger research and development staff, greater expertise in large scale pharmaceutical manufacturing, and/or well-established marketing and sales teams. In addition, smaller or early-stage companies may compete with us through collaborative arrangements with more established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these enterprises. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our competitors, either alone or with partners, may succeed in developing, acquiring or licensing compounds, drugs or biologic products that are more effective, safer, more easily commercialized, or less costly than our product candidates. Further, competitors may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. Our competitors also compete with us in recruiting and retaining qualified scientific and management personnel.

Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors’ products may limit demand for, or the price that we are able to charge for, our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances.

Our gene-editing technology is relatively new, and if we are unable to use this technology in all of our intended applications, our revenue opportunities will be limited.

Even if the use of gene editing technologies increases, our technology involves a relatively new approach to gene editing, using sequence-specific deoxyribonucleic acid (DNA)-cutting enzymes, or nucleases, to perform precise and stable modifications in the DNA of living-cells and organisms. Although we have generated nucleases for many specific gene sequences, we have not created nucleases for all gene sequences that we may seek to target, and we may not be able do so, which could limit the usefulness of our technology. Our technology may also not be shown to be effective in clinical studies that we or our strategic licensees or other licensees of our technology may conduct, or may be associated with safety issues that may negatively affect our development programs. For example, gene-editing may create unintended changes to the DNA such as a non-target site gene-editing, a large deletion, or a DNA translocation, any of which could lead to oncogenesis. The gene-editing of our product candidates may also not be successful in limiting the risk of graft-versus-host-disease (GvHD) or premature rejection by the patient.

In addition, the field of gene-editing is rapidly developing, and our competitors may introduce new technologies that render our technology obsolete, uneconomical or less attractive. New technology could emerge at any point in the development cycle of our product candidates. As competitors use or develop new technologies, any failures of such technology could adversely impact our programs. We also may be placed at a competitive disadvantage, and competitive pressures may force us to implement new technologies at a substantial cost. In addition, our competitors may have greater financial, technical and personnel resources that allow them to enjoy technological advantages and may in the future allow them to implement new technologies before we can. We cannot be certain that we will be able to implement technologies on a timely basis or at a cost that is acceptable to us. If we are unable to maintain technological advancements consistent with industry standards, our operations and financial condition may be adversely affected.

We are subject to various risks related to public health crises, including the COVID-19 pandemic, that could have material and adverse impacts on our business, financial condition, liquidity, and results of operations.

Any outbreaks of contagious diseases and other adverse public health developments could have a material and adverse impact on our business, financial condition, liquidity, and results of operations. As has occurred with the COVID-19 pandemic, a global pandemic could cause significant disruption to the global economy, including in regions in which we or our raw materials suppliers do business or where our clinical trials are being conducted. A regional epidemic or global pandemic and efforts to manage it, including those by governmental authorities, could have significant impacts on national and global financial markets, and could have a significant, negative impact on our clinical trials or operating results. Disruptions could include partial shutdowns of our facilities, as mandated by government decree, significant travel restrictions, “work-from-home” orders, limited availability of our workforce, supplier and raw materials constraints, supply chain interruptions, logistics challenges and limitations, and reduced participation in our clinical trials by patients.

The COVID-19 pandemic has had, and could continue to have, these effects on the economy and our business, including:

- Disruptions to, and delays in, the clinical trials for the product candidates that we are developing resulting from suspensions or delays in enrollment or difficulties in enrolling patients; increased patient withdrawals from, or restrictions imposed on, patients participating in, the clinical trials; diversion of healthcare resources away from the conduct of the clinical trials; or interruptions in data collection, monitoring and/or processing due to governmental restrictions imposed in response to the COVID-19 pandemic.

- Disruptions and delays to our research and development programs resulting from a shutdown of our laboratory facilities due to expanded governmental restrictions or illness among laboratory personnel as a result of COVID-19, increased absenteeism among scientific or laboratory employees, or delays with respect to raw material or starting material necessary for research and development activities.

- Delays with respect to operations at our manufacturing facilities resulting from increased, expanded or additional government restrictions in Paris, France or Raleigh, North Carolina, or as a result of supply chain disruptions affecting raw materials required for our manufacturing processes.

- Overall reduced operational productivity resulting from challenges associated with remote work arrangements, limited resources to employees, and increased cybersecurity risks as a result of remote access to our information systems.

- Constraints on financing opportunities resulting from dislocations in the capital markets, which may make it too costly or difficult for us to pursue public or private equity or debt financings on acceptable terms.

The degree to which the COVID-19 pandemic will continue to impact our business and results will depend on future developments, which are highly uncertain and cannot be predicted, including, but not limited to, the severity, duration and geographic spread of the outbreak, potential resurgence events and the emergence of additional variant strains, the effectiveness of available vaccines (including with respect to emerging variants of COVID-19) and the effective distribution thereof, as well as the global, national and regional actions to contain the virus and address its impact. The resumption of normal business operations after interruptions caused by the COVID-19 pandemic may be delayed or constrained by lingering effects of the COVID-19 pandemic on us or our suppliers and third-party service providers. Even after the COVID-19 outbreak has subsided, we may experience material and adverse impacts as a result of the global economic impact of the COVID-19 outbreak.

The impact of COVID-19 may also exacerbate other risks discussed in this Annual Report, any of which could have a material effect on us. This situation is continuing to evolve and additional impacts may arise that we are not aware of currently.

We may need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

The process of developing and manufacturing CAR T-cell product candidates and conducting clinical studies is expensive, lengthy and risky. We are currently sponsoring three clinical studies, preparing regulatory filings to commence new clinical studies and/or to add additional investigational sites for ongoing studies, advancing pre-clinical testing for additional product candidates, and beginning in-house manufacturing at our in-house manufacturing facilities. Accordingly, we expect our operational expenses to increase substantially in connection with our ongoing activities. In addition, subject to obtaining regulatory approval of any biopharmaceutical product candidates, we expect to incur significant commercialization expenses.

As of December 31, 2021, Cellectis, excluding Calyxt, had cash and cash equivalents and current financial assets of approximately $171.8 million. Based on the current operating plan and financial projections, we believe our cash and cash equivalents and current financial assets, together with our cash flow from operations (including payments we expect to receive pursuant to our strategic licensing agreements) and government funding of research programs will be sufficient to fund Cellectis' Therapeutics' operations into early 2024. However, our operating plans, including product development plans, may change in light of changed circumstances or as a result of factors currently unknown to us, which may require us to seek additional funds sooner than planned. To commercialize our products, if approved, we will require significant working capital to operate our business and maintain our operations.

Our ability to raise additional capital may be limited. If we raise additional capital through the sale of additional equity or convertible securities, current ownership interests may be diluted and the terms of these securities may include liquidation or other preferences that adversely affect stockholders' rights. Debt financing, if available, would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness. In addition, debt financing may involve agreements that include restrictive covenants that impose operating restrictions, such as restrictions on the incurrence of additional debt, the making of certain capital expenditures or the declaration of dividends. To the extent we raise additional funds through arrangements with research and development partners or otherwise, we may be required to relinquish some of our technologies, product candidates or revenue streams, license our technologies or product candidates on unfavorable terms, or otherwise agree to terms unfavorable to us. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of specific strategic considerations.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research and development programs or product candidate development programs, or the commercialization of any product candidate that may receive regulatory approval, which could materially affect our business, operating results and prospects.

We are limited in our ability to raise additional share capital, which may make it difficult for us to fund our operations.

Under French law, our share capital generally may be increased with the approval of a two-thirds majority of the votes cast of the shareholders present, represented by proxy, or voting by mail at an extraordinary general shareholders' meeting following the recommendation of our board of directors. The shareholders may delegate to our board of directors either the authority (*délégation de compétence*) or the power (*délégation de pouvoir*) to carry out any increase in the share capital. Accordingly, our board of directors may be precluded from issuing additional share capital if the prior approval of the shareholders is not duly obtained.

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

Our therapeutic product candidate development programs are in various phases of development and may be unsuccessful.

Our therapeutic product candidates are in various phases of development. At each stage of development, there is typically an extremely high rate of attrition from the failure of product candidates advancing to subsequent stages of development.

Because some of our product candidates are in the early stages of discovery or pre-clinical development, there can be no assurance that our research and development activities will result in these product candidates advancing into clinical development. Product candidates in these development phases undergo testing in animal studies, and the results from these animal studies may not be sufficiently compelling to warrant further advancement. Moreover, even if results from animal studies are positive, such results are not necessarily predictive of positive results in clinical studies. Even where product candidates do progress into and through clinical studies, these product candidates may fail to show the desired safety and efficacy in clinical development despite demonstrating positive preliminary clinical data and/or results in animal studies. Because of the early stages of our currently ongoing clinical studies, the safety, specificity and clinical benefits of our clinical-stage product candidates have not yet been demonstrated, and we cannot assure you that the results of any clinical trials will demonstrate the value and efficacy of our platform. The results of clinical studies are subject to a variety of factors, and there can be no assurance that any product candidate will advance to regulatory approval, be approved by applicable regulatory agencies, or be successfully commercialized.

Although there are a large number of drugs and biologics in development globally, only a very small percentage obtain regulatory approval, even fewer are approved for commercialization, and only a small number of these achieve widespread physician and consumer acceptance. Accordingly, despite expending significant resources in pursuit of their development, our product candidates may never achieve commercial success, and any time, effort and financial resources we expend on the product candidate development programs that we pursue may adversely affect our ability to develop and commercialize other product candidates.

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

From time to time, we or our strategic licensee partners may publish initial, interim or preliminary data from clinical studies. Interim and preliminary data from clinical trials 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. For instance, while we and our strategic licensees have published preliminary data from on-going clinical studies, because such data is preliminary in nature, has not established statistical significance, and should not be viewed as predictive of the ultimate success of the respective clinical trials. It is possible that such results will not continue or may not be repeated in ongoing or future clinical trials for the same product candidates or in clinical trials for other allogeneic Chimeric Antigen Receptor T-cells ("UCART") product candidates.

Preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, initial, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between initial, preliminary or interim data and final data could significantly harm our business prospects.

We may encounter substantial delays in our clinical trials, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Clinical trials are long, expensive and unpredictable processes that can be subject to extensive delays. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. It will take several years to complete the clinical development necessary to obtain adequate data to file for a marketing authorization or to commercialize a product candidate, and failure can occur at any stage.

Positive interim or preliminary results of clinical trials do not necessarily predict positive final results, and success in early clinical trials does not ensure that later clinical trials will be successful. Product candidates in later stages of clinical trials may still fail to show the desired safety and efficacy profile despite having successfully progressed through initial clinical trials. A number of pharmaceutical and biopharmaceutical companies have suffered significant setbacks—lack of efficacy, insufficient durability of efficacy or unacceptable safety issues (including a number of patient deaths in CAR-T trials conducted in the United States)—in advanced clinical trials, even after promising results in earlier trials.

We cannot be certain that our product candidates will not face similar setbacks. An unfavorable outcome in one or more clinical trials would be a major setback for our product candidates and for us and may require us or our strategic licensees to delay, reduce or re-define the scope of, or eliminate one or more product candidate development programs, any of which could have a material adverse effect on our business, financial condition and prospects.

In addition, a number of events, including any of the following, could delay clinical trials, negatively impact the ability to obtain regulatory approval for, and to market and sell, a particular product candidate, or result in suspension or termination of a clinical trial:

- conditions imposed by the FDA or any foreign regulatory authority regarding the scope or design of clinical trials;
- inability to generate sufficient preclinical, toxicology or other in vivo or in vitro data to support initiation of clinical studies;
- delays in obtaining, or the inability to obtain, regulatory agency approval for the conduct of the clinical trials or required approvals from institutional review boards, or IRBs, or other reviewing entities at clinical sites selected for participation in our clinical trials;
- the identification of flaws in the design of a clinical trial;
- changes in regulatory requirements and guidance that necessitate amendments to clinical trial protocols;
- delays in sufficiently developing, characterizing or controlling manufacturing processes suitable for clinical trials;
- insufficient supply or deficient quality of the product candidates or other materials necessary to conduct the clinical trials, including as a result of manufacturing issues at our in-house manufacturing facilities; ;
- difficulty in sourcing healthy donor material of sufficient quality and in sufficient quantity to meet our development needs;
- lower-than-anticipated enrollment and retention rate of subjects in clinical trials for a variety of reasons, including size of patient population, sites selection, nature of trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications and competition from approved products;

- delays in reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical study sites and obtaining required institutional review board (IRB) approval at each clinical study site;
- the placing of a clinical hold on our strategic licensees' clinical trials—for example, clinical holds were placed on our AMELI-01 Study in September 2018 and on our MELANI-01 Study in July 2020 and on all of our strategic licensee Allogene's AlloCAR T clinical trials in October 2021 and remained in place until the FDA permitted these trials to restart in November 2018, November 2020 and January 2022, respectively;
- unfavorable interpretations by FDA or similar foreign regulatory authorities of interim data;
- determinations by the FDA or similar foreign regulatory authorities that a clinical trial protocol is deficient in design to meet its stated objectives;
- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- serious and unexpected safety issues, including drug-related side effects experienced by patients in clinical trials;
- failure of our or our strategic licensees' third-party contractors to meet their contractual obligations in a timely manner; or
- lack of, or failure to, demonstrate efficacy of our products candidate.

Our product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and obtaining regulatory approval.

We have concentrated our research, development and manufacturing efforts on our gene-edited CAR T-cell immunotherapy product candidates, and our future success depends on the successful development of this therapeutic approach. We are in the early stages of developing our UCART product candidates' platform and there can be no assurance that any development problems we experience in the future will not cause significant delays or unanticipated costs, or that such development problems can be overcome. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process, or effectively implementing such process at our new manufacturing facilities, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all. Our expectations with regard to the scalability and cost of manufacturing may change significantly as we further progress the development of our product candidates.

In addition, the clinical study requirements of the FDA, EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate are determined according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more complex and consequently more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. Approvals by the European Commission, on the basis of the opinion issued by the EMA, and FDA for existing autologous CAR T-cell therapies may not be indicative of what these regulators may require for approval of our therapies. More generally, approvals by any regulatory agency may not be indicative of what any other regulatory agency may require for approval or what such regulatory agencies may require for approval in connection with new product candidates.

Our business is highly dependent on the success of our lead product candidates, and we cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, these product candidates.

Our business and future success depends on our ability to successfully develop, obtain regulatory approval for, and successfully commercialize our most advanced product candidates, UCART123, UCART22 and UCARTCS1, as well as the ability of our strategic licensees to advance the product candidates that they are developing pursuant to licenses from us. Each of these UCART product candidates is in an early stage of development, and preliminary results to date may not predict results for our, or our strategic licensees', ongoing or planned clinical studies. Because our lead product candidates, and UCART product candidates of our strategic licensees, are among the first allogeneic products to be clinically evaluated, the failure of any such product candidate, or the failure of other allogeneic T cell therapies, may impede our ability to develop our product candidates, and significantly influence physicians' and regulators' opinions in regards to the viability of our entire pipeline of allogeneic T cell therapies. If significant events, such as significant GvHD or chromosomal abnormality events, are observed with the administration of our product candidates, or if any of the product candidates is viewed as less safe or effective than autologous therapies, our ability to develop other allogeneic therapies may be significantly harmed.

Our therapeutic product candidates will require substantial additional clinical development, testing, and regulatory review and approval in multiple jurisdictions, substantial investment, implementation and scaling of our commercial manufacturing capabilities, and significant marketing efforts before we can generate any revenue from product sales. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate, with substantial evidence gathered in well-controlled clinical trials and to the satisfaction regulatory authorities (including the FDA in the United States and the EMA in the EU) that the product candidate is safe and effective for use in each target indication. Following this extensive regulatory process, the manufacturing and marketing of our product candidates will be subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to pursue commercialization.

Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. The process can take many years and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources beyond our existing cash on hand. There can be no assurance that any of our product candidates will successfully complete the foregoing regulatory approval processes. We do not expect any of the product candidates we or our strategic licensees develop to be commercially available for many years and some or all may never become commercially available.

The size of the initial market for our product candidates may be limited.

We expect that, if approved, several of the product candidates we develop will initially receive regulatory approval as treatment for advanced disease or rare diseases with few other treatment options. This could limit the initial size of the market for these product candidates, and we cannot predict when, if ever, such product candidates would receive regulatory approval for indications treating a more expansive patient population.

Any issues that arise in the highly complex manufacturing process for our product candidates could have an adverse effect on our business, financial position or prospects.

Our CAR T-cell immunotherapy products undergo a complex, highly-regulated manufacturing process. The process is subject to strict controls and procedures to ensure no more than very minimal batch-to-batch variability. As a result, our manufacturing process is subject to multiple risks, and the cost to manufacture our products is generally higher than traditional small molecule chemical compounds. The complexity of our manufacturing process makes it susceptible to product loss or failure due to issues associated with the collection of T-cells from healthy donors, manufacturing or supply of raw material or starting material, shipping such material to the manufacturing site, ensuring standardized production batch-to-batch in the context of mass production, freezing the manufactured product, shipping the final product globally, and infusing patients with the product.

Manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling out and validating initial production and ensuring the absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, inconsistency in cell growth, quality assurance testing, improper installation or operation of equipment, operator error, shortages of qualified personnel, shortage of raw material or starting material and other procurement issues, as well as compliance with strictly enforced federal, state and foreign regulations.

Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our supply of product candidates or in the manufacturing facilities in which our product candidates are made, such supply may have to be discarded and the manufacturing may be stopped or such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.

While we currently use third-party contract manufacturing organizations, or CMOs, to manufacture our product candidates, we completed construction of an in-house manufacturing facility in Paris, France. This manufacturing facility is now operational and dedicated to the manufacturing of certain raw and starting material for our investigational products, with the potential of manufacturing of certain raw and starting material for commercial products in the future. In addition, we completed and qualified our in-house manufacturing facility in Raleigh, North Carolina, which is dedicated to the production of clinical UCART products, with the potential for production of commercial products in the future. The production of the first batch of one of our product candidate started in third quarter of 2021. We have very limited experience in operating a manufacturing infrastructure for clinical or commercial pharmaceutical products, and we may never be successful in effectively exploiting such in-house manufacturing capabilities. In addition to all the challenges discussed above regarding manufacturing of cell therapy products, we may face potential problems associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, process scale-up and/or scale-out, process reproducibility, stability issues, lot consistency, and timely availability of reagents or raw materials. Further, the application of new regulatory guidelines or parameters, such as those related to release testing, may also adversely affect our ability to manufacture our product candidates.

