UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

or

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

For the transition period from _____ to _____

Commission File Number: 001-38207

Celcuity Inc.

(Exact name of registrant as specified in its charter)

Delaware	**82-2863566**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
16305 36th Avenue North, Suite 100 Minneapolis, MN	**55446**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (763) 392-0767

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	CELC	The Nasdaq Stock Market LLC

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

None

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

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

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

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

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

Large accelerated filer ☐	Accelerated filer ☐
Non-accelerated filer ☒	Smaller reporting company ☒
	Emerging growth company ☒

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). ☐ Yes ☒ No

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on $24.00, the closing price of the shares of common stock on June 30, 2021 (the last business day of the registrant's most recently completed second fiscal quarter) as reported by The Nasdaq Capital Market on such date, was approximately $198,263,160.

As of March 15, 2022, there were 14,920,302 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED IN PART BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2022 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

2021 Annual Report on Form 10-K

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The Private Securities Litigation Reform Act of 1995 provides a "safe harbor" for forward-looking statements. This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements regarding us, our business prospects and our results of operations that are subject to certain risks and uncertainties that could cause our actual business, prospects and results of operations to differ materially from those that may be anticipated by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those described in Part I, Item 1A, "Risk Factors" and elsewhere in this Annual Report. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report. We expressly disclaim any intent or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. Readers are urged to carefully review and consider the various disclosures made by us in this Annual Report and in our other reports filed with the Securities and Exchange Commission (the "SEC") that advise interested parties of the risks and uncertainties that may affect our business.

All statements, other than statements of historical facts, contained in this Annual Report, including statements regarding our plans, objectives and expectations for our business, operations and financial performance and condition, are forward-looking statements. In some cases, you can identify forward-looking statements by the following words: "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "target," "ongoing," "plan," "potential," "predict," "project," "should," "will," "would," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our results, performance or achievements to be materially different from the information expressed or implied by the forward-looking statements in this Annual Report. Additionally, our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make. Forward-looking statements may include, among other things, statements relating to:

- our plans to develop and commercialize gedatolisib, our first drug candidate;
- the focus and expected results of our initial clinical development program and upcoming clinical trials for gedatolisib, including but not limited to our planned Phase 3 clinical trial;
- our ability to capitalize on the exclusive global development and commercialization rights obtained from our license agreement with Pfizer with respect to gedatolisib;
- expectations with respect to clinical trials and collaborations with third parties, including anticipated outcomes and timing of interim and final results;
- statements relating to the potential efficacy of our gedatolisib drug in the treatment of cancer, including in combination with our CELsignia diagnostic platform;
- our ability to obtain approval from the U.S. Food and Drug Administration (the "FDA") to commercialize gedatolisib;
- the size and growth potential of the markets for both our CELsignia platform and gedatolisib, and our ability to serve those markets;
- the potential rate and degree of market acceptance, both in the United States and internationally, and clinical utility of our therapeutics, diagnostic platform and tests;
- our plans to develop and commercialize our CELsignia platform and CELsignia tests for patients with cancer and our expectations regarding the various cancer sub-types our CELsignia tests will identify;
- any perceived advantage of our CELsignia platform and CELsignia tests as compared to traditional molecular or other diagnostic tests, including, without limitation, the ability of our platform and tests to help physicians treat their patients' cancers or to identify new patient populations not diagnosable with currently available diagnostic tests;
- our expected first-mover advantage in providing products to culture living tumor cells on a commercial scale, or the sustainability of our competitive advantages;
- our ability to partner with and generate revenue from pharmaceutical partners and physicians, and the market opportunity for HER2 and c-Met therapies and other CELsignia programs for our pharmaceutical partners as a result of our CELsignia platform;
- the success of competing tests and therapeutics that are or may become available;
- expectations with respect to our CELsignia Multi-Pathway Test, which combines our CELsignia HER2 Pathway Activity Test with additional tests to analyze c-Met and PI3K signaling function and the expected capabilities of such test;
- the ability of our CELsignia platform and tests to impact clinical trials by our pharmaceutical partners, such as streamlining FDA approval of targeted therapeutics;

- the success, cost and timing of our CELsignia platform development activities;
- our commercialization, marketing and manufacturing capabilities and strategy with respect to both our gedatolisib drug candidate and CELsignia platform;
- expectations regarding federal, state, and foreign regulatory requirements and developments, such as potential FDA review and regulation of our gedatolisib drug candidate, our CELsignia platform and CELsignia tests, our operations and our laboratory;
- our plans with respect to pricing in the United States and internationally, and our ability to obtain reimbursement for both our CELsignia tests and gedatolisib drug candidate, including expectations as to our ability or the amount of time it will take to achieve successful reimbursement from third-party payors, such as commercial insurance companies and health maintenance organizations, and from government insurance programs, such as Medicare and Medicaid;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our drug product candidates and CELsignia tests;
- our expectations with respect to our facility needs;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our expectations regarding future agreements with third parties about the commercialization of our CELsignia diagnostic platform and tests, as well as our gedatolisib drug candidate;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates, including our gedatolisib drug candidate and our CELsignia platform and and tests;
- our ability to attract and retain key scientific or management personnel;
- our expectations regarding the period during which we qualify as an emerging growth company defined under the Jumpstart Our Business Startups Act of 2012 (the “JOBS Act”);
- the impact on our business of the requirements of being a public company;
- our anticipated use of the net proceeds from our initial public offering (“IPO”); and
- our expectations regarding the impact that the COVID-19 pandemic and related economic effects will have on our business and results of operations.

SUMMARY OF RISK FACTORS

Below is a summary of the material factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found in the "Risk Factors" section of Part I, Item 1A of this Annual Report and should be carefully considered, together with other information in this Annual Report and our other filings with the Securities and Exchange Commission before making investment decisions regarding our common stock.