Even as we successfully deploy and scale our in-house manufacturing capabilities, we may be adversely affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures, regulatory issues and numerous other factors that could prevent us from realizing the intended benefits of our internalized manufacturing capabilities and have a material adverse effect on our business. We may ultimately be unable to reduce the cost of goods for the product candidates to levels that will allow for an attractive return on investment if and when those product candidates are commercialized. In addition, we may never obtain the regulatory approvals to manufacture our commercial products in our in-house manufacturing facilities.

Any changes to manufacturing processes may result in additional regulatory approvals.

The manufacturing process for any products that we may develop is subject to FDA and foreign regulatory authority approval for the jurisdictions in which we or our strategic licensees will seek marketing approval for commercialization as well as ongoing compliance requirements. If the manufacturing process is changed during the course of product development or subsequent to a product’s commercialization, FDA or foreign regulatory authorities could require us to repeat some or all previously conducted trials or conduct additional bridging trials, which could delay or impede our ability to obtain marketing approval. If we or our CMOs are unable to reliably produce product candidates or products to specifications acceptable to the FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to further develop, conduct clinical trials for, and commercialize such products in the relevant territories.

Negative publicity and increased regulatory scrutiny of genetic research and therapies involving gene editing may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Our gene-editing technologies are novel. Public perception may be influenced by claims that gene editing is unsafe, and products incorporating gene editing may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in our targeted diseases prescribing our product candidates as treatments in lieu of, or in addition to, existing, more familiar, treatments, including those for which greater clinical data may be available. Any increase in negative perceptions of gene editing may result in fewer physicians prescribing our treatments or may reduce the willingness of patients to utilize our treatments or participate in clinical trials for our product candidates. Increased negative public opinion or more restrictive government regulations in response thereto, would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for such product candidates.

For example, there have been patient deaths in CAR-T trials conducted in the United States by our competitors as well as in our UCART123 and UCARTCS1 clinical studies, which have led to clinical trial holds. In addition, on October 7, 2021, the FDA placed a clinical hold on our sublicensee Allogene Therapeutics’ clinical trials following a chromosomal abnormality detected in a patient in Allogene’s ALLO-501A study, which hold was removed by the FDA in January 2022. Adverse events in clinical studies for the product candidates we develop or those of our competitors, even if not ultimately attributable to the respective product candidates and any resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays, stronger labeling for approved product candidates and a decrease in demand for any such product candidates.

Difficulty enrolling patients could delay or prevent clinical studies of product candidates.

Identifying and qualifying patients to participate in clinical studies is critical to the success of the relevant product candidate. The timing of clinical studies depends, in part, on the speed of recruitment of patients to participate in testing such product candidates as well as completion of required follow-up periods. We or those evaluating product candidates pursuant to licenses from us may not be able to identify, recruit and enroll a sufficient number of patients or patients with required or desired characteristics to achieve the objectives of the study. If patients are unable or unwilling to participate in such studies, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our technology, failure to meet study endpoints or objectives or termination of the clinical studies altogether.

In addition, competition among clinical trials in the same therapeutic areas may reduce the number and types of patients available to participate in our or our strategic licensees’ clinical trials. Because the number of qualified clinical investigators is limited, we expect to conduct some clinical trials at the same sites as our competitors, which may reduce the number of patients available for our clinical trials at such sites. Certain of our competitors may have greater success than us in enrolling patients as a result of a variety of factors. Moreover, because of the novel nature of our product candidates, potential patients and their doctors may be less likely to enroll in our clinical trials relative to clinical trials for more conventional therapies.

Patient enrollment is affected by a variety of factors, including:

- severity of the disease under investigation;
- incidence and prevalence of the disease under investigation;
- design of the clinical trial protocol;
- size and nature of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial, including relative to other available therapies;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- patient referral practices of physicians;
- our ability to monitor patients adequately during and after treatment, and
- ability of the clinical sites to have sufficient resources and avoid any backlogs.

If we or our strategic licensees' are unable to enroll a sufficient number of patients to conduct clinical studies as planned, it may be necessary to delay, limit or terminate such clinical studies, which could have a material adverse effect on our business and financial condition. Even if we are able to enroll a sufficient number of patients in our clinical trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of the product candidates we develop.

Our product candidates may cause undesirable side effects that could halt their clinical development, delay or prevent their regulatory approval, limit their commercial potential, or result in other significant negative consequences.

Undesirable or unacceptable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, suspend or halt clinical trials, could result in the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities, or could lead to a more restrictive label for our product candidates.

Our product candidates have only had limited clinical trial application, and results of our clinical trials could reveal a high and unacceptable incidence and severity of side effects or unexpected characteristics. Approved autologous CAR T therapies and those under development have shown frequent rates of CRS and neurotoxicity, and adverse events have resulted in the death of patients. We expect similar adverse events for allogeneic CAR T product candidates. Our allogeneic CAR T cell product candidates undergo gene engineering by using lentivirus and TALEN nucleases that can cause insertion, deletion, or chromosomal translocation. These changes can cause allogeneic CAR T cells to cause adverse events. In addition, the allogeneic nature of our CAR T cell product candidates may cause unique adverse events related to the differences between the donor material used to manufacture the product candidates and patients, such as GvHD.

In the currently ongoing UCART product candidate clinical studies, the most common severe or life-threatening adverse events include CRS, cytopenia and infections. There have also been patient deaths in the UCART19 Studies, the AMELI-01 Study and the MELANI-01 Study, including deaths attributable to UCART immuno-therapy. In the future, patients may experience additional severe adverse events related to UCART product candidates, some of which may result in death. Additionally, as more patients are included in our and our strategic licensee's clinical trials, previously less common, side effects may also emerge. Additional UCART product candidates that enter clinical development may also cause similar or more severe toxicities, particularly if such product candidates require higher dose levels or are administered to higher risk patient populations.

Any undesirable side effects could cause us, our strategic licensees or regulatory authorities to interrupt, delay, halt or terminate clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. Treatment-related side effects could also adversely affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. In addition, certain side effects of UCART product candidates are not normally encountered in the general patient population or by medical personnel familiar with more conventional therapies. Although we provide training to medical personnel involved in clinical trials for our product candidates, failure of medical personnel to recognize or manage potential side effects of our product candidates could exacerbate adverse outcomes and potentially result in patient deaths.

Any of these occurrences could prevent our product candidates from achieving or maintaining market acceptance and could increase the cost of development and commercialization, and may harm our business, financial condition and prospects significantly.

The administration of lymphodepletion agents, including the incorporation of an anti-CD52 monoclonal antibody, prior to administration of UCART product candidates may increase the risk of adverse side effects.

In certain of our clinical trials, we utilize an anti-CD52 monoclonal antibody as part of a lymphodepletion regimen to be infused prior to infusing patients with our product candidates. We believe that using an anti-CD52 antibody in a lymphodepletion regimen may delay rejection of our allogeneic T cells by the patient’s immune system, and therefore improve window of persistence during which such engineered allogeneic T cells can expand and actively target and destroy cancer cells.

However, the anti-CD52 antibody may not have the benefits that we anticipate and could result in adverse effects or confounding other adverse effects. For instance, our lymphodepletion regimen, including the use of an anti-CD52 antibody, will cause a transient and sometimes prolonged lymphocyte suppression, which is associated with an increased risk of infection.

We currently use alemtuzumab, a monoclonal antibody that binds CD52, as the anti-CD52 antibody for our lymphodepletion regimen. Alemtuzumab is known to have risk of causing certain adverse events. On November 14, 2019, the EMA completed a pharmacovigilance review of alemtuzumab in the context of the treatment of multiple sclerosis (Lemtrada®) following reports of immune-related disorders and cardiovascular disorders, including fatal cases. The EMA has recommended that alemtuzumab only be used to treat relapsing-remitting multiple sclerosis if the disease is highly active despite treatment with at least one disease-modifying therapy, or If the disease is worsening rapidly. Also, the EMA recommended that alemtuzumab should not be used in patients with certain heart, circulation or bleeding disorders or in patients who have autoimmune disorders other than multiple sclerosis. The EMA also recommended that alemtuzumab only be given in a hospital with ready access to intensive care facilities and specialists who can manage serious adverse reactions. Similarly, because of the risk of autoimmunity, infusion reactions, and malignancies, Lemtrada®is available in the United States only through restricted distribution under an FDA-approved and mandated Risk Evaluation and Mitigation Strategy (REMS) Program.

We are reviewing EMA’s and FDA’s recommendations with respect to the use of alemtuzumab in our clinical trials, which are currently conducted at specialized centers. If the EMA, FDA or other regulatory agencies further limit the use of alemtuzumab or anti-CD52 antibodies, our clinical programs would be adversely affected.

On May 11, 2021, we entered into a partnership agreement and a supply agreement with Sanofi regarding alemtuzumab to be used as part of the lymphodepleting regimen in certain Cellectis sponsored UCART clinical trials. As part of the agreement, Sanofi will supply alemtuzumab to support Cellectis’ clinical studies and the parties agreed to enter into discussions to execute an agreement for the commercial supply of alemtuzumab under pre-agreed financial conditions. We also continue to explore sourcing of alternative anti-CD52 antibodies for use in our clinical trials or for commercial purposes.

If we are unable to successfully secure an adequate source of anti-CD52 or to do so in the timeframe we anticipate, or if regulatory authorities do not approve the use of the anti-CD52 in combination with our UCART product candidates, our UCART product candidates may be less effective, which could result in delays in our product development efforts and/or the commercial potential of our product candidates.

If the product candidates we develop do not achieve projected development and commercialization in the announced or expected timeframes, the further development or commercialization of our product candidates may be delayed, and our business may be harmed.

We sometimes estimate, or may in the future estimate, for planning purposes, the timing of the accomplishment of various scientific, clinical, manufacturing, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings, the receipt of marketing approval or commercialization objectives. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions, including assumptions regarding capital resources and constraints, progress of development activities, and the receipt of key regulatory approvals or actions, any of which may cause the timing of achievement of the milestones to vary considerably from our estimates.

If we or our strategic licensees fail to achieve announced milestones in the expected timeframes, the commercialization of the product candidates may be delayed, our credibility may be undermined, and our business and results of operations may be harmed.

Even if we or our strategic licensees successfully complete clinical trials of product candidates, those candidates may not be commercialized successfully for other reasons.

Even if we or our strategic licensees successfully complete clinical trials for one or more product candidates, those candidates may not be commercialized for other reasons, including:

- failing to receive regulatory approvals required to market them as drugs;
- being subject to proprietary rights held by others;
- failing to comply with GMP requirements;
- being difficult or expensive to manufacture on a commercial scale;
- having adverse side effects that make their use less desirable;
- being inferior to existing approved drugs or therapies;
- failing to compete effectively with existing or new products or treatments commercialized by competitors; or
- failing to show long-term benefits sufficient to offset associated risks.

In addition, for any product candidates developed by a strategic licensee or other collaboration partner pursuant to a licensing agreement, we will depend entirely upon such party for marketing and sales of that product. These parties may not devote sufficient time or resources to the marketing and commercialization, or may determine not to pursue marketing and commercialization at all, which could prevent the affected products from reaching milestones or sales that would trigger payments to Cellectis.

Even if any of our product candidates are commercialized, they may not be accepted by physicians, patients, or others in the medical community.

The use of engineered T-cells as a cancer treatment is a recent development and may not become broadly accepted by physicians, patients, cancer treatment centers or others in the medical community. Even if any of our product candidates receive marketing approval, the medical community may not accept such products as adequately safe and efficacious for their indicated use. Moreover, physicians may choose to restrict the use of the product, if, based on experience, clinical data, side-effect profiles and other factors, they are not convinced that the product is preferable to alternative drugs or treatments.

Additional factors that may influence whether our product candidates are accepted in the market, include:

- the clinical indications for which product candidates are approved;
- the potential and perceived advantages and risks of our product candidates relative to alternative treatments;
- the prevalence and severity of side effects;
- the demonstration of the clinical efficacy and safety of the product;
- the approved labeling for the product and any required limitations or warnings;
- the timing of market introduction of the product candidate as well as of competing products;
- the effectiveness of educational outreach to the medical community about the product;
- the coverage and reimbursement policies of government and commercial third-party payors pertaining to the product; and
- the market price of the product relative to competing treatments.

We cannot predict the degree of market acceptance of any product candidate that receives marketing approval. If our product candidates are approved but fail to achieve market acceptance in the medical community, we will not be able to generate significant revenue. Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.

Successful sales of our product candidates, if approved, depend, in part, on the availability of adequate coverage and reimbursement from third-party payors.

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. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial third-party payors, such as private health insurers and health maintenance organizations, are critical to new product acceptance. Coverage and reimbursement may depend upon a number of factors, including determinations as to whether a product is:

- a covered benefit under applicable policies or plans;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Coverage and reimbursement policies vary, and obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us or our strategic licensees to furnish on a payor-by-payor basis supporting scientific, clinical and cost-effectiveness data for the use of our products, with no assurance that coverage or adequate reimbursement will be obtained. Even if coverage for a product is obtained, reimbursement rates may be inadequate to achieve profitability or may require co-payments that patients find unacceptably high.

If coverage is unavailable or reimbursement rates are inadequate, patients may not use our products. Because our product candidates represent a new approach to treatment, they may have a higher cost than conventional therapies and may require long-term follow-up evaluations, which may increase the risk that coverage and/or reimbursement rates may be inadequate for us to achieve profitability.

Our future profitability, if any, depends, in part, on our ability to penetrate global markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability, if any, will depend, in part, on our ability and the ability of our strategic licensees to commercialize the product candidates we develop in markets throughout the world. Commercialization of our product candidates in various markets could subject us to additional risks and uncertainties, including:

- obtaining, on a country-by-country basis, the applicable marketing authorization from the competent regulatory authority;
- the burden of complying with complex and changing regulatory, tax, accounting and legal requirements in each jurisdiction that we pursue;
- differing medical practices and customs affecting acceptance in the marketplace;
- import or export licensing requirements;
- country specific requirements related to the cells used as starting material for manufacturing;
- language barriers for technical training, healthcare professionals and patients documents;
- reduced protection of intellectual property rights in some foreign countries;
- foreign currency exchange rate fluctuations;
- potential imposition of governmental controls; and
- patients’ ability to obtain reimbursement for products in various markets.

Risks Related to Our Reliance on Third Parties

Third parties on whom we rely to conduct some aspects of our development programs may not perform satisfactorily.

We do not, and do not expect in the future to, independently conduct all aspects of our development programs. We rely, and will continue to rely, on third parties for certain aspects of manufacturing, quality control, protocol development, material supply, research and pre-clinical development, translational activities, and clinical testing, clinical trial conduct and distribution activities. With respect to the clinical trials that we sponsor, we rely on a clinical research organization, or CRO, medical institutions and clinical investigators to conduct our clinical studies. Such reliance on third parties reduces our control over these activities, but does not relieve us of our responsibility to ensure compliance with all required regulations and study and trial protocols.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct their activities in accordance with regulatory requirements and our stated study and trial plans and protocols, or if there are disagreements between us and these third parties, we may not be able to complete, or may be delayed in completing, the pre-clinical studies and clinical trials required to support future regulatory submissions and approval of the product candidates we develop.

Reliance on such third-parties entails additional risks to which we would not be subject if we conducted the above-mentioned activities ourselves, including:

- that we may be unable to negotiate agreements with third parties under reasonable terms or that termination or non-renewal of an agreement occurs in a manner or time that is costly or damaging to us;
- that such third-parties may have limited experience with our or comparable products and may require significant support from us in order to implement and maintain the infrastructure and processes required to manufacture, test or distribute our product candidates;
- that such third parties may not perform as agreed or in compliance with applicable laws and requirements, or may not devote sufficient resources to our products;
- that we may not have sufficient rights or access to the intellectual property or know how relating to improvements or developments made by our third-party service providers in the course of their providing services to us;
- that regulators object to or disallow the performance of specific tasks by certain third parties or disallow data provided by such third parties;
- that such third parties may experience business disruptions, such as bankruptcy or acquisition, or failures or deficiencies in their supply chains, that disrupt their ability to perform their obligations to us.

Under certain circumstances, third party service providers may be entitled to terminate their engagements with us. In such circumstances, product development activities could be delayed while we seek to identify, validate, and negotiate an agreement with a replacement service provider. In some such cases an appropriate replacement may not be readily available or available on acceptable terms, which could cause additional delays to our development process.

Any of these events could lead to manufacturing, supply and/or clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products, which could, in each case, have a material adverse effect on our business, financial condition, results of operations and prospects.

Third parties on whom we rely to conduct, supervise and monitor clinical studies may not perform satisfactorily.

We and our strategic licensees rely on medical institutions, clinical investigators, contract research organizations, or CROs, and contract laboratories to carry out, or otherwise assist with, clinical trials or to perform data collection and analysis. While we and our strategic licensees have agreements governing these services, we and our strategic licensees have limited control over such third parties’ actual performance. Nevertheless, we or our strategic licensees, as applicable, are responsible for ensuring that such clinical trial is conducted in accordance with the applicable protocol, legal, regulatory, ethical and scientific standards. Reliance on a third party does not relieve the sponsor of a clinical trial of any regulatory responsibilities, including compliance with the FDA’s and other regulatory authorities’ good clinical practices, or GCP, good manufacturing practices, or GMP, good laboratory practices, or GLP, and other applicable requirements for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected.

If we, our strategic licensees, our respective CROs, or our respective investigators or trial sites fail to comply with applicable GCP, GLP, GMP or other applicable regulatory requirements, the clinical data generated in the applicable clinical trial may be deemed unreliable or otherwise not usable and the regulatory authorities and they may require the performance of additional clinical trials before issuing any marketing authorizations for the relevant product candidates.

Third party performance failures may increase our costs, delay our ability to obtain regulatory approval, and delay or prevent starting or completion of clinical trials and delay or prevent commercialization of our product candidates. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without incurring delays or additional costs.

We are party to strategic licensing relationships, which may not advance or be successful.

We have entered into strategic licensing agreements with partners, such as Allogene and Servier, under which our partners have exclusive development and commercialization rights with respect to certain product candidates. We may in the future enter into additional strategic relationships. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report apply to the activities of our strategic licensees.

Our reliance on strategic licensing arrangements may pose a number of risks, including the following:

- strategic licensees may not perform or prioritize their obligations as expected;
- clinical trials conducted pursuant to strategic licensing agreements may not be successful;
- strategic licensees may not pursue development and commercialization of product candidates that achieve regulatory approval or may elect not to pursue development or commercialization of product candidates based on clinical trial results, changes in the partners’ focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- strategic licensees may delay clinical trials, provide insufficient funding for clinical trials, stop a clinical trial, or abandon a product candidate;
- strategic licensees could develop, independently or with third parties, products that compete directly or indirectly with our product candidates;
- product candidates developed pursuant to strategic licensing agreements may be viewed by our partners as competitive with their independently developed product candidates or products, which may cause them to devote limited resources to the product candidate’s development or commercialization;
- a collaborator may not commit sufficient resources to the commercialization, marketing and distribution of any product candidate;
- disagreements with strategic licensees, including over proprietary rights, contract interpretation, or the preferred course of development, may cause delays or termination of the development or commercialization of such product candidates, or may result in time- consuming and expensive legal proceedings;
- strategic licensees may not properly obtain, maintain, protect, defend or enforce intellectual property rights or may improperly use proprietary information;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our strategic licensing agreements;
- strategic licensees may infringe, misappropriate or otherwise violate third-party intellectual property rights, which may expose us to litigation and potential liability;
- strategic licensing agreements may be terminated for convenience by the collaborator and, if terminated, the development of product candidates may be delayed or stopped;
- the negotiation of strategic licensing agreements may require substantial attention from our management team; and
- we could face significant competition in seeking appropriate strategic licensees, and the negotiation process is time-consuming and complex.

We rely on these strategic licensing arrangements to help us finance the development and commercialization of our own biopharmaceutical products. Our success depends, in part, on our ability to collect milestone and royalty payments from our strategic licensees. To the extent our strategic licensees do not aggressively and effectively pursue product candidates for which we are entitled to such payments, we will not realize these significant revenue streams, which may slow our overall development progress and could have an adverse effect on our business and future prospects.

In addition, our strategic license agreements are generally terminable at will upon specified prior notice. If one or more collaborator terminates a strategic license agreement, this could have an adverse effect on our revenues. If we do not receive anticipated payments, our development of product candidates could be delayed and we may need additional resources to develop our product candidates.

Access to raw materials, starting material and products necessary for the conduct of clinical trials and manufacturing of our product candidates is not guaranteed.

We are dependent on third parties for the supply of various of materials, including certain biological materials, that are necessary to produce our product candidates. The supply of these materials could be reduced or interrupted at any time. In such case, we may not be able to find other acceptable suppliers or on acceptable terms. If key suppliers or manufacturers are lost or the supply of the materials is diminished or discontinued, we may not be able to develop, manufacture, and market our product candidates in a timely and competitive manner. In addition, biological materials are subject to stringent manufacturing process and rigorous testing. Delays in the completion and validation of manufacturing processes for these materials could adversely affect the ability to complete trials and commercialize our products candidates. In addition, our suppliers or manufacturers may, from time to time, change their internal manufacturing or testing processes and procedures. Such changes may require us to perform or have performed studies to demonstrate equivalence of the materials produced or tested under such new procedures. Such equivalence testing may impose significant delays in the development of our product candidates. Furthermore, our suppliers may face quality issues or findings from regulatory authorities' inspections that could lead to delays or interruption of the supply of our product candidates.

We may enter into agreements with third parties to sell, distribute and/or market any of the products candidates we develop for which we obtain regulatory approval, which may adversely affect our ability to generate revenues.

Given the early development stage of our product candidates, we have no experience in sales, marketing and distribution of biopharmaceutical products. However, if any of our product candidates obtain marketing approval, we intend to develop sales and marketing capacity, either alone or with partners. Outsourcing sales, distribution and marketing may subject us to a variety of risks, including:

- our inability to exercise direct control over sales, distribution and marketing activities and personnel;
- potential failure or inability of contracted sales personnel to successfully market our products to physicians;

and

- potential disputes with third parties concerning distribution, sales and marketing expenses, calculation of royalties, and sales and marketing strategies.

If we are unable to partner with a third party that has adequate sales, marketing, and distribution capabilities, we may have difficulty commercializing our product candidates, which would adversely affect our business, financial condition, and ability to generate product revenues.

Our reliance on third parties and our strategic licensees 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.

Because we rely on third party service providers for certain activities in our development process, we must, at times, share trade secrets with them. In addition, we are required to share certain trade secrets with our strategic licensees pursuant to the terms of our strategic licensing agreements. We also conduct joint research and product development that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements.

We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, licensing agreements, consulting agreements or other similar agreements with our strategic licensees, subcontractors, advisors, employees and consultants prior to beginning research, services or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite these contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are incorporated into the technology of others, or are disclosed or used in violation of these agreements. Parties with whom we share confidential information may also be acquired by competitors, which may increase the risk that these entities might breach their confidentiality obligations and share our confidential information with the acquirer. For example, in April 2019, Novartis announced its acquisition of CellForCure, which serves as a CMO for us.

Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

Risks Related to Operational Compliance and Risk Management

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

As of December 31, 2021, we had 294 full-time employees (excluding employees of Calyxt). As our development, manufacturing and commercialization programs develop, and as we continue to comply with our obligations as a public company in both France and the United States, we have rapidly expanded our employee base. To manage our anticipated continued development and expansion, including the operation of our manufacturing facilities and the commercialization of our product candidates, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel.

Current and future growth imposes significant responsibility on our management team, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- effectively managing our internal development efforts, including the clinical and regulatory review process for our product candidates; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company. To achieve this, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these activities.

If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy.

Product liability lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our product candidates.

The risk that we may be sued on product liability claims is inherent in the development and commercialization of biopharmaceutical products. Side effects of, or manufacturing defects in, products that we develop could result in the deterioration of a patient’s condition, injury or even death. For example, our liability could be sought by patients participating in the clinical trials for our product candidates as a result of unexpected side effects resulting from the administration of these product candidates. Once a product is approved for sale and commercialized, the likelihood of product liability lawsuits increases. Criminal or civil proceedings might be filed against us by patients, regulatory authorities, our strategic licensees, biopharmaceutical companies and any other third party using or marketing our products. These actions could include claims resulting from acts by our partners, licensees and subcontractors, over which we have little or no control.

In addition, regardless of merit or eventual outcome, product liability claims may result in: impairment of our business reputation; withdrawal of clinical trial participants; initiation of investigations by regulators; costs due to related litigation; distraction of management’s attention from our primary business; substantial monetary awards to trial participants, patients or other claimants; loss of revenue; exhaustion of any available insurance and our capital resources; the inability by us and our strategic licensees to commercialize our product candidates; and decreased demand for our product candidates, if approved for commercial sale.

We maintain product liability insurance coverage for damages caused by our product candidates, including clinical trial insurance coverage, with coverage limits that we believe are customary for companies in our industry. This coverage may be insufficient to reimburse us for any expenses or losses we may suffer. In addition, in the future, we may not be able to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product or other legal or administrative liability claims by us or our partners, licensees or subcontractors, which could prevent or inhibit the commercial production and sale of any of our product candidates that receive regulatory approval, which could adversely affect our business.

We may use hazardous chemicals and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, manufacture and disposal of hazardous materials and wastes. Our research and development processes may involve the controlled use of hazardous materials, including chemicals and biological materials.

We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed any insurance coverage and our total assets. Federal, state, local or foreign laws and regulations govern to use, manufacture, storage, handling and disposal of these hazardous materials and specified waste products, as well as the discharge of pollutants into the environment and human health and safety matters. Compliance with environmental laws and regulations may be expensive and may impair our research and development efforts. If we fail to comply with these requirements, we could incur delays, substantial costs, including civil or criminal fines and penalties, clean-up costs or capital expenditures for control equipment or operational changes necessary to achieve and maintain compliance. In addition, we cannot predict the impact on our business of new or amended environmental laws or regulations or any changes in the way existing and future laws and regulations are interpreted and enforced. These current or future laws and regulations may impair our research, development or production efforts.

Our internal computer systems, or those of our third-party contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs or loss of personal data.

Despite the implementation of security measures, our internal computer systems and those of our third-party contractors and consultants are vulnerable to damage from computer viruses, cyber-attacks, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we do not believe that we have experienced any significant system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in significant damages including without limitation in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

Data privacy regulations could adversely affect our business, results of operations and financial condition.

We are subject to data privacy and protection laws and regulations that impose requirements relating to the collection, transmission, storage and use of personally-identifying information, including comprehensive regulatory systems in the U.S. and EU. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information, including regulations promulgated pursuant to HIPAA that establish privacy and security standards for the use and disclosure of individually identifiable health information and require the implementation of administrative, physical and technological safeguards to protect the privacy of such protected health information.

Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. If we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties.

In the EU, we are subject to the European Regulation (EU) No. 2016/679, known as the General Data Protection Regulation (GDPR), as well as EU Member State legislations complementing the GDPR. GDPR and EU Member State legislation apply to the collection and processing of personal data, including health-related information, of individuals in the EU by companies established in the EU and, in certain circumstances established outside of the EU. These laws impose strict obligations on the ability to process personal data, including health-related information, in particular in relation to their collection, use, disclosure and transfer. These include several requirements relating to (i) obtaining, in some situations, the informed consent of the individuals to whom the personal data relates, (ii) the information provided to the individuals about how their personal information is used, (iii) ensuring the security and confidentiality of the personal data, (iv) the obligation to notify personal data breaches to regulatory authorities and, as applicable, to communicate such breaches to affected individuals, (v) extensive internal privacy governance obligations, and (vi) obligations to honor rights of individuals in relation to their personal data (for example, the right to access, correct and delete their data). The GDPR also imposes restrictions on the transfer of personal data to most countries in the world outside of the European Economic Area (EEA), including the U.S., unless the parties to the transfer have implemented specific safeguards to protect the transferred personal information. One of the primary safeguards allowing U.S. companies to import personal information from the EEA has been the European Commission's Standard Contractual Clauses (SCCs). However, the Court of Justice of the EU (CJEU) issued a decision that called into question whether the SCCs can lawfully be used for transfers of personal information from Europe to the United States or most other countries. At present, there are few, if any, viable alternatives to the SCCs, on which we have relied for personal information transfers from Europe to the United States and other countries outside of the EEA. Following this CJEU judgment, new sets of SCCs were published on June 4, 2021. Entities having entered into the old SCCs before September 27, 2021 will be able to rely on them for a transition period ending December 27, 2022. Most importantly, the use of SCCs no longer automatically ensures compliance with the GDPR. Instead, companies remain required to conduct a data transfer impact assessment for each transfer, which adds a compliance burden. The GDPR has thus increased our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional potential mechanisms to ensure compliance with the new EU data protection rules. Also, some uncertainty remains around the legal and regulatory environment for these evolving privacy and data protection laws and regulations. Potential pecuniary fines for noncompliant companies may be up to €20 million or 4% of annual global revenue, whichever is higher.

We may become the subject of investigations and/or claims in respect of privacy matters and unfavorable outcomes in any of such matters could preclude the commercialization of products, harm our reputation, negatively affect the profitability of our products and subject us to substantial fines. In addition, our ongoing efforts to comply with evolving laws and regulations in the US, EU and elsewhere may be costly and require ongoing modifications to our policies, procedures and systems.

Provisions in our collaboration agreement with Servier may prevent or delay a change in control.

Our strategic licensing agreement with Servier provides that if a third party, meeting certain criteria, acquires control of us, directly or indirectly, by any means, or in the event that we sell or otherwise convey to a third party all or substantially all of our assets (or all or substantially all of our assets that are material to the performance of our obligations under the collaboration agreement), and such third party successor conducts research, development, manufacturing or commercialization activities on the primary CD19 target or any other CAR-T products within the indications developed by Servier, then Servier has the right to acquire for one lump sum payment an exclusive fully paid-up worldwide license under our intellectual property, subject to certain exceptions including TAL technologies, to develop, manufacture and commercialize UCART19 products for use in anti-tumor immuno-therapy (the "Servier buy out"). If we and Servier fail to agree on the amount of payment for the Servier buy out within ten days following Servier's provision of a buy-out notice, then the amount of the buy-out payment would be determined based a valuation process involving third-party valuators selected by us and Servier, respectively.

The Servier buy-out mechanism may have the effect of delaying or preventing a change in control transaction involving us, or may reduce the number of companies interested in acquiring us. If Servier were to exercise the Servier buy-out upon a change of control, our successor would not receive milestone payments or royalty payments on net sales of any of the UCART19 products acquired by Servier in the Servier buy-out.

Risks Related to Regulatory Approvals for Our Product Candidates

The regulatory landscape that governs our product candidates is uncertain; regulations relating to more established gene therapy and cell therapy products are still developing, and changes in regulatory requirements could result in delays or discontinuation of development of our product candidates or unexpected costs in obtaining regulatory approval.

Because we are developing novel CAR T-cell immunotherapy product candidates that are unique biological entities, the regulatory requirements that we will be subject to are not entirely clear. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing, and requirements have changed frequently and may continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies (OTAT, formerly known as the Office of Cellular, Tissue and Gene Therapies, or OCTGT) within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. Although the FDA decides whether individual gene therapy protocols may proceed, review processes and determinations of other reviewing bodies can impede or delay the initiation of a clinical study, even if the FDA has reviewed the study and allowed its initiation. Conversely, the FDA can place an IND application on clinical hold even if such other entities have provided a favorable review. Furthermore, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which a clinical trial will be conducted. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

Complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. For example, in the EU a special committee called the Committee for Advanced Therapies (CAT) was established within the EMA in accordance with Regulation (EC) No 1394/2007 on advanced-therapy medicinal products (ATMPs) to assess the quality, safety and efficacy of ATMPs, and to follow scientific developments in the field. ATMPs include gene therapy products as well as somatic cell therapy products and tissue engineered products. In this regard, on May 28, 2014, the EMA issued a recommendation that Cellectis' UCART19 be considered a gene therapy product under Regulation (EC) No 1394/2007 on ATMPs. We believe this recommendation is likely to be applicable to each of our UCART product candidates; however, this recommendation is not definitive until such products obtain regulatory approval for commercialization.

These various regulatory review committees and advisory groups and new or revised guidelines that they promulgate from time to time may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. Because the regulatory landscape for our CAR T-cell immunotherapy product candidates is new, we may face even more cumbersome and complex regulations than those emerging for gene therapy products and cell therapy products. Furthermore, even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in regulations or the interpretation of regulations by applicable regulatory agencies.

As we or our collaborators advance product candidates, we and they will be required to consult with these regulatory groups and comply with all applicable guidelines, rules and regulations. Because the UCART19 Studies are being sponsored by Servier and Allogene, they are directly interacting with the relevant regulatory agencies and we are not able to direct such interactions. Some of the discussions among our strategic licensees and relevant regulatory agencies could generate additional unexpected requirements from regulatory agencies that may apply to our wholly-controlled UCART product candidates, including UCART123, UCARTCS1 and UCART22 and could lead to potential delays or additional requirements, such as additional studies or modifications to our controlled clinical studies.

Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to ongoing regulatory requirements.

Even if we obtain regulatory approval in a jurisdiction for the product candidates we develop, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, and submission of safety and other post-market information. Any regulatory approvals received for the product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. For example, the holder of an approved BLA in the United States is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. Similarly, in the EU, pharmacovigilance obligations are applicable to all medicinal products. In particular, any marketing authorization holder has legal obligations to continuously collect data and conduct pharmacovigilance, i.e., the activities relating to the detection, assessment, understanding and prevention of adverse reactions and other medicine-related problems. Data have to be transmitted to the authorities within defined timelines, and any emerging concern about the benefit-risk balance has to be notified immediately. If necessary, competent authorities may request further investigations, including formal studies. Regulatory procedures exist for updating product information and implementing other safety measures. In addition to those obligations, holders of a marketing authorization for gene or cell therapy products must detail, in their application, the measures they envisage to ensure follow-up of the efficacy and safety of these products. In cases of particular concern, marketing authorization holders for gene or cell therapy products in the EU may be required to design a risk management system with a view to identifying, characterizing, preventing or minimizing risks related to those products, and may be obliged to carry out post-marketing studies and submit them to the EMA for review. In the United States, the holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Similar provisions apply in the EU. In particular, any amendment to the marketing authorization (e.g., manufacturing processes, therapeutic indication(s), product information, etc.) must be reviewed by the EMA for medicinal products having received a centralized marketing authorization valid across the entire EU. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Similarly, in the EU any promotion of medicinal products is highly regulated. For example, in the EU, it is prohibited to promote prescription medicinal products to the general public and is permitted exclusively to healthcare professionals. Additional and stricter rules may applyto promotional materials and activities, depending on the specific jurisdiction involved, and these may may require their prior vetting by the competent national regulatory authorities.

In addition, product manufacturers and their facilities 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 agency discovers 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 agency disagrees with the promotion, marketing or labeling of that product, a regulatory agency may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market, suspension or revocation of the marketing authorization or suspension of manufacturing.

If we or our strategic licensees fail to comply with applicable regulatory requirements following approval of any of the product candidates we develop, national competent authorities may:

- issue a warning letter asserting a violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend or terminate any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic licensees;
- restrict the marketing, distribution or manufacturing of the product;
- seize or detain product or otherwise require the withdrawal or recall of product from the market;
- destroy or require destruction of products;
- refuse to permit the import or export of products; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any of the foregoing regulatory actions 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 the ability to commercialize products and generate revenues. In addition, the FDA’s policies, and policies of foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our strategic licensees are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our strategic licensees are not able to maintain regulatory compliance, marketing approval that has been obtained may be lost and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We expect the product candidates we develop will be regulated as biological products, or biologics, and therefore they may be subject to competition sooner than anticipated.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the 2010 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, to establish an abbreviated pathway for the approval of products that are biosimilar to or interchangeable with an FDA-approved biological product. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

We believe that if any of our product candidates is approved in the United States as a biological product under a BLA, it should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject 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 the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

Similarly in EU, a biosimilar is typically defined as a biological medicine highly similar to another already approved biological medicine (the ‘reference medicine’). Developers of biosimilars are required to demonstrate through comprehensive comparability studies with the reference medicine that:

- their biological medicine is highly similar to the reference medicine, notwithstanding natural variability inherent to all biological medicines; and
- there are no clinically meaningful differences between the biosimilar and the reference medicine in terms of safety, quality and efficacy.

Biosimilars can only be commercialized in the EU once the period of market exclusivity on the reference medicine has expired. In general, this means that the biological reference medicine must have been authorized for at least eight years before another company can apply for approval of a similar biological medicine (that protection is referred to data exclusivity). Also, this typically means that the biological reference medicine must have been commercialized for at least ten years before another company’s biosimilar medicine can be commercialized (that protection is referred to as market exclusivity). The overall ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are deemed to bring a significant clinical benefit in comparison with existing therapies. However, data and market exclusivity can be challenged under certain circumstances and there is therefore no guarantee that our products will benefit from the associated protection.

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

We must obtain regulatory approval to market and sell our product candidates. For example, in the U.S., we must obtain FDA approval for each product candidate that we intend to commercialize, and in the EU we must obtain approval from the European Commission (EC), based on the opinion of the EMA. The approval processes are typically expensive, and the time required to obtain approval by the FDA, the EC and comparable foreign authorities is inherently unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions. We have not obtained regulatory approval for the commercialization of any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain such regulatory approval.