- We have a limited operating history and we may never generate revenue or profit;
- An inability to raise additional capital on acceptable terms in the future may limit our ability to develop and commercialize our integrated therapeutic (Rx) and companion diagnostic (CDx) strategy;
- We are currently conducting and will continue to conduct clinical trials. Clinical trials are expensive and complex with uncertain outcomes, which may prevent or delay commercialization of any drug product candidates or CELsignia tests;
- The COVID-19 pandemic may materially and adversely impact our business, including ongoing clinical trials;
- Our future strategy is dependent on the success of our initial drug product, gedatolisib, as well as other drug products we may develop. If we are unable to successfully complete clinical development of, obtain regulatory approval for or commercialize our drug products, or if we experience delays in doing so, our business will be materially and adversely impacted;
- The successful development of biopharmaceuticals such as gedatolisib is highly uncertain;
- We were not involved in the early development of gedatolisib; therefore, we are dependent on third parties having accurately generated, collected, interpreted and reported data from certain preclinical and clinical trials;
- As an organization, we have never successfully completed any registrational clinical trials, and we may be unable to do so for any drug candidates we may develop;
- If we encounter difficulties enrolling patients in any of our clinical trials, our clinical development activities could be delayed or otherwise adversely affected;
- If we are unable to obtain and maintain intellectual property protection for our products and technology, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products or technology similar or identical to ours, and our ability to successfully commercialize our technology and diagnostic tests may be impaired;
- We depend on intellectual property licensed from third parties, including from Pfizer for our lead product candidate, gedatolisib, and termination of this license could result in the loss of significant rights, which would materially and adversely impact our business;
- If we fail to comply with our obligations under our patent license with Pfizer, we could lose certain license rights that are important to our business;
- Our success with CELsignia is heavily dependent on the success of our first CELsignia trials and we cannot be certain of the outcomes of such trials;
- We may not be successful in finding pharmaceutical company partners for continuing development of additional CELsignia tests;
- While our CELsignia HER2 Pathway Activity Test and CELsignia Multi-Pathway Activity Test are commercially ready, we have not attempted to market these to physicians or their patients as stand-alone tests and have no ability to determine if these tests or any of our other tests will be commercially viable;
- We will be dependent on our ability to attract and retain key personnel; and
- We face significant competition from other pharmaceutical and diagnostic companies.

PART I

ITEM 1. Business

Overview

Unless otherwise provided in this Annual Report, references to the "Company," "we," "us," and "our" and similar references refer to Celcuity Inc., a Delaware corporation. We own various unregistered trademarks and service marks, including our corporate logo. Solely for convenience, the trademarks, trade names and service marks in this Annual Report, including those owned by third parties, may be referred to without the ®,™ or ℠ symbols, but such references should not be construed as any indicator that the owner of such trademarks, trade names and service marks will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend the use or display of other companies' trademarks, trade names and service marks to imply an endorsement or sponsorship of us by any other companies.

We are a clinical-stage biotechnology company seeking to extend the lives of cancer patients by pursing an integrated therapeutic (Rx) and companion diagnostic (CDx) strategy. Our therapeutic efforts are focused on developing potential first-in-class or best-in-class molecularly targeted therapies that address the same cancer driver a CELsignia companion diagnostic can identify. CELsignia is uniquely able to analyze live patient tumor cells to identify new groups of cancer patients likely to benefit from targeted therapies. This enables a CELsignia CDx to support advancement of new indications for already approved targeted therapies. We believe this integrated Rx and CDx strategy will maximize the impact our drug development efforts have on the treatment landscape for cancer patients.

The first drug candidate we are developing internally is gedatolisib, a potent, well-tolerated, small molecule dual inhibitor, administered intravenously, that selectively targets all class I isoforms of PI3K and mammalian target of rapamycin (mTOR). In April 2021, we obtained exclusive global development and commercialization rights to gedatolisib under a license agreement with Pfizer, Inc. Our initial clinical development program for gedatolisib will focus on the treatment of patients with hormone receptor positive (HR+), HER2-negative, advanced or metastatic breast cancer. Additional clinical development programs are expected to focus on other tumor types that involve a hormonal signaling pathway, such as prostate, endometrial, or ovarian cancer.

Supporting the development of a potential first-in-class targeted therapy for breast cancer, like gedatolisib, with our CELsignia platform is a natural extension of our strategy to use our CELsignia CDx to enable new indications for other companies' targeted therapies. By combining companion diagnostics designed to enable proprietary new drug indications with targeted therapies that treat signaling dysregulation our CDx identifies, we believe we are uniquely positioned to improve the standard-of-care for many early and late-stage breast cancer patients. Our goal is to play a key role in the multiple treatment approaches required to treat breast cancer patients at various stages of their disease.

Therapeutic (Rx) Product Development

Gedatolisib

Gedatolisib is a potent, reversible dual inhibitor that selectively targets PI3K and mTOR. Gedatolisib was originally developed by Wyeth and clinical development was continued by Pfizer after it acquired Wyeth. We exclusively licensed global rights to gedatolisib from Pfizer in April 2021. A Phase 1b trial evaluating patients with HR+/HER2- metastatic breast cancer was initiated in 2016 and subsequently enrolled 138 patients.

On January 13, 2022, gedatolisib was granted Fast Track designation for the treatment of patients with HR+/HER2- metastatic breast cancer after progression on CDK4/6 therapy. Fast Track designation is granted by the FDA for products that are intended for the treatment of serious or life-threatening disease or conditions and which demonstrate the potential to address an unmet medical need. The designation offers the opportunity for frequent interactions with the FDA to discuss the drug's development plan and to ensure collection of appropriate data needed to support drug approval, as well as eligibility for rolling submission of a New Drug Application.

Based on the favorable preliminary results reported to date from the Phase 1b trial, we are preparing to initiate a Phase 3 clinical trial (VIKTORIA-1) evaluating gedatolisib and fulvestrant with or without palbociclib in patients with HR+/HER2- advanced or metastatic breast cancer whose disease progressed on prior treatment with a CDK4/6 therapy and an aromatase inhibitor. We expect to initiate the (VIKTORIA-1) study in the first half of 2022.

Background

Breast cancer is the most prevalent cancer in women, accounting for 30% of all female cancers and 13% of cancer-related deaths in the United States. The National Cancer Institute estimated that approximately 281,000 new cases of breast cancer would be diagnosed in the United States in 2020, and approximately 43,600 breast cancer patients would die of the disease. Approximately 190,000, or 70%, of these new cases are for HR+/HER2- breast cancer.

Four different breast cancer subtypes are currently identified using molecular tests that determine the level of ER and HER2 expression. About 70% of breast cancers are HR+/HER2-, which is indicative of hormone dependency. Despite progress in treatment strategies, metastatic HR+/HER2- breast cancer (MBC) remains an incurable disease, with a median overall survival (OS) of three years and a five-year survival rate of 29%.

Four different classes of targeted therapies are currently used to treat HR+/HER2- tumors: endocrine-based therapies, CDK4/6 inhibitors, PI3K inhibitors and mTOR inhibitors. Each of the CDK4/6 inhibitors, PI3K inhibitors and mTOR inhibitors are generally used to respond to the related mechanisms of resistance to endocrine therapy, namely, activation of the CDK4/6, PI3K and mTOR pathways.

As specifically relates to gedatolisib, activation of the PI3K/mTOR pathway has been implicated in a wide variety of human cancers, involving either activating mutations, or other unknown drivers of pathway amplification. These include cancers of the breast, prostate, endometrial, colon, rectum, and lung, among others.