The FDA or other regulatory authority, as applicable, may delay, limit or deny approval of our product candidates for many reasons, including disagreement with clinical trial design or implementation, determinations that a product candidate is not sufficiently safe or efficacious, objections to the statistical significance of data or our interpretation of data, objections to the production, formulation or labeling of our product candidates, and any other discretionary factors such regulators deem relevant.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market the product candidates we develop, which would significantly harm our business, results of operations and prospects. In addition, even if we or our strategic licensees were able to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for the product candidates we develop.

We plan to seek orphan drug status for some or all of our product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with such status, which may cause our revenue, if any, to be reduced.

We plan to seek orphan drug designation for some or all of our product candidates in specific orphan indications in which there is a medically plausible basis for the use of these products. 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 in the United States, or a patient population greater than 200,000 in the United States 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. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Although we intend to seek orphan product designation for some or all of our product candidates, we may never receive such designations.

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 FDA may grant orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA, to market the same biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority of the subsequent product to the product with orphan product exclusivity or if 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. Even if we obtain orphan drug designation for a product candidate, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective, the disease or condition exceeded the population threshold, or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

Similarly, in EU, a medicinal product may receive orphan designation under Article 3 of Regulation (EC) No 141/2000 (Orphan Regulation). This applies to products that are intended for a life-threatening or chronically debilitating condition and either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would unlikely generate sufficient return in the EU to justify the necessary investment. Moreover, in order to obtain orphan designation in the EU it is necessary to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. Orphan designation is lost if it is established that the product no longer meets the orphan criteria before market authorization is granted.

In EU, orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and applicants can benefit from specific regulatory assistance and scientific advice. Products receiving orphan designation in the EU can receive ten years of market exclusivity from the date on which they are granted a market authorization in the EU, during which time no similar medicinal product for the same indication may be placed on the market. The period of market exclusivity is extended by two years for orphan drug products that have also complied with an agreed Pediatric Investigation Plan (Article 37 of the Orphan Regulation). However, the 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, i.e. the prevalence of the condition has increased above the orphan designation threshold or it is judged that the product is sufficiently profitable so as not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same therapeutic indication at any time if:

- the second applicant can establish that its product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization of the orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization of the orphan medicinal product cannot supply sufficient quantities of the orphan medicinal product.

If we do not obtain, or if – despite having obtained it - we subsequently loose, orphan exclusivity for our products that do not have broad patent protection, our competitors may sell the same drug to treat the same condition and our revenues will be reduced.

Although we may seek fast-track designation from the FDA for some or all of our product candidates, there is no assurance that such designation will be granted or, if granted that it will lead to a faster development or regulatory review or approval process.

We may seek fast-track designation and review for some or all of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition or disease, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation. Thus, even if we believe a particular product candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Moreover, even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures and such designation does not assure ultimate approval. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Although we may seek a regenerative medicine advanced therapy (RMAT) designation, a breakthrough therapy designation and/or priority medicines (PRIME) support for our product candidates, there is no assurance that such designations will be granted or, if granted that they will lead to a faster development or regulatory review or approval process.

We may seek special designations for some or all of our product candidates, including RMAT designation or breakthrough therapy designation from the FDA, or PRIME support from the EMA.

A drug is eligible for RMAT designation if, (i) the drug is a regenerative medicine therapy, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations; (ii) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition.

A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

The EMA’s PRIME scheme focuses on medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options. To be accepted for PRIME support, a medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data. Through PRIME, the EMA offers early, proactive and enhanced support to drug developers to optimize the generation of robust data on a therapy’s benefits and risks and enable accelerated assessment of medicinal products applications.

For product candidates that obtain an RMAT, breakthrough therapy or are accepted for PRIME support, interaction and communication between the FDA or the EMA, as applicable, and the sponsor of the trial can help to identify the most efficient path for clinical development. However, the granting of such designations and support, is within the discretion of the FDA or the EMA, respectively. Accordingly, even if we believe, after completing early clinical trials, that one of our product candidates meets the criteria for RMAT, breakthrough therapy, or PRIME support, the FDA or EMA, as the case may be, may disagree and instead decide not to grant such designation or support. In any event, the receipt of RMAT, breakthrough therapy or PRIME support for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional regulatory procedures and does not assure ultimate regulatory approval. In addition, even if one or more of our product candidates qualify for RMAT, breakthrough therapy or PRIME support, the FDA or EMA, as the case may be, may later decide that such product candidates no longer meet the conditions for qualification.

Even if we or our strategic licensees obtain and maintain approval for product candidates in the United States or another jurisdiction, we or our strategic licensees may never obtain approval for the same product candidates in other jurisdictions, which would limit market opportunities and adversely affect our business.

Approval of a product candidate in the United States by the FDA or in another jurisdiction by the requisite regulatory agencies in such other jurisdiction does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. The approval process varies among countries and may limit our or our strategic licensees' ability to develop, manufacture, promote and sell our product candidates internationally. Failure to obtain marketing approval in international jurisdictions would prevent the product candidates from being marketed outside of the jurisdictions in which regulatory approvals have been received. In order to market and sell the product candidates in the EU and many other jurisdictions, we and our strategic licensees must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and may involve additional pre-clinical studies or clinical trials both before and post approval. In many countries, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the intended price for the product is also subject to approval. Further, while regulatory approval of a product candidate in one country does not ensure approval in any other country, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. If we or our strategic licensees fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, the target market will be reduced and the ability to realize the full market potential of the subject product candidates will be harmed and our business may be adversely affected.

Depending on the results of clinical trials and the process for obtaining regulatory approvals in other countries, we or our strategic licensees may decide to first seek regulatory approvals of a product candidate in countries other than the United States, or we or our strategic licensees may simultaneously seek regulatory approvals in the United States and other countries, in which case we or our strategic licensees will be subject to the regulatory requirements of health authorities in each country in which we seek approvals. Obtaining regulatory approvals from health authorities in countries outside the United States and the EU is likely to subject us or our strategic licensees to risks in such countries that are substantially similar to the risks associated with obtaining approval in the United States or the EU described herein.

Government restrictions on pricing and reimbursement, as well as other healthcare payor cost-containment initiatives, may negatively impact our ability to generate revenues if we obtain regulatory approval for any of our product candidates.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. The continuing efforts of various governments, insurance companies, managed care organizations and other payors to contain or reduce healthcare costs may adversely affect our ability or our strategic licensees' ability to set a price for our products that we believe is fair, to achieve profitability, and to obtain and maintain market acceptance by patients and the medical community.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory initiatives to contain healthcare costs. By way of example, in the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ACA) was enacted in March 2010.

The ACA expanded health care coverage through Medicaid expansion and the implementation of a tax penalty for individuals who do not maintain mandated health insurance coverage (the so-called 'individual mandate'). The ACA also contains a number of provisions that affect coverage and reimbursement of drug products. Uncertainty remains regarding the implementation and impact of the ACA. There have been sustained Congressional and legal efforts to modify or repeal all or certain provisions of the ACA. For example, tax reform legislation was enacted at the end of 2017 that eliminated the individual mandate beginning in 2019. We cannot predict the ultimate content, timing or effect of any changes to the ACA or other federal and state reform efforts, and there can be no assurance that any such health care reforms will not adversely affect our future business and financial results.

U.S. federal and state governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, waivers from Medicaid drug rebate law requirements, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. The private sector has also sought to control healthcare costs by limiting coverage or reimbursement or requiring discounts and rebates on products. We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures could significantly decrease the available coverage and the price we might establish for our potential products, which would have an adverse effect on our net revenues and operating results.

Likewise, in many EU Member States, legislators and other policymakers continue to propose and implement healthcare cost-containing measures in response to the increased attention being paid to healthcare costs in the EU. Certain of these changes could impose limitations on the prices we will be able to charge for our products and any approved product candidates or the amounts of reimbursement available for these products from governmental and private third-party payers, may increase the tax obligations on pharmaceutical companies or may facilitate the introduction of generic competition with respect to our products.

Further, an increasing number of EU countries Member States and other non-U.S. countries use prices for medicinal products established in other countries as “reference prices” to help determine the price of the product in their own territory. If the price of one of our products decreases substantially in a reference price country, that could impact the price for such product in other countries. Consequently, a downward trend in prices of our products in some countries could contribute to similar downward trends elsewhere, which would have a material adverse effect on our revenues and results of operations. Also, in order to obtain reimbursement for our products in some countries, we may be required to conduct clinical trials that compare the cost-effectiveness of our products to other available therapies.

Moreover, this political and legislative uncertainty could harm our and our strategic licensees’ ability to market any products and generate revenues. Cost containment measures that healthcare payors and providers are instituting and the effect of further healthcare reform could significantly reduce potential revenues from the sale of any of our product candidates approved in the future, and could cause an increase in our compliance, manufacturing, or other operating expenses.

In some countries, the proposed pricing for a biopharmaceutical product must be approved before it may be lawfully marketed. In addition, in certain foreign markets, the pricing of a biopharmaceutical product is subject to government control and reimbursement may in some cases be unavailable. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. An EU Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, biopharmaceutical products launched in the EU do not follow price structures of the United States and generally tend to have significantly lower prices.

We believe that pricing pressures will continue and may increase, which may make it difficult for us to sell our potential products that may be approved in the future at a price acceptable to us or any of our future collaborators.

We are subject to healthcare laws and regulations, which could expose us to the potential for criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of our products, if approved. Our arrangements with such persons and third-party payors must be structured in accordance with the broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our products, if we obtain marketing approval. Restrictions under applicable federal, state and foreign healthcare laws and regulations include but are not limited to the following:

- The federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase or lease, order or recommendation of, any item, good, facility or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid.
- The federal civil and criminal false claims laws and civil monetary penalties laws, which impose criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program or knowingly and willingly falsifying, concealing or covering up a material fact or making false statements relating to healthcare matters.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, which impose certain requirements on covered entities and their business associates, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.
- The federal transparency requirements under the Physician Payments Sunshine Act, enacted as part of the ACA, that require applicable manufacturers of covered drugs, devices, biologics and medical supplies to track and annually report to CMS payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians or their immediate family members.

- Analogous laws and regulations in various U.S. states, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state marketing and/or transparency laws applicable to manufacturers that may be broader in scope than U.S. federal requirements, state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. government, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA.

  Similar legislation is applicable in other countries, including by way of example and without limitation: the UK's Bribery Act 2010 or Article D1453-1 to D1453-9 of the French Public Health Code on Transparency of Benefits Given by Companies Manufacturing or Marketing Health and Cosmetic Products for Human Use. Furthermore, in the EU, harmonized rules prohibit gifts, pecuniary advantages or benefits in kind to Health Care Professionals (HCPs) unless they are inexpensive and relevant to the practice of medicine or pharmacy. Similarly, strict rules apply to hospitality at sales promotion events. Based on these rules, a body of industry guidelines and sometimes national laws in force in individual EU Member States has been introduced to fight improper payments or other transfers of value to HCPs, and in general inducements that may have a broadly promotional character.

Ensuring that our business practices and that our business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations were found to be in violation of any laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations. If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Significant regulation applies to the manufacturing of our products and the manufacturing facilities on which we rely may not meet regulatory requirements or may have limited capacity.

All entities involved in the preparation of products for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates as well as our in-house manufacturing facilities in Raleigh, North Carolina, and Paris, France, are subject to extensive regulations. For example, in the United States, components of a finished CAR T-cell immunotherapy product approved for commercial sale or used in clinical studies must be manufactured in accordance with the current Good Manufacturing Practices (cGMP) requirements. Similarly, in the EU, manufacturers and importers of active substances and/or medicinal products must be authorized to carry out these activities. Each of their facilities must comply with cGMP to obtain a manufacturing or import authorization. Also, applicants for a marketing authorization are responsible to ensure that the proposed manufacturing sites included in the marketing authorization application comply with cGMP.

The FDA's cGMP regulations and comparable regulations in other jurisdictions govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of the product candidates we develop that may not be detectable in final product testing. In the United States, we or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's cGMP requirements enforced by the FDA through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, inspect a manufacturing facility involved with the preparation and/or control of our product candidates as well as the associated quality systems for compliance with the regulations applicable to the activities being conducted.

Similarly, in the EU, Directive 2003/94/EC, Regulation (EU) No 1252/2014 and Regulation (EU) 2017/1569 lay down the principles and guidelines of cGMP in respect of active substances for medicinal products for human use as well as investigational and medicinal products for human use and require that products are consistently produced and controlled in accordance with the applicable quality standards. EU legislation also requires that medicinal products and investigational medicinal products that are imported from third countries are manufactured in accordance with standards at least equivalent to the GMP standards laid down in the EU. These rules, together with the detailed EU Guidelines on cGMP that are laid down in EudraLex - Volume 4, provide guidance on, inter alia, quality management, personnel, premises, documentation, production operations, quality control, outsources activities, complaints and product recall and self-inspection. GMP inspections are performed by the competent authorities of the EU Member States, and are coordinated by the EMA in the case of medicinal products that are authorized through the EU centralized procedure. Furthermore, specific guidance laying down GMP requirements for the manufacturing of ATMPs that have been granted a marketing authorization and of ATMPs used in a clinical trial setting have been adopted by the EMA.

If we or any of our third-party manufacturers fail to provide appropriate products or maintain regulatory compliance, the regulator can impose regulatory sanctions including, among other things, the imposition of a hold on clinical trials, the refusal to permit a clinical trial to commence, the refusal to use certain batches of product candidates intended to be used in the clinical trials, the refusal to approve a pending application for a new product, the revocation or non-renewal of a pre-existing approval, or the refusal to accept some non-clinical and/or clinical data generated with material for which that third-party was responsible. As a result, our business, financial condition and results of operations may be materially harmed.

Manufacturing and increasing manufacturing scale at our in-house manufacturing facilities will require significant resources and substantial regulatory engagement. Our commercial manufacturing facility that we are completing in Raleigh, North Carolina, will be subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and other foreign agencies to ensure strict compliance with cGMPs, and other government regulations. Accordingly, operating our own manufacturing facilities and maintaining compliant manufacturing capabilities at scale may be costlier than we anticipate or may result in delays.

In addition, if supply from one approved manufacturer or supplier, including our own in-house manufacturing facilities, is interrupted, there could be a significant disruption in commercial and/or clinical supply of our products. Identifying and engaging an alternative manufacturer or supplier that complies with applicable regulatory requirements could result in further delay. Applicable regulatory agencies may also require additional studies if a new manufacturer or supplier is relied upon in connection with commercial production. Switching manufacturers or suppliers may involve substantial costs and time and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause commercialization of our product candidates to be delayed, cause us to incur higher costs, or prevent us from commercializing our products successfully. Furthermore, if our manufacturing facilities are unable to produce high quality product for our clinical and commercial needs, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

Risks Related to Calyxt, Inc.

As of February 23, 2022, we owned 56.1% of Calyxt, Inc. As a consolidated subsidiary and one of our operating subsidiaries, Calyxt’s business performance, financial condition and results of operations affect our financial condition and results of operations. Accordingly, to the extent any of the risks to which Calyxt is subject occur, there may be a corresponding adverse effect on our business, financial condition or results of operations and such effect may be material.

Calyxt’s ability to continue as a going concern will depend on its ability to obtain additional financing which may not be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force it to delay, limit or terminate its product development efforts or other operations.

As of December 31, 2021, Calyxt had $14.4 million of cash, cash equivalents, and restricted cash. Calyxt’s restricted cash is associated with its equipment financing leases and was $0.6 million as of December 31, 2021, with $0.5 million scheduled to be returned in December 2022. Current liabilities were $4.9 million as of December 31, 2021, and Calyxt used $18.8 million of cash for operating activities for the year then ended.

On February 23, 2022 (the February 2022 Offering), Calyxt issued 3,880,000 shares of its common stock, pre-funded warrants to purchase up to 3,880,000 shares of its common stock, and common warrants to purchase up to 7,760,000 shares of its common stock. In the aggregate, Calyxt received net proceeds of $10.0 million, after deducting approximately $0.9 million of underwriting discounts and estimated other offering expenses.

Calyxt has incurred losses since its inception and anticipates that it will continue to generate losses for the next several years. Over the longer term and until Calyxt can generate cash flows sufficient to support its operating capital requirements, it expects to finance a portion of future cash needs through (i) cash on hand, (ii) commercialization activities, which may result in various types of revenue streams from (a) future product development agreements and technology licenses, including upfront and milestone payments, annual license fees, and royalties; and (b) product sales from its proprietary BioFactory production system; (iii) government or other third-party funding, which the Company expects to be more readily available if Cellectis were to own less than 50 percent of Calyxt's common stock, (iv) public or private equity or debt financings, or (v) a combination of the foregoing. However, additional capital may not be available on reasonable terms, if at all.

For example, based on Calyxt's public float, as of the date of the filing of this Annual Report, Calyxt is only permitted to utilize a "shelf" registration statement, including the registration statement under which Calyxt's Open Market Sale Agreement℠ with Jefferies LLC (the "Calyxt ATM Facility"), is operated, subject to Instruction I.B.6 to Form S-3, which is referred to as the "baby shelf" rules. For so long as Calyxt's public float is less than $75,000,000, it may not sell more than the equivalent of one-third of its public float during any 12 consecutive months pursuant to the baby shelf rules. Although alternative public and private transaction structures are expected to be available, these may require additional time and cost, may impose operational restrictions on Calyxt, and may not be available on attractive terms.

Calyxt's ability to continue as a going concern will depend on its ability to obtain additional public or private equity or debt financing, obtain government or private grants and other similar types of funding, attain further operating efficiencies, reduce or contain expenditures, and, ultimately, to generate revenue. Calyxt's cash, cash equivalents, and restricted cash as of December 31, 2021, considering its plan to continue to invest in the growth and scaling of its BioFactory production system and AIML capabilities and the $10.0 million of net proceeds from the February 2022 Offering, is sufficient to fund its operations into late 2022. Calyxt's management has concluded there is substantial doubt regarding its ability to continue as a going concern because it anticipates that it will need to raise additional capital to support this business plan for a period of 12 months or more from the date of this filing.

If Calyxt is unable to raise additional capital in a sufficient amount or on acceptable terms, management may be required to implement various cost reduction and other cash-focused measures to manage liquidity and Calyxt may have to significantly delay, scale back, or cease operations, in part or in full. If Calyxt raises additional funds through the issuance of additional debt or equity securities, it could result in dilution to its existing stockholders and increased fixed payment obligations, and these securities may have rights senior to those of Calyxt's shares of common stock. Any of these events could significantly harm Calyxt's business, financial condition, and prospects.

Cellectis S.A. may experience substantial future dilution as a result of future equity offerings by Calyxt.

As of February 23, 2022, Cellectis S.A. owns approximately 56.1% of Calyxt's 42,718,930 outstanding shares of common stock. On February 23, 2022, Calyxt issued (i) pre-funded warrants (the "Pre-Funded Calyxt Warrants") to purchase 3,880,000 shares of Calyxt common stock at an exercise price of $0.0001 per share and (ii) common warrants (the "Common Calyxt Warrants" and together with the Pre-Funded Calyxt Warrants, the "Calyxt Warrants") to purchase 7,760,000 shares of Calyxt common stock at an exercise price of $1.41 per share. Based on Calyxt's 42,718,930 outstanding common stock as of February 23, 2022, if all Pre-Funded Calyxt Warrants were fully exercised, Cellectis S.A.'s ownership of Calyxt's outstanding common stock would be reduced to 51.4%, and if all Warrants were fully exercised, Cellectis S.A.'s ownership of Calyxt's outstanding common stock would be reduced to 44.1% .

In order to raise additional capital, Calyxt expects in the future to offer additional shares of Calyxt's common stock or other securities convertible into or exchangeable for Calyxt's common stock, including sales of Calyxt's common stock pursuant to an "at-the-market" offering facility (the "Calyxt ATM Facility"), pursuant to which Calyxt may, from time to time, sell shares of its common stock having an aggregate offering price of up to $50,000,000 through a sales agent, under which approximately $45.4 million of availability remained at January 31, 2022. Any such further issuances by Calyxt would further dilute Cellectis S.A.'s ownership level.

Furthermore, if outstanding options are exercised, Cellectis S.A. could experience further dilution. As of December 31, 2021, approximately 11,483,525 shares of Calyxt common stock are either subject to outstanding options, issuable upon vesting of outstanding restricted stock units and performance stock units, or reserved for future issuance under Calyxt's equity incentive plans. To the extent such equity compensation awards are exercised or otherwise vest, Cellectis's ownership interest in Calyxt would be further diluted.

Certain securities offered and sold by Calyxt in future offerings may be made at prices that are lower than current trading prices and may provide investors in such securities with future rights that are superior to those of existing stockholders, including Cellectis S.A.

Certain rights under the Stockholder's Agreement with Calyxt terminate when Cellectis S.A.'s ownership level falls below 50%.

Pursuant to Cellectis S.A.'s stockholders agreement with Calyxt, Cellectis S.A. has significant contractual rights, which also form part of Calyxt's certificate of incorporation, for so long as Cellectis S.A. beneficially owns at least 50% (the "Majority-Level Cellectis Rights") of the then outstanding shares of Calyxt's common stock, including those described under "ITEM 7. Major

Shareholders and Related Party Transactions—B. Related Party Transactions—Transactions with subsidiaries: Calyxt Offerings and Key Arrangements—Stockholders Agreement.” Based on Calyxt’s 42,718,930 outstanding common stock as of February 23, 2022, if all Pre-Funded Calyxt Warrants were fully exercised, Cellectis S.A.’s ownership of Calyxt’s outstanding common stock would be reduced to 51.4%, and if all Warrants were fully exercised, Cellectis S.A.’s ownership of Calyxt’s outstanding common stock would be reduced to 44.1% .

Although Cellectis S.A. will continue to retain important rights with respect to Calyxt for so long as it beneficially owns at least 15% of the outstanding shares of Calyxt’s common stock (“Continuing Cellectis Rights”), these Continuing Cellectis Rights are substantially more limited than the Majority-Level Cellectis Rights. While the Majority-Level Cellectis Rigths require Cellectis S.A. to approve substantially all major decisions made by Calyxt S.A., the Continuing Cellectis Rights include the following more limited rights:

- the right to nominate a number of designees for Calyxt’s board of directors representing a majority of the directors, to designate the Chairman of the board of directors and to have at least one designated director serve on each board committee;
- information rights with respect to Calyxt;
- approval of certain changes to Calyxt’s constitutive documents;
- approval of Calyxt’s making of any regular or special dividends;
- approval of Calyxt’s commencement of any voluntary bankruptcy proceeding or any consent to any bankruptcy proceeding;
- approval of any appointment to or removal from the Calyxt board of directors; and
- approval of the consummation of any public or private offering, merger, amalgamation or consolidation of Calyxt, the spinoff of a business of Calyxt, or any sale, conveyance, transfer or other disposition of Calyxt’s assets.

Risks Related to Calyxt, Inc.—Risks Related to Calyxt’s Business and Operations

Calyxt’s operational and financial success depends on its ability to successfully deliver synthetic biology solutions for an expanded group of end markets, which is subject to a variety of risks and uncertainties.

Since Calyxt’s inception, it has deployed its technology platform toward delivering plant-based innovations and solutions, primarily to the agriculture end market. In October 2021, Calyxt announced a strategic initiative to focus it on engineering plant-based synthetic biology solutions across an expanded group of end markets, including Calyxt’s initial target end-markets—the cosmeceutical, nutraceutical and pharmaceutical markets—as well as other potential end markets, including advanced materials and chemical industries, in addition to the agriculture end market. This expanded and diversified focus places significant demands on Calyxt’s management, requires adaptations to Calyxt’s operational infrastructure, and necessitates incremental capital expenditures. If Calyxt fails to effectively and efficiently manage and implement the strategic initiative, its business, financial condition, and results of operations would be adversely impacted. Calyxt would face similar adverse impacts if it is unable to differentiate its offerings and capabilities from competitors in the synthetic biology industry, who may have a more established position in the synthetic biology industry, greater financial and operational resources than Calyxt, and other competitive advantages over Calyxt, or if Calyxt is otherwise not successful in marketing its offerings and capabilities to new target customers.

In addition, to the extent Calyxt faces technological and other challenges, including unanticipated costs or delays in the development of compounds intended to be produced using Calyxt’s BioFactory production system, challenges adapting its technology platform for specific customer-driven plant-based chemistry needs, or the inability to effectively or efficiently scale production, Calyxt’s business, financial condition and results of operations would be adversely impacted.

The AIML capabilities that Calyxt is developing for its PlantSpring platform remain in the early stages of development, and their implementation and effectiveness could be adversely affected by flawed algorithms, insufficient datasets, or errors resulting from human intervention. Further, Calyxt’s BioFactory production system and Calyxt’s ability to produce plant-based chemistries remain relatively unproven and may not be successful at scale or at all.

The market, including customers and potential investors, may be skeptical of the viability and benefits of Calyxt’s PlantSpring technology platform, its AIML capabilities, and its BioFactory production system because they are based on a novel approach and the adoption of complex and emerging technologies. There can be no assurance that Calyxt’s technology will be understood, approved, or accepted by customers, regulators, and potential investors or that Calyxt will be able to sell its services and products profitably at competitive prices and with features sufficient to establish demand. If potential investors are skeptical of Calyxt’s technology, its ability to raise capital and the value of its common stock may be adversely affected.

Moreover, because of the novelty and complexity of Calyxt’s PlantSpring platform and BioFactory production system, achieving broad commercial success may require that Calyxt overcomes potential customer skepticism regarding its capabilities, particularly in light of the historical challenges of scaling production in the field of synthetic biology. If Calyxt does not achieve the technical specifications required by its customers or successfully manage new product development processes, or if development work is not performed according to schedule, then Calyxt's revenue growth from new pipeline products may be prevented or delayed, and Calyxt's business and operating results may be harmed.

In order for novel products from Calyxt's PlantSpring technology platform and its BioFactory production system to be successfully commercialized, it will be important for Calyxt to establish relationships not only with customers, but also with their suppliers in order to gain visibility into market trends, feature and specification demands, and manufacturing, regulatory, and distribution challenges. If Calyxt is unable to convince potential customers or their suppliers of the value of its synthetic biology products, Calyxt will not be successful in entering these markets and its business and results of operations will be adversely affected.

Calyxt has a limited operating history, which makes it difficult to evaluate its current business and prospects and may increase the risk of an investment in Calyxt.

Calyxt is an early-stage synthetic biology company with a limited operating history that to date has been focused primarily on R&D and Calyxt's previous go-to-market strategies. Calyxt's limited operating history may make it difficult to evaluate its current business and prospects. Calyxt's operating results for periods prior to October 2021 reflect results under Calyxt's prior go-to-market strategies, which involved different areas of focus, different cost structures, and different sources of revenues, which, in combination with its limited operating history, may make it difficult to evaluate its current business and prospects.

In implementing Calyxt's current strategic focus on the development of plant-based synthetic biology products, Calyxt will encounter risks and difficulties frequently experienced by companies in rapidly developing and changing emergent industries, including challenges in developing products, determining appropriate investments of its limited resources, capital raising, and gaining customers for its novel products and innovations.

Investment in plant-based synthetic biology product development is a highly speculative endeavor. It entails significant upfront R&D investment to scale Calyxt's BioFactory production system to sufficient levels to support commercialization, and there is significant risk that Calyxt will not be able to scale Calyxt's BioFactory to these levels, or at all.

To commercialize its products, Calyxt must be successful in using its PCMs to produce target molecules at commercial scale and at a commercially viable cost. If Calyxt cannot achieve commercial scale production levels or commercially viable production economics for enough products to support its business plan, including through establishing and maintaining sufficient commercial scale and volume, it will be unable to achieve a sustainable business. Calyxt's commercial scale production costs depend on many factors that could have a negative effect on its ability to sell products developed for customers at competitive prices, including, Calyxt's ability to establish and maintain sufficient commercial scale and volume to attract third party contract manufacturing, referred to as infrastructure partners. There can be no assurance that Calyxt will be able to engage infrastructure partners on acceptable terms, including reasonable costs per unit of production, or at all.

If Calyxt is unable to achieve these economies of scale and targeted unit commercial production, its revenues, profitability, and financial condition will be adversely affected.

Calyxt faces significant competition and many of its competitors have substantially greater financial, technical, and other resources than Calyxt.

The market for products developed with synthetic biology is highly competitive, and Calyxt faces significant direct and indirect competition in several aspects of its business. Many of these competitors have substantially greater financial, technical, marketing, sales, distribution, and other resources than Calyxt. Many of Calyxt's competitors engage in ongoing R&D, and technological developments by its competitors could render Calyxt's technology less competitive or obsolete, resulting in reduced revenues compared to expectations. As a result, Calyxt may be unable to compete successfully against its current or future competitors, which may result in reductions in revenue, reduced margins, and the inability to achieve market acceptance for its products. Calyxt expects to continue to face significant competition.

The synthetic biology industry is still emerging and is characterized by rapid and significant technological changes, frequent new product introductions and enhancements, and evolving industry demands and standards. Calyxt's future success will depend on its ability to sign and initiate commercial programs using its customer demand-driven approach to selecting compounds for development and scaling the production of those compounds in its BioFactory production system. Once commercial scale production occurs those customers will need to purchase the compound and integrate it into their business. Calyxt's development activity needs to occur on a timely and cost-effective basis, and it will need to continue to advance its technology. Additionally, Calyxt's customers may face significant competition or other risks that may adversely impact their business and results of operations.

Calyxt's ability to compete effectively and to achieve commercial success also depends, in part, on its ability to identify and attract customers who contract with Calyxt to develop products for use in their production and contracting with those same third parties for the commercialization of those products. Calyxt may not be successful in achieving these factors and any such failure may adversely affect its business, results of operations and financial condition. Due to the lead time involved in developing a product for a customer using Calyxt's platform, its potential customers will be required to make a number of assumptions and estimates regarding the commercial feasibility of the plant-based chemistry, including assumptions and estimates regarding the demand for those end-products and processes that will utilize the plant-based chemistry developed with Calyxt's technology, the existence or non-existence of products being simultaneously developed by competitors, potential market penetration and obsolescence, whether planned or unplanned. As a result, it is possible that Calyxt may reach an agreement with a customer who wishes to develop a product that has been displaced by the time of launch, addresses a market that no longer exists or is smaller than previously thought, that end-consumers do not like or otherwise is not competitive at the time of launch, in each case, after the incurrence of significant opportunity costs by Calyxt to develop such a product.

From time to time, third parties who may have competed in the agriculture end market once pursued by Calyxt may seek to license its technology. Calyxt has, in the past, entered such licensing arrangements and may enter such arrangements in the future. In certain circumstances, competitors who license Calyxt's technology could use those technologies to develop their own products that would compete with products commercialized by Calyxt's agriculturally focused collaboration partners, which may impact Calyxt's future royalties.

Calyxt also anticipates increased competition in the future as new companies enter the market and new technologies become available. Calyxt's technology may be rendered obsolete or uneconomical by technological advances or entirely different approaches developed by one or more of its competitors that are more effective or that enable them to develop and commercialize products more quickly or with lower expense than Calyxt is able to. At the same time, the expiration of patents covering existing technologies reduces the barriers to entry for competitors. If for any reason Calyxt's technology becomes obsolete or uneconomical relative to competitors' technologies, this would prevent or limit Calyxt's ability to generate revenues from the commercialization of its products.

If Calyxt cannot enter into new customer partnerships and successfully execute on the underlying product development projects to bring a customer's plant-based chemistry to commercial scale production and ultimately sell them the product, its business will be adversely affected.

Calyxt's approach to product development is customer demand-driven and as a result, its success depends on the number, size, and scope of customer collaborations. Calyxt's ability to win new business depends on many factors, including its reputation in the market, the differentiation of its PlantSpring technology platform and BioFactory production system relative to alternatives, the pricing and efficiency of its offerings relative to alternatives, its financial stability, and its technical capabilities. If Calyxt fails to establish a position of strength in any of these factors, its ability to either sign new customer agreements may suffer and this could adversely affect its prospects.

Calyxt engages in conversations about collaborations with potential customers regularly. Calyxt may spend considerable time and money engaging in these conversations and feasibility assessments, including understanding the technical specifications of a particular plant-based chemistry, customer concerns and limitations, and the legal or regulatory landscape of a potential program or offering, which may not result in a commercial agreement. Even if an agreement is reached, the resulting relationship may not be successful for many reasons, including Calyxt's inability to complete the development of a plant-based chemistry to the customers' specifications or within the customers' time frames, or unsuccessful development or commercialization of products or processes by Calyxt's customers. In such circumstances, Calyxt's revenues from such an agreement might be meaningfully reduced.

Development of new or improved plant-based synthetic biology products that meet customer demand-driven specifications involves risks of failure inherent in the deployment of innovative and complex emerging technologies. Accordingly, if Calyxt or its infrastructure partners experience any significant delays in the development of new products or if new products do not meet customer specifications, Calyxt's business, operating results, and financial condition would be adversely affected.

Calyxt intends to rely on third parties for at-scale BioFactory production and other services, and any performance issues by such third parties, or Calyxt's inability to engage third parties on acceptable terms, may impact Calyxt's ability to successfully meet its commercial obligations.

Calyxt's current plan is to contract with third-party infrastructure partners for at-scale BioFactory production and for other R&D services. Although Calyxt intends to provide for audit and/or inspection rights and will provide the infrastructure partners with protocols regarding the production and handing of its plant-based chemistries, it will have limited control over the execution of their activities. Poor execution, failure to follow required protocols or regulatory requirements, or mishandling of the plant-based chemistry by these infrastructure partners could impair success, delay production, cause Calyxt to incur incremental costs, or damage the customer relationship.

Even if Calyxt's infrastructure partners adhere to protocols, production runs and other R&D activities may fail to succeed for a variety of other reasons. Ultimately, Calyxt remains responsible for ensuring work performed is conducted in accordance with the applicable protocol and standards, and reliance on infrastructure partners does not relieve Calyxt of its responsibilities. Should these infrastructure partners fail to comply with these standards, Calyxt's ability to develop plant-based chemistries in accordance with customer specifications or in a timely manner could be adversely impacted.

Additionally, if Calyxt is unable to maintain or enter into agreements with infrastructure partners on acceptable terms, or if engagement is terminated prematurely, Calyxt may be unable to conduct or complete research, development, and production in the anticipated manner. For example, establishing and operating infrastructure partner facilities may require Calyxt to make significant capital expenditures, which reduces its cash and places such capital at risk. Also, infrastructure partner agreements may contain terms that commit Calyxt to pay for other costs and amounts incurred or expected to be earned by the plant operators and owners, which can result in contractual liability and losses for it even if it terminates a particular infrastructure partner arrangement or decides to reduce or stop production under such an arrangement. Further, Calyxt cannot be sure that contract manufacturers will be available when it needs their services, that they will be willing to dedicate a portion of their capacity to Calyxt's projects, or that it will be able to reach acceptable price, delivery, and other terms with the infrastructure partners for the provision of their production services.

If Calyxt's relationship with any of these infrastructure partners is terminated, it may be unable to enter arrangements with alternative infrastructure partners on commercially reasonable terms, or at all. Switching or adding infrastructure partners can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when any new infrastructure partners commences work. As a result, delays may occur, which could materially impact Calyxt's ability to meet desired development timelines, and its achievement of product-related revenues and profitability.

If Calyxt's technology licensees are delayed or unsuccessful in their development activities associated with their license of the technology, its financial results could be affected.

Calyxt expects to license its technology and its historically developed seed-trait product candidates for traditional agriculture to third parties. If Calyxt's licensees are delayed, are unsuccessful in their development and commercialization efforts, or if they fail to devote sufficient time and resources to support the marketing and selling efforts of products developed using the licenses of Calyxt's technology, it may not receive milestone and/or royalty payments as expected, and its financial results could be harmed. Further, if these licensee customers fail to market the licensed seed-trait products or products developed with Calyxt's licensed technology at prices that will achieve or sustain market acceptance for those products, Calyxt's future royalty revenues could be further harmed. If a product is commercialized by a licensee, its performance may also be impact by numerous risks, including competition from alternative products, product defects, changes in end-consumer demand, changes in law or regulation, or changes in economic conditions. Moreover, licensees have significant discretion in determining the efforts and resources applied to commercializing products utilizing the plant-based chemistries developed by Calyxt, and they may not commit sufficient resources to successfully advance a product candidate or achieve commercial success. Disputes may arise with licensees that cause the delay or termination of commercial contracts for current or future products or that results in costly litigation or arbitration that diverts management attention and resources.

Any outdoor agriculture product development agreements that Calyxt may enter in the future may be delayed or may be unsuccessful, which could adversely affect its financial results.

Calyxt may opportunistically enter into product development arrangements with third parties for the development and commercialization of certain outdoor agriculture seed traits. For example, in the third quarter of 2021, Calyxt announced that it had entered into a research collaboration with a global food ingredient manufacturer based in Asia to develop an improved soybean capable of producing an oil as a commercial alternative to palm oil.