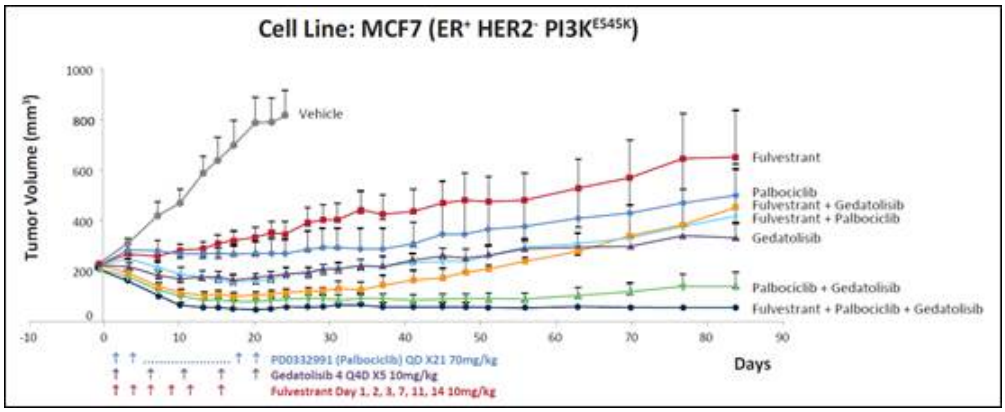
Activities associated with PI3K involve complex essential cell regulatory mechanisms including feedforward and feedback signaling loops. Overactivation of the pathway is frequently present in human malignancies and plays a key role in cancer progression. Four catalytic isoforms of class I PI3K preferentially mediate signal transduction and tumor cell survival based on the type of malignancy and the genetic or epigenetic alterations an individual patient harbors. Due to the multiple subcellular locations, activities, and importance of the different PI3K complexes in regulating many types of cancer cell proliferation, control of PI3K activity is an important target in cancer therapy.

mTOR is a critical effector in cell-signaling pathways commonly dysregulated in human cancers. The mTOR signaling pathway integrates both intracellular and extracellular signals and serves as a central regulator of cell metabolism, growth, proliferation, and survival. mTOR is a serine/threonine protein kinase, a downstream effector of PI3K, and regulated by hormones, growth factors, and nutrients, that is contained in two functionally distinct protein assemblies – mTORC1 and mTORC2: In cancer, dysfunctional signaling leads to various constitutive activities of the mTOR complexes, making mTOR a good therapeutic target.

In addition, the PI3K/mTOR pathway, like other mitogenic pathways, can also promote the activities of cyclin D and CDK4/6 to drive proliferative cell cycling. The available evidence indicates that resistance to CDK4/6 inhibition in patients with HR+/HER2- advanced breast cancer is a transient adaptive mechanism, most likely involving the PI3K/mTOR pathway. This data indicates that CDK4/6 signaling is restored in CDK4/6 resistant tumors when PI3K/mTOR inhibitors are applied. Thus, continuing CDK4/6 inhibitor treatment in combination with a PI3K/mTOR inhibitor in patients who progressed on their prior CDK4/6 inhibitor, would both blockade the reactivated CDK4/6 pathway and prevent adaptive activation of the PI3K/mTOR pathway. This suggests the limited efficacy induced by current standard-of-care (SOC) therapies in patients who have progressed on a CDK4/6 therapy reflects the mechanistic inadequacy of relying on partial PI3K/mTOR inhibition (e.g., alpelisib or everolimus) and no CDK4/6 inhibition to address this complex disease mechanism.

We believe the complex connection between PI3K/mTOR and CDK4/6 regulated cell cycling can enable gedatolisib to adaptively reactivate CDK4/6 signaling that reportedly occurs in CDK4/6 resistant tumors when the PI3K/mTOR pathway is completely blockaded. By re-activating CDK4/6 signaling, we believe gedatolisib can restore the therapeutic effect of CDK4/6 inhibition when it is combined with a CDK4/6 inhibitor. The contributory effect of a CDK4/6 inhibitor when combined with gedatolisib would thus largely reflect the interaction between the two therapies that gedatolisib initiates.

Evidence of gedatolisib anti-tumor in vivo activity was provided in a study evaluating the combination of gedatolisib and a CDK4/6 inhibitor in cell-line xenograft model where response to endocrine therapy was improved and tumor regressions were induced. In a study evaluating the MCF7 xenograft model (ER+/HER2-/PIK3CA mutant), the combination of gedatolisib with palbociclib and fulvestrant caused 90% tumor regression with no tumor regrowth observed for more than 60 days after the final dose.



Advantages of Gedatolisib over Other PI3K and mTOR Inhibitors

The important role the PI3K/mTOR pathway plays in cancer has led to significant investment in the development of many different PI3K and mTOR inhibitors for solid tumors. However, developing efficacious and well-tolerated therapies that target this pathway has been challenging. This reflects the inherent adaptability and complexity of the PI3K pathway, where numerous feedforward and feedback loops, crosstalk with other pathways, and compensatory pathways enable resistance to PI3K inhibition. Another major hurdle for the development of PI3K pathway inhibitors has been the inability to achieve optimal drug-target blockade in tumors while avoiding undue toxicities in patients.

We believe there is significant potential for gedatolisib to address previously treated breast cancer tumors and has the potential to be used in other tumor types where the PI3K/mTOR pathway is either: i) driving tumorigenesis directly; ii) cooperating with other dysregulated signaling pathways; or iii) a mechanism of resistance to other drug therapies.

As a result, we believe gedatolisib's unique mechanism of action, favorable pharmacokinetic properties, and intravenous formulation offer distinct advantages over currently approved and investigational therapies that target PI3K or mTOR alone or together.

- **Overcomes limitations of therapies that only inhibit a single class I PI3K isoform or only one mTOR kinase complex**

  Gedatolisib is a pan-class I isoform PI3K inhibitor with low nanomolar potency for the p110α, p110β, p110γ, and p110δ isoforms. Because gedatolisib inhibits all four PI3K isoforms and both mTOR complexes, it prevents the confounding effect of isoform interaction that may occur with isoform-specific PI3K inhibitors and the confounding interaction between PI3K isoforms and mTOR. This compares to therapies that only inhibit a single class I isoforms (e.g., alpelisib, a PI3K-α inhibitor) or only one mTOR kinase complex (e.g., everolimus, an mTORC1 inhibitor), which cross-activate uninhibited sub-units due to numerous feedforward and feedback loops between the PI3K isoforms and mTOR, which in turn induces compensatory resistance that reduces the efficacy of isoform specific PI3K or single mTOR kinase complex inhibitors.

- **Better tolerated by patients than oral PI3K and mTOR drugs.**

  Gedatolisib is administered intravenously (IV) on a four-week cycle of three weeks-on, one week-off, in contrast to the orally administered pan-PI3K or dual PI3K/mTOR inhibitors that are no longer being clinically developed. Oral pan-PI3K or PI3K/mTOR inhibitors have repeatably been found to induce significant side effects that were not well tolerated by patients. This typically leads to a high proportion of patients requiring dose reductions or treatment discontinuation, despite showing promising efficacy. By contrast, gedatolisib stabilizes at lower concentration levels in plasma compared to orally administered PI3K inhibitors, resulting in less toxicity, while maintaining concentrations sufficient to inhibit PI3K/mTOR signaling.