To the extent Calyxt enters into such product development agreements, their success will depend heavily on the efforts and activities of its customer's commercialization efforts and as a result its ability to achieve milestone payments or generate royalties will not be within its direct control. If an outdoor agriculture product is commercialized by a licensee, its performance may also be impacted by numerous risks, including:

- Adverse weather conditions, natural disasters, crop disease, pests and other natural conditions;
- Climate change that may cause changes in weather patterns and conditions, including changes in rainfall and storm patterns and intensities, water shortages, changes in sea levels, and changes in temperature levels;
- Licensee field trials may be unsuccessful;
- Licensee products, and food containing those products, may fail to meet standards established by third-party non-GMO verification organizations;
- The unintended presence of Calyxt's traits in other products or plants may have a negative effect on the licensee's operations.

Risks Related to Calyxt, Inc.—Risks Related to Calyxt’s Regulatory and Legal Matters

Ethical, legal, and social concerns about products using genetically modified or edited plant cells could limit or prevent the use of Calyxt’s products and technologies and could harm its business.

Calyxt’s technologies and products involve the use of genetically modified or edited plant cells. Public perception about the safety of, and ethical, legal, or social concerns over, genetically engineered products, including genetically modified or edited plant genetic materials, could affect public acceptance of Calyxt’s products. If Calyxt is not able to overcome any such concerns relating to its products, these technologies may not be accepted by its customers or end-users of the customers’ products that incorporate Calyxt’s products. In addition, the use of genetically modified or edited plant cells has in the past received negative publicity, which could lead to greater regulation or restrictions on imports of Calyxt’s products. If Calyxt’s technologies and products are not accepted by its customers or their end-users due to negative publicity or lack of public acceptance, Calyxt’s business could be materially harmed.

Calyxt may become subject to increasing regulation as a result of its hemp development activities, which could require it to incur additional costs associated with compliance requirements.

Calyxt has developed hemp product candidates and is currently exploring licensing opportunities in the crop. Hemp is legally distinct from marijuana and recognized as an agricultural crop by the United States government. Federal and state laws and regulations on hemp address production, monitoring, manufacturing, distribution, and laboratory testing to ensure that that the hemp has a THC concentration of not more than 0.3 percent on a dry weight basis. Federal laws and regulations may also address the transportation or shipment of hemp or hemp products. It is difficult to predict whether regulators, such as the USDA or the MDA, will alter the manner in which they interpret existing federal and state laws and regulations on hemp or institute new regulations, or otherwise modify regulations in a way that will render compliance more burdensome. As Calyxt continues to pursue hemp as a product candidate, it may become subject to increasing regulation particular to hemp, which could require it to incur additional costs associated with compliance requirements.

The regulatory environment outside the United States varies greatly from jurisdiction to jurisdiction and there is less certainty how Calyxt’s products will be regulated.

The regulatory environment around gene editing and genetic modification in plants is greatly uncertain outside of the United States and varies greatly from jurisdiction to jurisdiction. Each jurisdiction may have its own regulatory framework regarding genetically modified and gene edited products and materials, which continue to evolve, and which may encapsulate Calyxt’s products. To the extent regulatory frameworks outside of the United States are not receptive to Calyxt’s genetic modification and gene editing technologies, this may limit its ability to expand into other global markets.

Complying with the regulatory requirements outside the United States will be costly and time-consuming, and there is no guarantee Calyxt will be able to commercialize its products outside the United States. Such regulatory requirements may also inhibit Calyxt’s ability to market and sell its products to customers located outside of the United States.

Calyxt cannot predict whether or when any jurisdiction will change its regulations with respect to its products. Advocacy groups have engaged in publicity campaigns and filed lawsuits in various countries against companies and regulatory authorities, seeking to halt regulatory approval or clearance activities or influence public opinion against genetically engineered and/or gene edited products. In addition, governmental reaction to negative publicity concerning Calyxt’s products could result in greater regulation of genetic research and derivative products or regulatory costs that render its products cost prohibitive.

The scale of the industries in which Calyxt intends as the end markets for its products may make it difficult to monitor and control the distribution of Calyxt’s products. As a result, Calyxt’s products may be sold inadvertently within jurisdictions where they are not approved for distribution. Such sales may lead to regulatory challenges or lawsuits against Calyxt, which could result in significant expenses and management attention.

Calyxt may use biological materials in its business and is subject to numerous environmental, health and safety laws and regulations. Compliance with such laws and regulations and any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Calyxt is subject to numerous federal, state, local and foreign environmental, health and safety laws and regulations, including those governing laboratory procedures, the handling, use, storage, treatment, manufacture and disposal of hazardous materials and wastes, discharge of pollutants into the environment and human health and safety matters. Calyxt’s R&D processes involve the controlled use of hazardous materials, including biological materials. Calyxt may be sued for any injury or contamination that results from its use or the use by third parties of these materials, or may otherwise be required to remediate such contamination, and its liability may exceed any insurance coverage and its total assets. Compliance with environmental, health and safety laws and regulations may be expensive and may impair Calyxt's R&D efforts. If Calyxt fails to comply with these requirements, it could incur substantial costs and liabilities, including civil or criminal fines and penalties, clean-up costs or capital expenditures for control equipment or operational changes necessary to achieve and maintain compliance. In addition, Calyxt cannot predict the impact on its business of new or amended environmental, health and safety laws or regulations or any changes in the way existing and future laws and regulations are interpreted and enforced. These current or future laws and regulations may impair Calyxt's research, development or production efforts or result in increased expense of compliance.

The regulatory environment in the United States is uncertain and evolving and may impact Calyxt's customers' willingness to utilize Calyxt's products.

Calyxt anticipates that its customers will be responsible for any regulatory activities associated with development of compounds commissioned from Calyxt. Such regulatory activities may involve significant expense and changes in applicable regulatory requirements could result in a substantial increases in the time and costs associated with such activities. It is difficult for Calyxt and its customers to predict whether regulators, such as the USDA or FDA, will alter the manner in which they interpret existing laws and regulations or institute new regulations, or otherwise modify regulations in a way that will subject products utilizing Calyxt's synthetic biology products to more burdensome standards, thereby substantially increasing the time and costs associated with the regulatory activities of Calyxt's customers. If the regulatory burden and expense required for the utilization of Calyxt's products becomes too significant, Calyxt's customers may seek alternatives that involve lesser regulatory costs.

If Calyxt is sued for defective products and if such lawsuits were determined adversely, it could be subject to substantial damages, for which insurance coverage is not available.

Calyxt expects that some applications of its products will be used as components of customers' end products and therefore its success will be tied, in part, to the success of such end products. Calyxt cannot be certain that material performance problems, defects, errors or delays will not arise in its products or the end products in which they are used as components.

Calyxt expects to provide warranties that its products will meet customer specifications. The costs incurred in correcting any failures to meet such specifications may be substantial and could adversely affect Calyxt's business. If Calyxt's products or the end products of which they are components, contain defects or are delayed, it may experience:

- a failure to achieve commercial traction with Calyxt's target customers;
- loss of customer contracts or delays in fulfilling Calyxt's contractual obligations;
- damage to Calyxt's brand reputation;
- product recalls or replacements;
- inability to attract new customers and collaboration opportunities;
- diversion of resources from Calyxt's R&D and sales activities; and
- legal and regulatory claims against Calyxt, including product liability claims, which could be costly, time consuming to defend, result in substantial damages and result in reputational damage.

Risks Related to Calyxt, Inc.—Risks Related to the Organization and Governance of Calyxt

Changes to Calyxt's strategic business focus have placed significant demands on Calyxt's management and Calyxt's infrastructure.

Since Calyxt's initial public offering, the strategic focus of the business has undergone changes. Most recently, in October 2021, Calyxt announced the launch of a strategic initiative which focused it on engineering synthetic biology solutions. The changes to Calyxt's strategic focus has placed, and may continue to place, significant demands on Calyxt's management and its operational and financial infrastructure. Managing a significant change in business focus requires significant expenditures and allocation of valuable management resources. If Calyxt fails to achieve the necessary level of efficiency in its organization as it evolves, its business, financial condition and results of operations would be adversely impacted.

Calyxt depends on key management personnel and attracting and retaining other qualified personnel, and its business could be harmed if it loses key management personnel or cannot attract and retain other qualified personnel.

Calyxt's success depends to a significant degree upon the technical skills and continued service of certain members of its management and other key employees. The loss of the services of Calyxt's management or key employees may delay or prevent the timely and successful execution of its business strategies and objectives. Calyxt's business is dependent on its ability to recruit and maintain a highly skilled and educated workforce with expertise in a range of disciplines, including biology, biochemistry, plant genetics, mathematics, and other subjects relevant to its operations. Calyxt's ability to successfully implement its strategic focus also depends on recruiting and retaining personnel with the necessary background and ability to understand its systems at a technical level to effectively identify and sell to potential new customers. Competition for these highly skilled employees is intense.

To attract top talent, Calyxt believes it will need to offer competitive compensation and benefits packages, including equity incentive compensation, which may require significant investment. If Calyxt is unable to offer competitive compensation this may make it more difficult for it to attract and retain key employees. Moreover, if the perceived value of Calyxt's equity awards declines, it may adversely affect Calyxt's ability to attract and retain key employees. Further, all of Calyxt's current employees are employed at-will and could depart with little or no prior notice. If Calyxt does not maintain the necessary personnel to accomplish its business objectives, it may experience staffing constraints that adversely affect its ability to support its R&D programs, customer acquisition efforts, and operations.

There can be no assurance that Calyxt will be successful in attracting or retaining such personnel and the failure to do so could have a material adverse effect on its business, financial condition, and results of operations.

Calyxt's business and operations would suffer in the event of computer system failures, cyber-attacks, or a deficiency in its cyber-security.

Increased information systems security threats, cyber- or phishing-attacks and more sophisticated, targeted computer invasions pose a risk to the security of Calyxt's systems and networks, and the confidentiality, availability, and integrity of its data, operations, and communications, and the exposure to such risks is enhanced in Calyxt's remote work environment as a result of the COVID-19 pandemic. Cyber-attacks against Calyxt's technology platform and infrastructure could result in exposure of confidential information, the modification of critical data, and/or the failure of critical operations. Likewise, improper or inadvertent employee behavior, including data privacy breaches by employees and others with permitted access to Calyxt's systems may pose a risk that sensitive data may be exposed to unauthorized persons or to the public. While Calyxt attempts to mitigate these risks by employing a number of measures, including security measures, employee training, comprehensive monitoring of networks and systems, maintenance of backup and protective systems, and incident response procedures, if these measures prove inadequate, Calyxt could be adversely affected by, among other things, loss or damage of intellectual property, proprietary and confidential information, data integrity, and communications or customer data, increased costs to prevent, respond to, or mitigate these cyber security threats and interruptions of its business operations.

Calyxt's business activities are currently conducted at a limited number of locations, which makes it susceptible to damage or business disruptions caused by natural disasters or acts of vandalism.

Calyxt's current headquarters and R&D facilities, which include an office, labs, the BioFactory pilot facility, greenhouses, and field-testing plots are in Roseville, Minnesota. Calyxt takes precautions to safeguard its facilities, including insurance, health and safety protocols, and off-site storage of critical research results and computer data. Although Calyxt maintains levels of insurance that it believes are customary for its industry, its insurance policies may not cover certain losses, or losses may exceed Calyxt's coverage limits. A natural disaster, such as a hurricane, drought, fire, flood, tornado, earthquake, or other intentional or negligent acts, including acts of vandalism, could damage or destroy Calyxt's equipment, inventory, development projects, data, and cause it to incur significant additional expenses to repair or replace the damaged physical facilities, which increase the development schedule for the products under development for customers.

Risks Related to Intellectual Property

Our ability to compete may decline if we do not adequately protect our proprietary rights.

Our commercial success depends, in part, on obtaining and maintaining proprietary rights to our and our licensors' intellectual property estate, including with respect to our product candidates, as well as successfully defending these rights against third-party challenges. We will only be able to protect our product candidates from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. Our ability to obtain patent protection for our product candidates is uncertain due to a number of factors, including:

- we or our licensors may not have been the first to invent the technology covered by our or their pending patent applications or issued patents;
- we cannot be certain that we or our licensors were the first to file patent applications covering our product candidates, including their compositions or methods of use, as patent applications in the United States and most other countries are confidential for a period of time after filing;
- others may independently develop identical, similar or alternative products or compositions or methods of use thereof;

- the disclosures in our or our licensors' patent applications may not be sufficient to meet the statutory requirements for patentability and the plausibility case law requirements that may exist in certain jurisdictions;
- any or all of our or our licensors' pending patent applications may not result in issued patents;
- we or our licensors may not seek or obtain patent protection in countries or jurisdictions that may eventually provide us a significant business opportunity;
- any patents issued to us or our licensors may not provide a basis for commercially viable products, may not provide any competitive advantages, or may be successfully challenged by third parties, which may result in our or our licensors' patent claims being narrowed, invalidated or held unenforceable;
- our compositions and methods may not be patentable;
- others may design around our or our licensors' patent claims to produce competitive products that fall outside of the scope of our or our licensors' patents; and
- others may identify prior art or other bases upon which to challenge and ultimately invalidate our or our licensors' patents or otherwise render them unenforceable.

Even if we own, obtain or in-license patents covering our product candidates or compositions, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights or other intellectual property rights of others. Others may have filed, and in the future may file, patent applications covering compositions, products or methods that are similar or identical to ours, which could materially affect our ability to successfully develop and, if approved, commercialize our product candidates. In addition, because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that our product candidates or compositions may infringe. These patent applications, including intermediate documents, may have priority over patent applications filed by us or our licensors.

Obtaining and maintaining a patent portfolio entails significant expense of resources. Part of such expense includes periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications due over the course of several stages of prosecuting patent applications, and over the lifetime of maintaining and enforcing issued patents. We or our licensors may or may not choose to pursue or maintain protection for particular intellectual property in our or our licensors portfolio. If we or our licensors choose to forgo patent protection or to allow a patent application or patent to lapse purposefully or inadvertently, our competitive position could suffer. In some cases, the prosecution and maintenance of our licensed patents is controlled by the applicable licensor. If such licensor fails to properly prosecute and maintain such patents, we could lose our rights to them, which could materially impair any competitive advantage afforded by such patents. Furthermore, we and our licensors employ reputable law firms and other professionals to help us comply with the various procedural, documentary, fee payment and other similar provisions we and they are subject to and, in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules.

There are situations, however, in which failure to make certain payments or noncompliance with certain requirements in the patent prosecution and maintenance process can result in abandonment or lapse of a 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, which would have a material adverse effect on our business.

Legal action that may be required to enforce our patent rights can be expensive and may involve the diversion of significant management time. In addition, these legal actions could be unsuccessful and could also result in the invalidation or transfer of ownership of our or our licensors' patents or a finding that they are unenforceable. We or our licensors may or may not choose to pursue litigation or other actions against those that have infringed on our or their patents, or have used them without authorization, due to the associated expense and time commitment of monitoring these activities. In some cases, the enforcement and defense of patents we in-license is controlled by the applicable licensor. If such licensor fails to actively enforce and defend such patents, any competitive advantage afforded by such patents could be materially impaired. In addition, some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we or our licensors can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging or claiming ownership over our intellectual property rights. If we fail to protect or to enforce our intellectual property rights successfully, our competitive position could suffer, which could harm our results of operations.

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

In addition to patent protection, because we operate in the highly technical field of development of therapies, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. 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 or sufficient.

In addition to contractual measures that we implement in our agreements with third-party service providers and in strategic licensing agreements, we try to protect the confidential nature of our proprietary information using physical and technological security measures. Such measures may not provide adequate protection for our proprietary information. For example, our security measures may not prevent an employee, consultant, or collaborator with authorized access from misappropriating our trade secrets and providing them to a competitor, and the recourse we have available against such misconduct may not provide an adequate or sufficiently swift remedy to protect our interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Furthermore, our proprietary information may be independently developed or lawfully reverse-engineered by others in a manner that could prevent legal recourse by us.

We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. If any of our confidential or proprietary information, including our trade secrets, were to be disclosed or misappropriated, or if any such information was independently developed by a competitor, our competitive position could be harmed.

Patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our competitive position.

The patent positions of biotechnology and biopharmaceutical companies and other actors in our fields of business can be highly uncertain and typically involve complex scientific, legal and factual analyses. In particular, the interpretation and breadth of claims allowed in some patents covering biological and biopharmaceutical compositions may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The standards of the United States Patent and Trademark Office, or USPTO, and foreign patent offices are sometimes uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated, narrowed or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings, post- grant review, inter partes review, or other administrative proceedings in the USPTO. Foreign patents as well may be subject to opposition or comparable proceedings in the corresponding foreign patent offices. Challenges to our or our licensors’ patents and patent applications, if successful, may result in the denial of our or our licensors’ patent applications or the loss or reduction in their scope. For example, on February 2022, following an opposition before the European Patent Office, the EP3004349 patent entitled “ a method for producing precise DNA cleavage using CAS9 double nickase activity” was revoked. In addition, any interference, reexamination, post-grant review, inter partes review, opposition proceedings and other administrative proceedings may be costly and involve the diversion of significant management time. Accordingly, rights under any of our or our licensors’ patents may not provide us with sufficient protection against competitive products or processes and any loss, denial or reduction in scope of any such patents and patent applications may have a material adverse effect on our business.

Furthermore, even if not challenged, our or our licensors’ patents and patent applications may not adequately protect our product candidates or technology or prevent others from designing their products or technology to avoid being covered by our or our licensors’ patent claims. If the breadth or strength of protection provided by the patents we own or license with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and could threaten our ability to successfully commercialize, our product candidates. Furthermore, 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 in order to determine who was the first to invent any of the subject matter covered by such patent claims.

In addition, changes in, or different interpretations of, patent laws in the United States and other countries may permit others to use our discoveries or to develop and commercialize our technology and products without providing any notice or compensation to us, or may limit the scope of patent protection that we or our licensors are able to obtain. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights.

If we or our licensors fail to obtain and maintain patent protection and trade secret protection of our product candidates and technology, we could lose our competitive advantage and competition we face would increase, reducing any potential revenues and have a material adverse effect on our business.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Our or our licensors' issued patents and pending patent applications will expire on dates ranging from 2021 to 2033, subject to any patent extensions that may be available for such patents. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. In the EU, Supplementary Protection Certificates (SPCs) are available to extend a patent term for up to five years to compensate for patent protection lost during regulatory review. Although all EU Member States must provide SPCs, SPCs must still be applied for and granted on a country-by-country basis and their protection is subject to exceptions. If we or our licensors do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on our product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we or our licensors do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we or our licensors have patent protection, but where the ability to enforce our or our licensors' patent rights is not as strong as in the United States. These products may compete with our products and our intellectual property rights and such rights may not be effective or sufficient to prevent such competition.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Patent protection must be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we or our licensors may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. In addition, the legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biopharmaceuticals or biotechnologies, and the requirements for patentability differ, in varying degrees, from country to country, and the laws of some foreign countries do not protect intellectual property rights, including trade secrets, to the same extent as federal and state laws of the United States. As a result, many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. Such issues may make it difficult for us to stop the infringement, misappropriation or other violation of our intellectual property rights. For example, many foreign countries, including the EU countries, have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors 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 and our licensors' 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. Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Furthermore, proceedings to enforce our and our licensors' patent rights and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our or our licensors' patents at risk of being invalidated or interpreted narrowly, could put our or our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded to us, if any, may not be commercially meaningful, while the damages and other remedies we may be ordered to pay such third parties may be significant. Accordingly, our or our licensors' 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.