  Isoform-specific PI3K inhibitors administered orally were developed to reduce toxicities in patients. While the range of toxicities associated with isoform-specific inhibitors is narrower than oral pan-PI3K or PI3K/mTOR inhibitors, administering them orally on a continuous basis still leads to challenging toxicities. The experience with an FDA approved oral p110-α specific inhibitor, Piqray, illustrates the challenge. In its Phase 3 pivotal trial Piqray was found to induce a Grade 3 or 4 adverse event (AE) related to hyperglycemia in 39% of patients evaluated. In addition, 26% of patients discontinued alpelisib due to treatment related adverse events. By contrast, in the 103-patient dose expansion portion of the Phase 1b clinical trial with gedatolisib, only 7% of patients experienced Grade 3 or 4 hyperglycemia and less than 10% discontinued treatment.

Clinical Experience with Gedatolisib

As of December 31, 2021, 492 patients with solid tumors have received gedatolisib in eight clinical trials sponsored by Pfizer. Of the 492 patients, 129 were treated with gedatolisib as a single agent in three clinical trials. The remaining 363 patients received gedatolisib in combination with other anti-cancer agents in five clinical trials. Additional patients received gedatolisib in combination with other anti-cancer agents in nine investigator sponsored clinical trials.

On January 13, 2022, gedatolisib was granted Fast Track designation for the treatment of patients with HR+/HER2- metastatic breast cancer after progression on CDK4/6 therapy. Fast Track designation is granted by the FDA for products that are intended for the treatment of serious or life-threatening disease or conditions and which demonstrate the potential to address an unmet medical need. The designation offers the opportunity for frequent interactions with the FDA to discuss the drug's development plan and to ensure collection of appropriate data needed to support drug approval, as well as eligibility for rolling submission of a New Drug Application.

Gedatolisib's safety, tolerability and pharmacokinetic profile were determined in a Phase 1 First-in-Human study. The favorability of preliminary results from our most recently completed clinical trial, a Phase 1b study which evaluated 138 patients with HR+/HER2- advanced breast cancer, led us to focus our initial clinical development program on advanced breast cancer.

Phase 1 First-in-Human Study

In 2013, Pfizer completed a Phase 1, open-label, dose-escalation first-in human study of single-agent gedatolisib in patients with advanced solid tumors. The primary objective of Part 1 of the study was to determine the safety, tolerability, and maximum tolerated dose (MTD) of single-agent gedatolisib administered once weekly as an intravenous (IV) infusion. Seventy-seven patients with advanced solid tumors received doses of gedatolisib and the MTD was determined to be 154 mg IV once weekly (n = 42). Subsequent analysis determined that the recommended Phase 2 dose could be increased to 180 mg IV once weekly.

At the MTD, the majority of patients enrolled in the MTD group experienced only grade 1 treatment-related adverse events (AEs). Grade 3 treatment-related adverse events were noted in 23.8% of patients, and the most frequently reported included mucosal inflammation and stomatitis (7.1%), increased alternative lengthening of telomeres (ALT) (7.1%), and increased aspartate aminotransferase (AST) (4.8%). Only 2% of patients experienced Grade 3 hyperglycemia. No treatment-related AEs of grade 4 or 5 severity were reported at any dose level.

Phase 1b HR+/HER2- MBC Clinical Trial Results (preliminary)

In 2016, Pfizer initiated a Phase 1b trial dose-finding trial with an expansion portion for safety and efficacy to evaluate gedatolisib when added to either the standard doses of palbociclib plus letrozole or palbociclib plus fulvestrant in patients with HR+/HER2- metastatic breast cancer. PI3K mutation status was not used as an eligibility criterion. Patient enrollment for the trial is complete.

A total of 138 patients with HR+/HER2- metastatic breast cancer were dosed in the clinical trial. Twelve patients from this study continue to receive study treatment, as of December 31, 2021, ten of whom have received study treatment for more than three years.

- 35 patients were enrolled in two dose escalation arms to evaluate the safety and tolerability and determine the MTD of gedatolisib when used in combination with the standard doses of palbociclib and endocrine therapies. The MTD was determined to be 180 mg administered intravenously once weekly.

- 103 patients were enrolled in one of four expansion arms (A, B, C, D) to determine if the triplet combination of gedatolisib plus palbociclib and letrozole or gedatolisib plus palbociclib and fulvestrant produced a superior objective response (OR), compared to historical control data of the doublet combination (palbociclib plus endocrine therapy). All patients received gedatolisib in combination with standard doses of palbociclib and endocrine therapy (either letrozole or fulvestrant). In Arms A, B, and C, patients received an intravenous dose of 180 mg of gedatolisib once weekly. In Arm D, patients received an intravenous dose of 180 mg of gedatolisib on a four-week cycle of three weeks-on, one week-off. Objective response was determined using Response Evaluation Criteria in Solid Tumors v1.0, or RECIST v1.0.

    - **Arm A**: MBC with progression and no prior endocrine-based systemic therapy or a CDK4/6 inhibitor in the metastatic setting. First-line endocrine-based therapy for metastatic disease (CDK4/6 treatment naive).

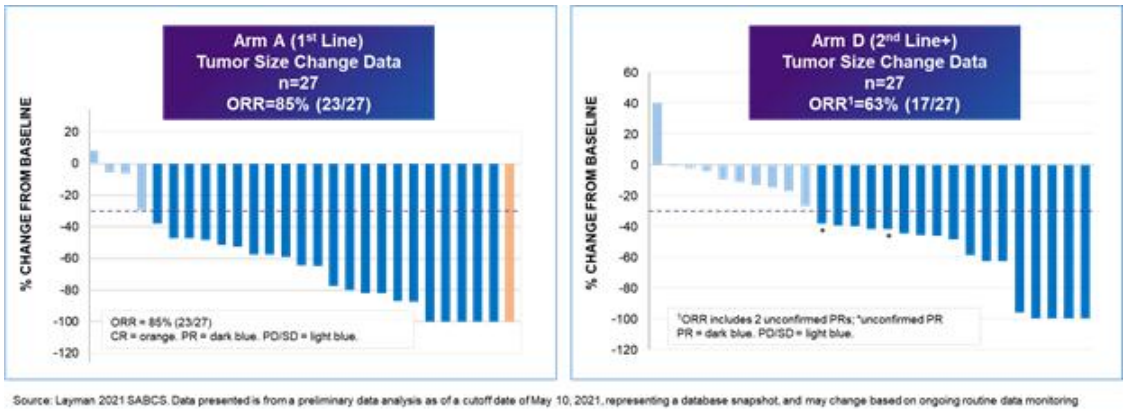
    - **Arm B**: MBC with progression during one or two prior endocrine-based systemic therapy in the metastatic setting, with no prior therapy with any CDK inhibitor. Second- or third-line endocrine-based therapy for metastatic disease.

    - **Arm C**: MBC with progression during one or two prior endocrine-based systemic therapies in the metastatic setting and following prior therapy with a CDK inhibitor. Second- or third-line endocrine-based therapy for metastatic disease.

- **Arm D**: MBC having progressed on a CDK inhibitor in combination with endocrine therapy as the most recent regimen for metastatic disease. Second- or third-line endocrine-based therapy for metastatic disease.

A preliminary analysis for the 103 patients enrolled in the expansion portion of the Phase 1b clinical trial, as of the database cutoff date of May 10, 2021, showed:

- Efficacy analysis for all arms in aggregate:
  - 62% objective response rate (ORR)
  - 92% clinical benefit rate (CBR)
- Best responses, as measured by RECIST v1.0, are shown in the following chart for Arm A (1st line patients) and Arm D (2nd/3rd line patients who received recommended dosing regimen). The dotted line represents the cutoff for partial response (PR), defined as a 30% reduction from the baseline tumor assessment.



Source: Layman 2021 SABCS. Data presented is from a preliminary data analysis as of a cutoff date of May 10, 2021, representing a database snapshot, and may change based on ongoing routine data monitoring

- Preliminary safety analysis:
  - For all arms in aggregate, all patients experienced at least one Grade 1 or Grade 2 treatment-emergent adverse event. The most commonly reported adverse events regardless of grade and occurring in at least 30% of patients included stomatitis (81%), neutropenia (80%), nausea (75%), fatigue (68%), dysgeusia (46%), vomiting (45%), anemia (40%), diarrhea (34%), decreased appetite (32%), leukopenia (32%).
  - For all arms in aggregate, the Grade 3 and 4 treatment-emergent adverse events occurring in at least 20% of patients were neutropenia (67%), stomatitis (27%) and rash (20%). Neutropenia is a known class effect of CDK4/6 inhibitors. Stomatitis was reversible in most patients with a steroidal mouth rinse. All grades of treatment-related adverse events related to hyperglycemia was reported in 22% of patients; Grade 3 or 4 hyperglycemia was reported in 7% of patients. Gedatolisib was discontinued in 10% of patients.
  - For the patients in Arm D, who received the Phase 3 dosing schedule, Grade 3 and 4 treatment-emergent adverse events occurring in at least 20% of patients were neutropenia (67%) and stomatitis (22%). All grades of treatment-related adverse events related to hyperglycemia was reported in 22% of patients; Grade 3 or 4 hyperglycemia was reported in 7% of patients. Gedatolisib was discontinued in 4% of patients.
- Preliminary best overall response and progression free survival data for each arm is presented in the table below:

Arm	**A (N=31)**	**B (N=13)**	**C (N=32)**	**D (N=27)**
Patients	1L: CDKi-naïve	2L+: CDKi-naïve	2L/3L: CDKi-pretreated	2L/3L: CDKi-pretreated
ORR[1] (evaluable patients)	85%	77%[2]	32%[2]	63%[2]
CBR (evaluable patients)	96%	100%	79%	96%
Median PFS (months) (95% CI)	31.1 (16.9, NR)	11.9 (3.7, NR)	5.1 (3.4, 7.5)	12.9 (7.4, 16.7)

(1) ORR represents PR, except in Arm A, which had 1 CR. Responses per RECIST 1.1
(2) Includes 2 unconfirmed PR

Abbreviations: CBR = clinical benefit rate; NR = not reached
Source: Layman 2021 SABCS

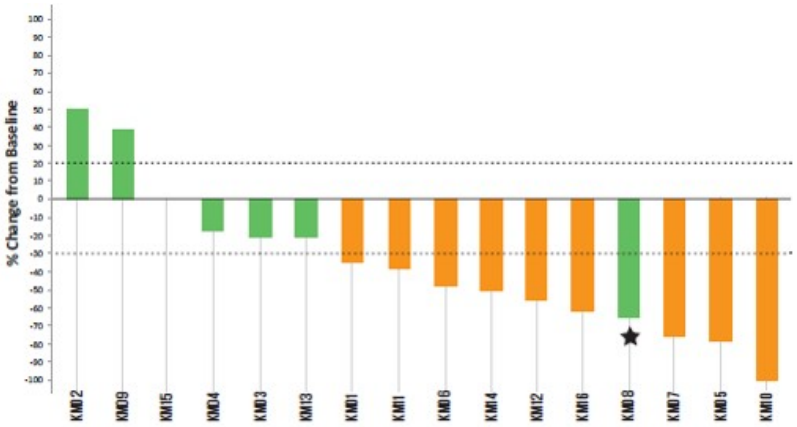
Other Gedatolisib Clinical Trials

Phase 2 Pilot Clinical Trial for HER2+/PIK3CA+ Patients

The Korean Cancer Study Group sponsored a Phase 2 pilot clinical trial to evaluate gedatolisib combined with a trastuzumab biosimilar (Herzuma®), in patients with HER2+/PIK3CA+ metastatic breast cancers whose disease had progressed after treatment with three or more prior HER2 targeted therapy regimens. The clinical trial commenced in December 2019 and interim efficacy data from the first 16 patients enrolled was presented at the San Antonio Breast Cancer Symposium in December 2020. Patients received a trastuzumab biosimilar (8 mg/kg IV for 1st cycle loading dose, and then 6 mg/kg IV every 3 weeks) plus gedatolisib (180 mg, weekly IV). The primary endpoint was objective response, a reduction of at least 30% in tumor volume by RECIST v1.1.

As of a data cutoff date of October 30, 2020, nine of 16 patients achieved a partial response, an ORR of 56%, and four patients had stable disease. Thirteen of 16 patients thus received either a partial response or stable disease, resulting in a clinical benefit rate of 81%. Best responses are shown in the following chart. The dotted lines represent the cutoff for progressive disease (>20% tumor growth) and for partial response (>30% tumor regression).

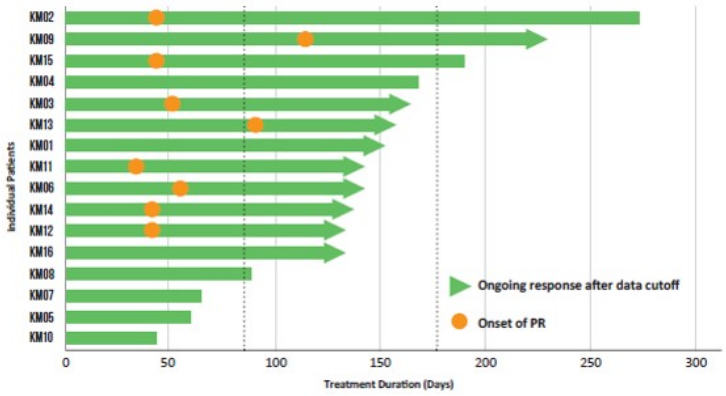
Best Response



* Patient whose target lesion decreased by 63% but a new leptomeningeal seeding occurred.