Third parties may assert rights to inventions we develop or otherwise regard as our own.

Third parties may in the future make claims challenging the inventorship or ownership of our or our licensors' intellectual property. We have written agreements with collaborators that provide for the ownership of intellectual property arising from our strategic licensing arrangements. These agreements provide that we must negotiate certain commercial rights with such collaborators with respect to joint inventions or inventions made by our collaborators that arise from the results of the strategic arrangement. In some instances, there may not be adequate written provisions to address clearly the allocation of intellectual property rights that may arise from the respective strategic licensing arrangement. If we cannot successfully negotiate sufficient ownership and commercial rights to the inventions that result from our use of a third-party collaborator's materials when required, or if disputes otherwise arise with respect to the intellectual property developed through the use of a collaborator's samples, we may be limited in our ability to capitalize on the full market potential of these inventions. In addition, we may face claims by third parties that our agreements with employees, contractors, or consultants obligating them to assign intellectual property to us are ineffective, or are in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and could interfere with our ability to capture the full commercial value of such inventions. Litigation may be necessary to resolve an ownership dispute, and if we are not successful, we may be precluded from using certain intellectual property and associated products and technology, or may lose our rights in that intellectual property. Either outcome could have a material adverse effect on our business.

In addition, the research resulting in certain of our in-licensed patent rights and technology was funded in part by the United States government. As a result, the United States government has certain rights to such patent rights and technology, which include march-in rights. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to the United States industry. Any exercise by the government of any of the foregoing rights could have a material adverse effect on our business.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop and market our products.

We cannot guarantee that any of our patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or 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 and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

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. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

We currently employ, and may in the future employ, individuals who were previously employed or worked as an intern at universities or other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. 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. 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.

A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business.

There is significant litigation in the biopharmaceutical industry regarding patent and other intellectual property rights. Although we are not currently subject to any material pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others.

Our success will depend in part on our ability to operate without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. Other parties may allege that our or our collaborators' products or product candidates or the use of our or our collaborators' technologies infringe, misappropriate or otherwise violate patent claims or other intellectual property rights held by them or that we or our collaborators' are employing their proprietary technology without authorization.

If our development activities are found to infringe any such patents or other intellectual property rights, we may have to pay significant damages or seek licenses to such patents or other intellectual property. A patentee could prevent us from using the patented drugs or compositions. We may need to resort to litigation to enforce a patent issued to us, to protect our trade secrets, or to determine the scope and validity of third-party proprietary rights.

If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. Any adverse ruling or perception of an adverse ruling in defending ourselves against these claims could have a material adverse impact on our cash position. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain.

Any legal action against us or our collaborators could lead to:

- payment of damages, potentially including treble or punitive damages if we are found to have willfully infringed a party's patent rights;
- injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products;
- our or our collaborators being required to obtain a license under third-party intellectual property, and such license may not be available on an exclusive basis, on commercially acceptable terms, or at all; or
- extensive discovery in which our confidential information could be compromised.

Any of these outcomes could have a material adverse impact on our cash position and financial condition and our ability to develop and commercialize our product candidates.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering our product candidate, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Furthermore, third parties may petition courts for declarations of invalidity or unenforceability with respect to our patents or individual claims. If successful, such claims could narrow the scope of protection afforded our product candidates and future products, if any. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a 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 our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

We may be unsuccessful in licensing or acquiring intellectual property that may be required to develop and commercialize our product candidates from third parties.

We have rights, through licenses from third parties and under patents that we own, to the intellectual property to develop our product candidates. Because our programs may involve additional product candidates or improved formulations of existing product candidates that may require the use of intellectual property or proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use such intellectual property and proprietary rights. We may be unable to acquire or in-license any third-party intellectual property or proprietary rights or to do so on commercially reasonable terms. For example, we sometimes collaborate with academic institutions to accelerate our research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution’s rights in technology resulting from the strategic collaboration. Regardless of such option, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us, and the institution may license such intellectual property rights to third parties, potentially blocking our ability to pursue our development and commercialization plans.

The licensing and acquisition of third-party intellectual property and proprietary rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property and proprietary rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size and greater capital resources and development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license intellectual property and proprietary rights to us.

If we are unable to successfully acquire or in-license rights to required third-party intellectual property and proprietary rights or maintain the existing intellectual property and proprietary rights we have, we may have to cease development of the relevant the relevant program, product or product candidate, which could have a material adverse effect on our business.

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.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, our licensors may have the right to terminate the license, in which event we would not be able to market products or product candidates covered by the license.

In addition, disputes may arise regarding the payment of the royalties or other consideration due to licensors in connection with our exploitation of the rights we license from them. Licensors may contest the basis of payments we retained and claim that we are obligated to make payments under a broader basis. In addition to the costs of any litigation we may face as a result, any legal action against us could increase our payment obligations under the respective agreement and require us to pay interest and potentially damages to such licensors.

In some cases, patent prosecution of our licensed technology is controlled solely by the licensor. If such licensor fails to obtain and maintain patent or other protection for the proprietary intellectual property we license from such licensor, we could lose our rights to such intellectual property or the exclusivity of such rights, and our competitors could market competing products using such intellectual property. In addition, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected products and product candidates, which could harm our business significantly. In other cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. We may also require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided. Moreover, we have obligations under these license agreements, and any failure to satisfy those obligations could give our licensor the right to terminate the agreement. Termination of a necessary license agreement could have a material adverse impact on our business.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the basis of royalties and other consideration due to our licensors;
- the extent to which our products, product candidates, technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- 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; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

Risks Related to Calyxt's Intellectual Property

Patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to Calyxt, could negatively impact its competitive position.

The patent positions of biotechnology companies and other actors in Calyxt's fields of business can be highly uncertain and involve complex scientific, legal, and factual analyses. The interpretation and breadth of claims allowed in some patents covering biological compositions may be uncertain and difficult to determine and are often affected materially by the facts and circumstances that pertain to the patented compositions and the related patent claims. The issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated, narrowed, or circumvented. Challenges to Calyxt or its licensors' patents and patent applications, if successful, may result in the denial of it or its licensors' patent applications or the loss or reduction in their scope. In addition, defending against such challenges may be costly and involve the diversion of significant management time. Accordingly, rights under any of Calyxt or its licensors' patents may not provide it with enough protection against competitive products or processes and any loss, denial, or reduction in scope of any of such patents and patent applications may have a material adverse effect on its business.

Even if not challenged, Calyxt or its licensors' patents and patent applications may not adequately protect its product candidates or technology or prevent others from designing their products or technology to avoid being covered by Calyxt or its licensors' patent claims. If the breadth or strength of protection provided by the patents Calyxt owns or licenses is threatened, it could dissuade companies from partnering with it to develop, and could threaten the ability to successfully commercialize, Calyxt's product candidates.

If Calyxt or its licensors fail to obtain and maintain patent protection and trade secret protection of its product candidates and technology, it could lose competitive advantage and competition Calyxt faces would increase, reducing any potential revenues and have a material adverse effect on its business.

Calyxt will not seek to protect its intellectual property rights in all jurisdictions throughout the world and it may not be able to adequately enforce its intellectual property rights even in the jurisdictions where it seeks protection.

Filing, prosecuting, and defending patents in all countries and jurisdictions throughout the world would be prohibitively expensive. Patent protection must be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Calyxt's intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, Calyxt may not be able to prevent third parties from practicing its inventions in all countries outside the United States, or from selling or importing products made using its inventions in and into the United States or other jurisdictions.

Competitors may use Calyxt's technologies in jurisdictions where it or its licensors do not pursue and obtain patent protection. Further, competitors may export otherwise infringing products to territories where Calyxt or its licensors have patent protection, but where the ability to enforce those patent rights is not as strong as in the United States. These products may compete with Calyxt's products and its intellectual property rights and such rights may not be effective or enough to prevent such competition.

In addition, changes in, or different interpretations of, patent laws in the United States and other countries may permit others to use Calyxt's discoveries or to develop and commercialize its technology and products without providing any notice or compensation or may limit the scope of patent protection that Calyxt or its licensors are able to obtain. The laws of some countries do not protect intellectual property rights to the same extent as United States laws and those countries may lack adequate rules and procedures for defending Calyxt's intellectual property rights.

Furthermore, proceedings to enforce Calyxt's licensors' and its patent rights and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert its efforts and attention from other aspects of its business, could put Calyxt or its licensors' patents at risk of being invalidated or interpreted narrowly, could put it or its licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against it or its licensors. Calyxt may not prevail in any lawsuits that initiates, and the damages or other remedies awarded to it, if any, may not be commercially meaningful, while the damages and other remedies Calyxt may be ordered to pay such third parties may be significant. Accordingly, Calyxt's licensors and its efforts to enforce its intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that it develops or licenses.

Third parties may assert rights to inventions Calyxt develops or otherwise regards as its own.

Third parties may in the future make claims challenging the inventorship or ownership of Calyxt or its licensors' intellectual property. Calyxt has written agreements with R&D partners that provide for the ownership of intellectual property arising from the relationship. Some agreements provide that Calyxt must negotiate certain commercial rights at a later date and others may not include or clearly address the allocation of intellectual property rights. If Calyxt cannot successfully negotiate sufficient ownership and commercial rights to the inventions that result from Calyxt's use of a third-party partner's materials, or if disputes otherwise arise with respect to the intellectual property developed through the use of a partner's samples, Calyxt may be limited in its ability to capitalize on the full market potential of these inventions. In addition, Calyxt may face claims by third parties that its agreements with employees, contractors, or consultants obligating them to assign intellectual property to it are ineffective or are in conflict with prior or competing contractual obligations of assignment. Litigation may be necessary to resolve an ownership dispute, and if Calyxt is not successful, it may be precluded from using certain intellectual property and associated products and technology, which could have a material adverse effect on its business.

In addition, the research resulting in certain of Calyxt's in-licensed patent rights and technology was funded in part by the United States government. As a result, the United States government has certain rights to such patent rights and technology, which include march-in rights. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf. The government can exercise its march-in rights if it determines that action is necessary because Calyxt fails to achieve practical application of the government-funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to United States industry. Any exercise by the government of any of the foregoing rights could have a material adverse effect on Calyxt's business.

Any infringement, misappropriation, or other violation by Calyxt of intellectual property rights of others may prevent or delay its product development efforts and may prevent or increase the costs of successful commercialization by Calyxt, its customers or its licensees.

Calyxt's success will depend in part on its ability to operate without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. Calyxt cannot assure that its business operations, products developed, historically developed agriculture-focused product candidates, and methods and the business operations, products, product candidates and methods of its customers or licensees do not or will not infringe, misappropriate, or otherwise violate the patents or other intellectual property rights of third parties.

The biotechnology industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that Calyxt's product development activities, products, product candidates or the use of its technologies infringe, misappropriate, or otherwise violate patent claims or other intellectual property rights held by them or that it is employing their proprietary technology without authorization. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against Calyxt may require it to pay substantial damages, including treble damages and attorneys' fees if it or its partners are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if Calyxt is forced to take a license. Such a license may not be available on commercially reasonable terms, or at all. Even if Calyxt was able to obtain a license, it could be non-exclusive, thereby giving its competitors access to the same intellectual property rights or technologies licensed to Calyxt. In addition, if any such claim were successfully asserted against Calyxt and it could not obtain a license, Calyxt or its partners may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing its products, product candidates or other infringing technology, or those it develops with its R&D partners.

Even if Calyxt is successful in these proceedings, it may incur substantial costs and divert management time and attention pursuing these proceedings, which could have a material adverse effect on the organization. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of Calyxt's confidential information could be compromised by disclosure during this type of litigation. 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 Calyxt's common stock. Such litigation or proceedings could substantially increase Calyxt's operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. If Calyxt is unable to avoid infringing the patent rights of others, it may be required to seek a license, defend an infringement action, or challenge the validity of the patents in court, or redesign its products. Patent litigation is costly and time consuming. Calyxt may not have enough resources to bring these actions to a successful conclusion.

Any of these risks coming to fruition could have a material adverse effect on Calyxt's business, results of operations, financial condition, and prospects.

Calyxt may be unsuccessful in developing, licensing, or acquiring intellectual property that may be required to develop and commercialize its product candidates.

Calyxt's programs may involve additional product candidates that may require the use of intellectual property or proprietary rights held by third parties; the growth of its business may depend in part on its ability to acquire, in-license or use these intellectual property and proprietary rights. However, Calyxt may be unable to acquire or in-license any third-party intellectual property or proprietary rights that may be key to development. Even if Calyxt can acquire or in-license such rights, it may be unable to do so on commercially reasonable terms. The licensing and acquisition of third-party intellectual property and proprietary rights is a competitive area, and several more established companies are also pursuing strategies to license or acquire third-party intellectual property and proprietary rights that Calyxt may consider attractive or necessary. These established companies may have a competitive advantage over Calyxt due to their size, capital resources and agricultural development and commercialization capabilities.

In connection with his appointment as chair of the Scientific Advisory Board, Dr. Dan Voytas is no longer Calyxt's Chief Science Officer, a position he held from Calyxt's founding in January 2010 through February 2021. The consulting agreement with Dr. Voytas, while he served as Chief Science Officer, and the current engagement letter with Dr. Voytas, as chair of the Scientific Advisory Board, each generally obligates Dr. Voytas to assign to Calyxt any intellectual property solely or jointly conceived, developed or reduced to practice by him in the course of the performance of his services to Calyxt. However, Calyxt does not have any rights, including any assignment or right of first refusal rights, to intellectual property conceived, developed, or reduced to practice by Dr. Voytas outside the course of the performance of his services to Calyxt, including in connection with his employment at the University of Minnesota.

In addition, companies that perceive Calyxt to be a competitor may be unwilling to assign or license intellectual property and proprietary rights to Calyxt. Calyxt also may be unable to license or acquire third-party intellectual property and proprietary rights on terms that would allow it to make an appropriate return on its investment or at all. If Calyxt is unable to successfully acquire or in-license rights to required third-party intellectual property and proprietary rights or maintain the existing intellectual property and proprietary rights Calyxt has, it may have to cease development of the relevant program, product, or product candidate, which could have a material adverse effect on its business.

Calyxt licenses a portion of its intellectual property from Cellectis S.A. and the University of Minnesota.

Calyxt relies on the intellectual property it licenses from Cellectis S.A. and the University of Minnesota. If it does not comply with obligations under the license agreements, it may be subject to damages, which may be significant, and in some cases Cellectis S.A. and/or the University of Minnesota may have the right to terminate the license agreement. Any termination of Calyxt's license agreement with Cellectis S.A. or the University of Minnesota could have a material adverse effect on its business and results of operations.

Moreover, any enforcement of the licensed intellectual property could be subject it to challenge by third parties and if any such challenge is successful, such intellectual property could be narrowed in scope or held to be invalid or unenforceable, which could materially impair any competitive advantage afforded to Calyxt by such intellectual property. There can be no assurance that Cellectis S.A. or the University of Minnesota will prosecute and maintain such intellectual property in the best interests of

Calyxt’s business or at all, and, if Cellectis S.A. or the University of Minnesota fails to properly prosecute and maintain such intellectual property, Calyxt could lose rights to such intellectual property, which would materially impair any competitive advantage afforded to it by such intellectual property. For more information regarding Calyxt’s license agreement with Cellectis or the license agreement between Cellectis and the University of Minnesota, please see “Business—Intellectual Property.”

Risks Related to Human Capital

We depend on key management personnel and attracting and retaining other qualified personnel, and our business could be harmed if we lose key management personnel or cannot attract and retain other qualified personnel.

Our success depends to a significant degree upon the technical skills and continued service of certain members of our management team, including Dr. André Choulika, our co-founder and Chief Executive Officer and Dr. David Sourdive, our co-founder and Executive Vice President, CMC and Manufacturing. Although we maintain “key person” insurance policies on the lives of our co-founders, the loss of the services of our co-founders or other key executive officers could have a material adverse effect on us.

Our success also will depend upon our ability to attract and retain additional qualified management, regulatory, medical, and technical executives and personnel. The failure to attract, integrate, motivate, and retain additional skilled and qualified personnel, or to find suitable replacements upon departures, could have a material adverse effect on our business. We compete for such personnel against numerous companies, including larger, more established companies with significantly greater financial resources than we possess. In addition, failure to succeed in our product candidates’ development may make it more challenging to recruit and retain qualified personnel. There can be no assurance that we will be successful in attracting or retaining such personnel and the failure to do so could have a material adverse effect on our business, financial condition, and results of operations.

In order to induce valuable employees to remain at Cellectis, we have provided from time to time free shares and stock options to purchase ordinary shares that vest over time. The value to employees of free shares and stock options that vest over time may be significantly affected by movements in the price of our ordinary shares that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. In addition, our board’s authority to grant equity incentive instruments is subject to an approval of a two-thirds majority of the votes cast of our shareholders. Our shareholders may vote against some or all resolutions giving authority to our board to grant such equity awards.

Risks Relating to Our Status as a Foreign Private Issuer and a French Company

Our By-laws and French corporate law contain provisions that may delay or discourage a takeover attempt.