The duration of treatment for the 16 patients evaluated is shown in the chart below. As of the October 30, 2020 data cutoff, 16 patients (80%) remained on therapy. Four patients discontinued treatment, one due to disease progression, one due to an adverse event of Grade 1 diarrhea, one participant decision, and one patient being unable to undergo the required MRI imaging due to a titanium rod implant from non-treatment related worsening of scoliosis. At the time of data cut-off, the median time on treatment for these 20 patients was 10.1 cycles (approximately 10 months) and all 10 patients who had achieved an objective response remained on therapy assessment. At the time of the analysis, nine patients had a continuing response. The dashed lines show the response at 3 months and 6 months.

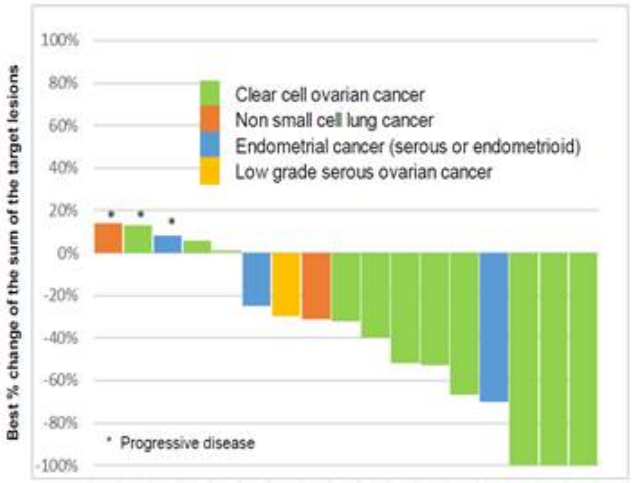
Duration of Treatment



Phase 1 Clinical Trial in Patients with Solid Tumors

A phase 1 study conducted at the Indiana University Simon Cancer Center evaluated the safety, tolerability, pharmacokinetics and preliminary activity of gedatolisib combined with carboplatin and paclitaxel in patients with advanced solid tumors previously who were treated with two or more prior chemotherapies. Seventeen patients were enrolled (10 clear cell ovarian, one low-grade serous ovarian, four endometrial, and two lung cancers). The ORR was 65% in all patients (11/17 patients: eight partial responses and three complete responses) and stable disease was 17% (3/17). Among patients with clear cell ovarian cancer, the ORR was 80%, with three patients achieving a complete response.

Best Response



Planned Gedatolisib Clinical Trials

Planned Phase 3 HR+/HER2- MBC Clinical Trial (VIKTORIA-1)

We are preparing to initiate VIKTORIA-1, a Phase 3, open-label, randomized clinical trial to evaluate the efficacy and safety of gedatolisib in combination with fulvestrant with or without palbociclib in adults with HR+/HER2- advanced breast cancer whose disease has progressed after prior CDK4/6 therapy in combination with an aromatase inhibitor. This multi-center, international trial is expected to enroll 651 total subjects at approximately 175 clinical sites across the U.S., Europe, and Asia. We expect to initiate the VIKTORIA-1 clinical trial in the first half of 2022.

The clinical trial will enable separate evaluation of subjects according to their *PIK3CA* status.

- Subjects who meet eligibility criteria and do not have confirmed *PI3KCA* mutations (WT) will be randomly assigned (1:1:1) to receive a regimen of either gedatolisib, palbociclib, and fulvestrant (Arm A), gedatolisib and fulvestrant (Arm B), or fulvestrant (Arm C). Up to 351 subjects who are PIK3CA WT will be enrolled. The three-arm design will also show the contribution of gedatolisib.

- Subjects who meet eligibility criteria and have confirmed *PI3KCA* mutations (MT) will be randomly assigned (1:1) to receive a regimen of either gedatolisib, palbociclib, and fulvestrant (Arm D) or alpelisib and fulvestrant (Arm E). Up to 300 subjects who are PIK3CA MT will be enrolled.

The clinical trial primary endpoints are progression free survival (PFS), per RECIST 1.1 criteria, as assessed by blinded independent central review (BICR). Two primary endpoints will be evaluated in subjects who are PI3KCA WT, and one primary endpoint will be evaluated in subjects who are PI3KCA MT. In subjects who are PI3KCA WT, the PFS of gedatolisib in combination with palbociclib and fulvestrant (Arm A) will be compared to fulvestrant monotherapy (Arm C), and the PFS in gedatolisib in combination with fulvestrant (Arm B) will be compared to fulvestrant monotherapy (Arm C). In subjects who are PI3KCA MT, the PFS of gedatolisib in combination with palbociclib and fulvestrant (Arm D) will be compared to alpelisib combined with fulvestrant (Arm E).

All subjects will receive treatment according to the assigned study arm until objective progressive disease, unacceptable toxicity, death, or withdrawal of consent, whichever occurs first. Subjects in Arm C will have the option to receive the treatment regimen provided in Arm A or Arm B upon radiographically confirmed disease progression. Subjects will be followed for AEs, safety laboratory testing, tumor assessment by RECIST v1.1, quality of life, and overall survival.

Planned Phase 2 Gedatolisib Clinical Trials

We expect to use the CELsignia PI3K Activity Test to help support development of gedatolisib for breast cancer indications. Our internal studies demonstrate how measurement of PI3K-involved signaling may provide a sensitive and specific method of identifying patients most likely to benefit from PI3K inhibitors. We believe CELsignia tests uniquely enable us to pursue indications simultaneously for unselected patient populations and CELsignia selected patient sub-groups. This approach can greatly reduce the risk of pursing an indication for a large, but unselected patient population, as we plan to do for the initial gedatolisib indication. By combining the capabilities of CELsignia PI3K Activity Test with a potent pan-PI3K/mTOR inhibitor like gedatolisib, we believe we are uniquely suited to maximize the probability of obtaining regulatory approval to market gedatolisib.

Accordingly, we plan to initiate two Phase 2 clinical trials to evaluate gedatolisib in HR+/HER2- breast cancer patients selected with a CELsignia PI3K Pathway Test. One trial is expected to evaluate gedatolisib in combination with fulvestrant in up to 25 patients with metastatic breast cancer. The second trial is expected to evaluate up to 15 patients with early-stage breast cancer with gedatolisib in combination with palbociclib and letrozole. These clinical trials are expected to be initiated at sites which are already participating in a trial that is screening patients with the CELsignia HER2 Pathway Test. Screened patients who provide a tumor biopsy will receive a CELsignia HER2 and PI3K Test. Patients found to have hyperactive HER2 signaling will be eligible to receive treatment with an anti-HER2 therapy and those with hyperactive PI3K signaling will be eligible to receive gedatolisib in combination with other targeted therapies. Patient enrollment is expected to begin for the two trials in late 2022.

Pfizer License Agreement

In April 2021, we entered into a license agreement, or the Gedatolisib License Agreement, with Pfizer pursuant to which we acquired exclusive (including as to Pfizer) worldwide sublicensable rights to research, develop and manufacture, and commercialize gedatolisib for the treatment, diagnosis and prevention of all diseases. Pursuant to the Gedatolisib License Agreement, we are obligated to use commercially reasonable efforts to develop and seek regulatory approval for at least one product in the U.S. and if regulatory approval is obtained, to commercialize such product in the U.S and at least one international major market.

We paid Pfizer a $5.0 million upfront fee upon execution of the Gedatolisib License Agreement and issued to Pfizer $5.0 million of our common stock. We are also required to make milestone payments to Pfizer upon achievement of certain development and commercial milestone events, up to an aggregate of $335.0 million. We will pay Pfizer tiered royalties on sales of gedatolisib at percentages ranging from the low to mid-teens, that may be subject to deductions for expiration of valid claims, amounts due under third-party licenses and generic competition. Unless earlier terminated, the Gedatolisib License Agreement will expire upon the expiration of all royalty obligations. The royalty period will expire on a country-by-country basis upon the later of (a) 12 years following the date of First Commercial Sale of such Product in such country, (b) the expiration of all regulatory or data exclusivity in such country for such Product or (c) the date upon which the manufacture, use, sale, offer for sale or importation of such Product in such country would no longer infringe, but for the license granted herein, a Valid Claim of a Licensed Patent Right. Capitalized terms in this paragraph have the meanings set forth in the Gedatolisib License Agreement.

We have the right to terminate the Gedatolisib License Agreement for convenience upon 90 days' prior written notice. Pfizer may not terminate the agreement for convenience. Either we or Pfizer may terminate the Gedatolisib License Agreement if the other party is in material breach and such breach is not cured within the specified cure period. In addition, either we or Pfizer may terminate the Gedatolisib License Agreement in the event of specified insolvency events involving the other party.

Manufacturing

We rely on third parties to manufacture gedatolisib. We expect to enter into agreements with contract manufacturing organizations, or CMOs, to produce drug substance for gedatolisib. We require all of our CMOs to conduct manufacturing activities in compliance with current good manufacturing practice, or cGMP, requirements. We anticipate that these CMOs will have the capacity to support both clinical supply and commercial-scale production, but we do not have any formal agreements at this time to cover commercial production. We may also elect to enter into agreements with other CMOs to manufacture supplies of drug substance and finished drug product.

Sales and Marketing

If any of our product candidates are approved, we intend to market and commercialize them in the U.S. and select international markets, either alone or in partnership with others. Cancer patients are managed by oncologists, medical geneticists and neurologists, and therefore we believe can be reached with a targeted sales force.

Competition for Gedatolisib

The pharmaceutical industry is characterized by rapid evolution of technologies and intense competition. While we believe that our product candidates, technology, knowledge, experience and scientific resources provide us with competitive advantages, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others. Any product candidates that we successfully develop and commercialize will compete with approved treatment options, including off-label therapies, and new therapies that may become available in the future. Key considerations that would impact our ability to effectively compete with other therapies include the efficacy, safety, method of administration, cost, level of promotional activity and intellectual property protection of our products. Many of the companies against which we may compete have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products.

There are several PI3K and mTOR inhibitors approved by the FDA, including Piqray and Afinitor from Novartis AG, Aliqopa from Bayer Corporation, Copiktra from Verastem, Inc. Zydelig from Gilead Sciences, Inc. and we are aware that other companies are, or may be, developing products for this indication, including AstraZeneca plc, BridgeBio Inc., Eli Lilly and Company, F. Hoffmann-La Roche Ltd, Kazia Therapeutics Limited, Infinity Pharmaceuticals, Inc., Revolution Medicines Inc., and Takeda Pharmaceutical Company Limited. There may be additional companies with programs suitable for addressing these patient populations that could be competitive with our efforts but that have not yet disclosed specific clinical development plans. Smaller or early-stage companies, including oncology-focused therapeutics companies, may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies may also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, enrolling patients in clinical trials and acquiring technologies complementary to, or necessary for, our programs. The availability of reimbursement from government and private payors will also significantly impact the pricing and competitiveness of our products. Our competitors may obtain FDA or other regulatory approvals for their products more rapidly than we may obtain approvals for our product candidates, which could result in our competitors establishing a strong market position before we are able to commercialize our product candidates.

CELsignia Development and CDx Programs

Overview

Our proprietary CELsignia diagnostic platform is the only commercially ready technology we are aware of that uses a patient's living tumor cells to identify the specific abnormal cellular process driving a patient's cancer and the targeted therapy that best treats it. This enables us to identify patients whose tumors may respond to a targeted therapy, even though they lack a previously associated molecular mutation. By identifying cancer patients whose tumors lack an associated genetic mutation but have abnormal cellular activity a matching targeted therapeutic is designed to inhibit, we believe our CELsignia CDx can expand the markets for a number of already approved targeted therapies. Our current CDx identifies breast and ovarian cancer patients whose tumors have cancer drivers potentially responsive to treatment with human epidermal growth factor receptor 2-negative (HER2), mesenchymal-epithelial transition factor (c-MET), or phosphatidylinositol 3-kinases (PI3K) targeted therapeutics.

Our CELsignia platform provides an important advantage over traditional molecular diagnostics. Current molecular diagnostics analyze fragmented cells to obtain a snapshot of the genetic mutations present in a patient's tumor. Using cell fragments prevents molecular diagnostics from analyzing the dynamic cellular activities, known as cell signaling, that regulate cell proliferation or survival. Cancer can develop when critical cell signaling, regulating physiologic activity such as cell proliferation, becomes abnormal or dysregulated. Since genetic mutations are often only weakly correlated to the dysregulated cell signaling activity driving a patient's cancer, a molecular diagnostic is prone to providing an incomplete diagnosis. CELsignia tests overcome this limitation by measuring dynamic cell signaling activity in a cancer patient's living tumor cells. When a CELsignia test detects abnormal signaling activity, a more accurate diagnosis of the patient's cancer driver is obtained.

We are supporting the advancement of new potential indications for four different targeted therapies, controlled by other pharmaceutical companies, that would rely on a CELsignia CDx to select patients. Our first analytically validated and commercially ready test using our CELsignia platform, the CELsignia HER2 Pathway Activity Test for breast cancer, diagnoses two new sub-types of HER2-negative breast cancer that traditional molecular diagnostics cannot detect. Our internal studies show that approximately 15-20% of HER2-negative breast cancer patients have abnormal HER2 signaling activity similar to levels found in HER2-positive breast cancer cells. As a result, these HER2-negative patients have undiagnosed HER2-driven breast cancer and would be likely to respond to the same anti-HER2 targeted therapies only HER2-positive patients receive today. We have four interventional clinical trials underway to evaluate the efficacy of HER2 targeted therapies in breast cancer patients selected with our CELsignia HER2 Pathway Activity Test.