Provisions contained in our By-laws and French corporate law could make it more difficult for a third party to acquire us, even if doing so might be beneficial to our shareholders. In addition, provisions of French law and our By-laws impose various procedural and other requirements, which could make it more difficult for shareholders to effect certain corporate actions. These provisions include the following:

- a merger (i.e., in a French law context, a stock-for-stock exchange after which our company would be dissolved without being liquidated into the acquiring entity and our shareholders would become shareholders of the acquiring entity) of our company into a company incorporated in the European Union would require the approval of our board of directors as well as a two-thirds majority of the votes cast of the shareholders present, represented by proxy or voting by mail at the relevant meeting;
- a merger of our company into a company incorporated outside of the European Union would require the unanimous approval of our shareholders;
- under French law, a cash merger is treated as a share purchase and would require the consent of each participating shareholder;
- our shareholders have granted and may in the future grant to our board of directors broad authorizations to increase our share capital or to issue additional ordinary shares or other securities (for example, warrants) to our shareholders, the public or qualified investors, which could be used as a possible defense following the launching of a tender offer for our shares;

- our shareholders have preferential subscription rights proportional to their shareholding in our company on the issuance by us of any additional shares or securities giving the right, immediately or in the future, to new shares for cash or a set-off of cash debts, which rights may only be waived by the extraordinary general meeting (by a two-thirds majority vote) of our shareholders or on an individual basis by each shareholder;
- our board of directors has the right to appoint directors to fill a vacancy created by the resignation or death of a director, subject to the ratification by the shareholders of such appointment at the next shareholders’ meeting, which prevents shareholders from having the sole right to fill vacancies on our board of directors;
- our board of directors can only be convened by its chairman (and our managing director, if different from the chairman, may request the chairman to convene the board) or, when no board meeting has been held for more than two consecutive months, by directors representing at least one-third of the total number of directors;
- our board of directors meetings can only be regularly held if at least half of the directors attend either physically or by way of videoconference or teleconference enabling the directors’ identification and ensuring their effective participation in the board of directors’ decisions;
- our shares take the form of bearer securities or registered securities, if applicable legislation so permits, according to the shareholder’s choice. Issued shares are registered in individual accounts opened by us or any authorized intermediary (depending on the form of such shares), in the name of each shareholder and kept according to the terms and conditions laid down by the legal and regulatory provisions;
- under French law, a non-French resident as well as any French entity controlled by non-French residents may have to file a declaration for statistical purposes with the Bank of France (Banque de France) following the date of certain direct or indirect investments in us; see the section of this Annual Report titled “Ownership of Shares and ADSs by Non-French Persons”;
- approval of at least a majority of the votes cast of the shareholders present, represented by a proxy, or voting by mail at the relevant ordinary shareholders’ general meeting is required to remove directors with or without cause;
- advance notice is required for nominations to the board of directors or for proposing matters to be acted upon at a shareholders’ meeting, except that a vote to remove and replace a director can be proposed at any shareholders’ meeting without notice;
- transfers of shares shall comply with applicable insider trading rules;
- in the event where certain ownership thresholds would be crossed, a number of disclosures should be made by the relevant shareholder in addition to other certain obligations; see the section of this Annual Report titled “Declaration of Crossing of Ownership Thresholds”; and
- pursuant to French law, the sections of the By-laws relating to the number of directors and election and removal of a director from office may only be modified by a resolution adopted by a two-thirds majority of the votes cast of our shareholders present, represented by a proxy or voting by mail at the meeting.

The rights of shareholders in companies subject to French corporate law differ in material respects from the rights of shareholders of corporations incorporated in the United States.

We are a French company with limited liability. Our corporate affairs are governed by our By-laws and by the laws governing companies incorporated in France. The rights of shareholders and the responsibilities of members of our board of directors are in many ways different from the rights and obligations of shareholders in companies governed by the laws of U.S. jurisdictions. For example, in the performance of its duties, our board of directors is required by French law to consider the interests of our company, its shareholders, its employees and other stakeholders, rather than solely our shareholders and/or creditors. It is possible that some of these parties will have interests that are different from, or in addition to, the interests of our shareholders. See the sections of this Annual Report titled “Memorandum and Articles of Association” and “Corporate Governance.”

French law may limit the amount of dividends we are able to distribute, and we do not currently intend to pay dividends.

We have never declared or paid any cash dividends on our share capital and do not currently intend to do so for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, holders of our ordinary shares and ADSs are not likely to receive any dividends for the foreseeable future and any increase in value will depend solely upon any future appreciation. Consequently, holders of our equity securities may need to sell all or part of their holdings after price appreciation, which may never occur, as the only way to realize any future gains.

Further, under French law, the determination of whether we have been sufficiently profitable to pay dividends is made on the basis of our statutory financial statements prepared and presented in accordance with standard applicable in France. Please see the section of this Annual Report titled "Memorandum and Articles of Association" for further details on the limitations on our ability to declare and pay dividends. Therefore, we may be more restricted in our ability to declare dividends than companies not based in France.

Our failure to maintain certain tax benefits applicable to French technology companies may adversely affect our results of operations.

As a French technology company, we have benefited from certain tax advantages, including the French research tax credit (*Crédit d'Impôt Recherche*), or CIR. The CIR is a French tax credit aimed at stimulating research and development. The CIR can be offset against French corporate income tax due and the portion in excess (if any) may be refunded at the end of a three fiscal-year period (or, sooner, in certain cases). The Research tax credit receivables as of December 31, 2021 include the accrual for a French research tax credit related to 2021 for $7.9 million and research tax credit related to previous periods for $1.2 million. The CIR is calculated based on our claimed amount of eligible research and development expenditures in France. The French tax authority with the assistance of the Research and Technology Ministry may audit each research and development program in respect of which a CIR benefit has been claimed and assess whether such program qualifies in their view for the CIR benefit, in accordance with the French tax code (*code général des impôts*) and the relevant official guidelines.

During December 2018, the French Tax Authority initiated an audit related to the 2014, 2015, 2016 and 2017 French research tax credits. As a result of the audit, the French Tax Authority withheld a portion of the 2017 and 2018 research tax credits payment corresponding to the nature of certain employee costs. The *Tribunal Administratif* of Paris seized by Cellectis, decided the restitution of the amount withheld by the French Tax Authority. The French Tax Authority may appeal such decision. Should the French tax authorities appeal and be successful, we may be liable for additional corporate income tax, and penalties and interest related thereto, or we may not obtain the refunds for which we have applied, which could have a significant impact on our results of operations and future cash flows.

Furthermore, if the French Parliament decides to eliminate, modify, or reduce the scope of the CIR benefit, which it could decide to do at any time, our results of operations could be adversely affected.

We may be exposed to significant foreign exchange risk, which may adversely affect our financial condition, results of operations and cash flows.

We incur portions of our expenses and may in the future derive revenues in currencies other than the euro, including, in particular, the U.S. dollar. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. While we are engaged in hedging transactions to minimize the impact of uncertainty in future exchange rates on cash flows, we may not hedge all of our foreign currency exchange rate risk. In addition, hedging transactions carry their own risks and costs, including the possibility of a default by the counterpart to the hedge transaction. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

Although not free from doubt, we do not believe we were a "passive foreign investment company," or PFIC, for U.S. federal income tax purposes for the taxable year ended December 31, 2021. However, we cannot assure you that we will not be classified as a PFIC for the taxable year ending December 31, 2022 or any future taxable year, which may result in adverse U.S. federal income tax consequences to U.S. holders (as defined in the section titled "Taxation—Material U.S. Federal Income Tax Considerations" in this Annual Report).

A non-U.S. corporation will be considered a PFIC for any taxable year if either (1) at least 75% of its gross income for such year is passive income or (2) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during such year) is attributable to assets that produce or are held for the production of passive income. Although the matter is not free from doubt, we do not believe that we were a PFIC for U.S. federal income tax purposes for the taxable year ended December 31, 2021. Because certain aspects of the PFIC rules are not entirely certain and because this determination is dependent upon a number of factors, there can be no assurance that we were not a PFIC for such taxable year or that the IRS will agree with any position we take regarding our PFIC statutes.

Further, no assurances may be given at this time as to our PFIC status for the current or future taxable years. The determination of PFIC status is fact-specific, and a separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). It is possible that we could be classified as a PFIC for the taxable year ending December 31, 2022 or future taxable years due to changes in the composition of our assets or income, as well as changes to the market value of our assets. The market value of our assets may be determined in large part by reference to our market capitalization (and, therefore, the market price of the ADSs and our ordinary shares, which has fluctuated and is likely to continue to fluctuate, substantially).

If we are a PFIC for any taxable year during which a U.S. holder holds ADSs, the U.S. holder may be subject to adverse tax consequences, including (1) the treatment of all or a portion of any gain on disposition of the ADSs as ordinary income, (2) the application of an interest charge with respect to such gain and certain dividends and (3) compliance with certain reporting requirements. Each U.S. holder is strongly urged to consult its tax advisor regarding these issues and any available elections to mitigate such tax consequences. See the section titled “Taxation—Material U.S. Federal Income Tax Considerations” in this Annual Report.

As a foreign private issuer, we are exempt from a number of rules under the U.S. securities laws and are permitted to file less information with the SEC than a U.S. company. This may limit the information available to holders of ADSs.

We are a “foreign private issuer,” as defined in the SEC’s rules and regulations and, consequently, we are not subject to all of the disclosure requirements applicable to public companies organized within the United States. For example, we are exempt from certain rules under the Exchange Act that regulate disclosure obligations and procedural requirements related to the solicitation of proxies, consents or authorizations applicable to a security registered under the Exchange Act, including the U.S. proxy rules under Section 14 of the Exchange Act. In addition, our officers and directors are exempt from the reporting and “short-swing” profit recovery provisions of Section 16 of the Exchange Act and related rules with respect to their purchases and sales of our securities. Moreover, while we currently make annual and quarterly filings with the SEC, we are not required to file periodic reports and financial statements with the SEC as frequently or as promptly as U.S. domestic public companies and are not required to file quarterly reports on Form 10-Q or current reports on Form 8-K under the Exchange Act. Accordingly, there may be less publicly available information concerning our company than there would be if we were a U.S. domestic issuer.

As a foreign private issuer, we follow certain home country practices in relation to corporate governance matters that differ significantly from Nasdaq corporate governance standards. These practices may afford less protection to shareholders than they would enjoy if we complied fully with Nasdaq’s corporate governance standards.

As a foreign private issuer listed on the Nasdaq Global Market, we are subject to Nasdaq’s corporate governance standards. However, as a foreign private issuer, Nasdaq’s rules permit us to follow the corporate governance practices of France, which differ significantly from certain corporate governance standards of the Nasdaq. For example, neither the corporate laws of France nor our By-laws require a majority of our directors to be independent and our independent directors are not required to hold regularly scheduled meetings at which only independent directors are present. In addition, French governance practice does not require us to maintain a nominating and corporate governance committee or to maintain a compensation committee composed entirely of independent directors. Currently, we follow home country practice in certain key respects. Therefore, our shareholders may be afforded less protection than they otherwise would have under corporate governance listing standards applicable to U.S. domestic issuers. A discussion of our corporate governance practices is set forth in the section titled “Management—Corporate Governance Practices.”

We may lose our foreign private issuer status in the future, which could result in significant additional cost and expense.

Based on our determination made on June 30, 2021 (the last business day of our most recently completed second fiscal quarter), we currently qualify as a foreign private issuer. The next determination will be made with respect to us on June 30, 2022.

We will lose our foreign private issuer status if, as of the relevant determination date, more than 50% of our securities are held by U.S. residents and (i) more than 50% of our executive officers or more than 50% of the members of our board of directors are residents or citizens of the United States, (ii) more than 50% of our assets are located in the United States, or (iii) our business is principally administered within the United States we could lose our foreign private issuer status.

As of June 30, 2021, approximately 54.1% of our securities were held by persons who were not U.S. residents.

The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic public company would be significantly more than the costs we currently incur as a foreign private issuer.

It may be difficult to enforce civil liabilities against our company and directors and senior management and the experts named in this Annual Report.

Certain members of our board of directors and senior management are not residents of the United States, and all or a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible to serve process on such persons or us in the United States or to enforce judgments obtained in U.S. courts against them or us based on civil liability provisions of the securities laws of the United States. Additionally, it may be difficult to assert U.S. securities law claims in actions originally instituted outside of the United States. Foreign courts may refuse to hear a U.S. securities law claim because foreign courts may not be the most appropriate forums in which to bring such a claim. Even if a foreign court agrees to hear a claim, it may determine that the law of the jurisdiction in which the foreign court resides, and not U.S. law, is applicable to the claim. Further, if U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process, and certain matters of procedure would still be governed by the law of the jurisdiction in which the foreign court resides. In particular, there is some doubt as to whether French courts would recognize and enforce certain civil liabilities under U.S. securities laws in original actions or judgments of U.S. courts based upon these civil liability provisions. In addition, awards of punitive damages in actions brought in the United States or elsewhere may be unenforceable in France. An award for monetary damages under the U.S. securities laws would be considered punitive if it does not seek to compensate the claimant for loss or damage suffered but is intended to punish the defendant. French law provides that a shareholder, or a group of shareholders, may initiate a legal action to seek indemnification from the directors of a company in the company’s interest if it fails to bring such legal action itself. If so, any damages awarded by the court are paid to the company and any legal fees relating to such action are borne by the relevant shareholder or the group of shareholders.

The enforceability of any judgment in France will depend on the particular facts of the case as well as the laws and treaties in effect at the time. The United States and France do not currently have a treaty providing for recognition and enforcement of judgments (other than arbitration awards) in civil and commercial matters.

Risks Related to Ownership of Our ADSs

Holders of our ADSs do not directly hold our ordinary shares.

Holders of ADSs are not treated as one of our shareholders and do not have ordinary shareholder rights. French law governs shareholder rights. The depositary, through the custodian or the custodian’s nominee, is the holder of the ordinary shares underlying all ADSs. Holders of ADSs have only ADS holder rights. Among other things, ADS holder rights do not provide for double voting rights, which otherwise would be available to holders of ordinary shares held in a shareholders’ name for a period of at least two years. The deposit agreement among us, the depositary and purchasers of ADSs in the U.S. offering, as an ADS holder, and all other persons directly and indirectly holding ADSs, sets out ADS holder rights, as well as the rights and obligations of us and the depositary.

Holders of our ADSs may not be able to exercise their right to vote the ordinary shares underlying such ADSs.

Holders of ADSs may exercise voting rights with respect to the ordinary shares represented by the ADSs only in accordance with the provisions of the deposit agreement and not as a direct shareholder. The deposit agreement provides that, upon receipt of notice of any meeting of holders of our ordinary shares, the depositary will fix a record date for the determination of ADS holders who shall be entitled to give instructions for the exercise of voting rights. Upon timely receipt of notice from us, if we so request, the depositary shall distribute to the holders as of the record date (1) the notice of the meeting or solicitation of consent or proxy sent by us and (2) a statement as to the manner in which instructions may be given by the holders.

Holders of ADSs may instruct the depositary of the ADSs to vote the ordinary shares underlying such ADSs. Otherwise, holders of our ADSs will not be able to exercise their right to vote, unless they withdraw the ordinary shares underlying such ADSs. However, holders of our ADSs may not know about the meeting far enough in advance to withdraw those ordinary shares. If we ask for instructions, the depositary, upon timely notice from us, will notify holders of our ADSs of the upcoming vote and arrange to deliver our voting materials to such holders. We cannot guarantee that holders of our ADSs will receive the voting materials in time to ensure that they can instruct the depositary to vote such ordinary shares or to withdraw such ordinary shares so as to vote them directly. If the depositary does not receive timely voting instructions from holders of our ADSs, it may give a proxy to a person designated by us to vote the ordinary shares underlying such ADSs in accordance with the recommendation of our board of directors. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. This means that holders of our ADSs may not be able to exercise their right to vote, and there may be nothing such holders can do if the ordinary shares underlying such ADSs are not voted as requested.

The right of holders of our ADSs to participate in any future preferential subscription rights or to elect to receive dividends in shares may be limited, which may cause dilution to holders of ADSs.

According to French law, if we issue additional shares or securities for cash, current shareholders will have preferential subscription rights for these securities proportionally to their shareholding unless they waive those rights at an extraordinary meeting of our shareholders (by a two-thirds majority vote) or individually by each shareholder. However, our ADS holders in the United States will not be entitled to exercise or sell such rights unless we register the rights and the securities to which the rights relate under the Securities Act or an exemption from the registration requirements is available. In addition, the deposit agreement for our ADSs provides that the depositary will not make rights available to holders of our ADSs unless the distribution to ADS holders of both the rights and any related securities are either registered under the Securities Act or exempted from registration under the Securities Act. Further, if we offer holders of our ordinary shares the option to receive dividends in either cash or shares, the depositary may require satisfactory assurances from us that extending the offer to holders of ADSs does not require registration of any securities under the Securities Act before making the option available to holders of ADSs. We are under no obligation to file a registration statement with respect to any such rights or securities or to endeavor to cause such a registration statement to be declared effective. Moreover, we may not be able to establish an exemption from registration under the Securities Act. Accordingly, ADS holders may be unable to participate in our rights offerings or to elect to receive dividends in shares and may experience dilution in their holdings and may receive no value for these rights.

Holders of our ADSs may be subject to limitations on the transfer of such ADSs and the withdrawal of the underlying ordinary shares.

ADSs, which may be evidenced by American Depositary Receipts, or ADRs, are transferable on the books of the depositary. However, the depositary may close its books at any time or from time to time when it deems expedient in connection with the performance of its duties. The depositary may refuse to deliver, transfer or register transfers of ADSs generally when our books or the books of the depositary are closed, or at any time if we or the depositary think it is advisable to do so because of any requirement of law, government or governmental body, or under any provision of the deposit agreement, or for any other reason subject to an ADS holders' right to cancel such ADSs and withdraw the underlying ordinary shares. Temporary delays in the cancellation of such ADSs and withdrawal of the underlying ordinary shares may arise because the depositary has closed its transfer books or we have closed our transfer books, the transfer of ordinary shares is blocked to permit voting at a shareholders' meeting or we are paying a dividend on our ordinary shares. In addition, holders of our ADSs may not be able to cancel such ADSs and withdraw the underlying ordinary shares when such holders owe money for fees, taxes and similar charges and when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADSs or to the withdrawal of ordinary shares or other deposited securities.

The market price for our ADSs may be volatile or may decline regardless of our operating performance.

The trading price of the ADSs has fluctuated, and is likely to continue to fluctuate, substantially. Since the ADSs were sold in our initial public offering in March 2015 at a price of $41.50 per share, the price per ADS has ranged as low as $4.1 and as high as $50.00 through March 3, 2022. The market price of the ADSs may fluctuate significant in response to numerous factors, including those described in this "Risk Factors" section, many of which are beyond our control. The market price and demand for our ADSs may also fluctuate substantially, regardless of our actual operating performance, which may limit or prevent holders from readily selling their ADSs and may otherwise negatively affect the liquidity of our capital shares.

Share ownership is concentrated in the hands of our principal shareholders and management, who will continue to be able to exercise substantial influence on us.

Our executive officers, directors and current 5% or greater shareholders beneficially own approximately 38.79% of our ordinary shares outstanding (including those underlying our ADSs, but excluding shares that may be acquired upon exercise of stock options or warrants) as of December 31, 2021. As a result, these shareholders have significant influence over all matters that require approval by our shareholders, including the election of directors and approval of significant corporate transactions. Corporate action might be taken even if other shareholders oppose them. This concentration of ownership might also have the effect of delaying or preventing a change of control of our company that other shareholders may view as beneficial.