Our second CELsignia test for breast cancer evaluates independent c-Met signaling activity and its involvement with HER family signaling in HER2-negative breast cancer tumor cells. Our internal studies show that approximately 20%-25% of HER2-negative breast cancer patients have abnormal c-Met signaling activity that is co-activated with abnormal HER family signaling. These studies suggest that this sub-group of HER2-negative breast cancer patients may best respond to treatment with a combination of HER family and c-Met inhibitors. We have one interventional clinical trial underway to evaluate the efficacy of HER2 and c-Met targeted therapies, in previously treated metastatic HER2-negative breast cancer patients selected with our CELsignia Multi-Pathway Activity Test, or CELsignia MP Test.

Our third CELsignia test for breast cancer evaluates PI3K signaling in HER2-negative breast cancer tumor cells. Our internal studies demonstrate how measurement of PI3K-involved signaling may provide a more sensitive and specific method of identifying patients most likely to benefit from PI3K inhibitors than current genetic tests that measure PI3K mutations. We intend to combine these three tests to expand the CELsignia MP Test. With this next generation CELsignia test, we plan to provide an analysis of EGFR/HER1, HER2, HER3, c-MET, and PI3K-node involved signaling activity for each patient tumor specimen received.

In addition, we completed development of our first CELsignia test for ovarian cancer in 2020. This test identifies a new sub-group of ovarian cancer patients with tumors that have abnormal c-Met and HER2 signaling activity. These findings suggest that a significant sub-group of ovarian cancer patients may respond to treatment with a combination of ErbB and c-Met inhibitors. Nearly 14,000 women a year die from ovarian cancer, a disease that has less than a 50% five-year survival rate and a limited range of targeted therapy options. There is thus a significant unmet need for additional therapeutic options for ovarian cancer patients. As a companion diagnostic, our CELsignia test for ovarian cancer will be intended to help pharmaceutical companies obtain new drug indications and expand treatment options for this challenging tumor type.

Our overall commercialization strategy is to develop diagnostics that expand the patient population eligible for targeted therapies. In furtherance of this strategy, we have been and will continue to seek collaborations with pharmaceutical companies to field clinical trials to advance the clinical development of their targeted therapies with the eventual goal of obtaining FDA approval of a new drug indication.

CELsignia Clinical Trials

We are currently collaborating on five Phase II clinical trials to evaluate the efficacy of our collaboration partners' targeted therapies in patients selected with one of our CELsignia tests. The goal of these trials is to support the development of five potential new drug indications to treat patient groups found responsive by our CELsignia test to their approved targeted therapies. These clinical trials include:

- FACT-1 Clinical Trial to Evaluate Efficacy of Genentech's HER2 Targeted Therapies. We are collaborating with NSABP Foundation, Inc. ("NSABP") and Genentech, Inc. ("Genentech") to evaluate the efficacy and safety of Genentech's drugs, Herceptin (trastuzumab) and Perjeta (pertuzumab), and chemotherapy in breast cancer patients selected with our CELsignia test. Based on NSABP's updated estimates of patient enrollment rates to reflect the impact of COVID-19, including the recent variants, interim results are expected to be available in the first half of 2023 and final results approximately nine months later. The goal is to demonstrate that patients who have an abnormal HER2 signaling pathway, as identified by our CELsignia test, respond to treatment with a matching targeted therapy.

- FACT-2 Clinical Trial to Evaluate Efficacy of Puma's HER2 Targeted Therapy. We are collaborating with Puma Biotechnology, Inc. ("Puma") and West Cancer Center to conduct a Phase II single-arm interventional trial to evaluate the efficacy and safety of Puma's drug, Nerlynx (neratinib), and chemotherapy in breast cancer patients selected with our CELsignia test. Based on West Cancer Center's updated estimates of patient enrollment rates to reflect the impact of COVID-19, including the recent variants, interim results are expected to be available in the first half of 2023 and final results approximately nine months later. The goal of the trial is to demonstrate that triple-negative breast cancer patients who have a hyperactive HER2 signaling tumor, as identified by the CELsignia test, respond to treatment with Nerlynx, a matching HER2 therapy.

- FACT-4 Clinical Trial to Evaluate Efficacy of Puma's HER2 Targeted Therapy. In December 2020, we announced a clinical trial collaboration with Massachusetts General Hospital and Puma, a biopharmaceutical company, to conduct a Phase II clinical trial. This open-label Phase II trial will evaluate the efficacy and safety of Puma's drug, Nerlynx (neratinib), and Faslodex (fulvestrant), an AstraZeneca drug, in previously treated metastatic EHR-positive (HR+), HER2-negative breast cancer patients selected with our CELsignia HER2 Pathway Activity Test. Based on Massachusetts General Hospital's estimates of patient enrollment rates, we expect to obtain interim results 12-15 months after the protocol is activated and final results 12 to 15 months later. The goal of the trial is to demonstrate that previously treated HR+, HER2-negative metastatic breast cancer patients who have hyperactive HER2 signaling tumors, as identified by the CELsignia test, respond to treatment with Nerlynx in combination with Faslodex, a hormonal therapy that targets the estrogen receptor.

- FACT-5 Clinical Trial to Evaluate Efficacy of Puma's pan-HER Inhibitor and chemotherapy. In October 2021, we announced a clinical trial collaboration with University of Rochester Wilmot Cancer Center and Puma, to conduct a Phase II clinical trial. This open-label Phase II trial will evaluate the efficacy and safety of Puma's drug, Nerlynx (neratinib), and the chemotherapy capecitabine, in previously treated metastatic HER2-negative breast cancer patients with brain metastases selected with our CELsignia HER2 Pathway Activity Test. Based on University of Rochester Wilmot Cancer Center estimates of patient enrollment rates, we expect to obtain interim results 12-15 months after the protocol is activated and the final results 12 to 15 months later. We expect enrollment to begin in the second half of 2022. The goal of the trial is to demonstrate that previously treated HER2-negative metastatic breast cancer patients with brain metastases who have hyperactive HER2 signaling tumors, as identified by the CELsignia test, respond to treatment with Nerlynx in combination with capecitabine.

- FACT-6 Clinical Trial to Evaluate Efficacy of Novartis's c-Met Inhibitor and Puma's pan-HER Inhibitor. In March 2021, we announced a clinical trial collaboration with MD Anderson Cancer Center, Novartis AG, and Puma, to conduct a Phase I/II clinical trial. This open-label Phase I/II trial will evaluate the efficacy and safety of Novartis' c-Met inhibitor, Tabrecta (capmatinib), and Puma's pan-HER inhibitor, Nerlynx (neratinib), in previously treated metastatic HER2-negative breast cancer patients selected with our CELsignia MP Test. Based on MD Anderson's estimates of patient enrollment rates, we expect to obtain interim results 12-15 months after the protocol is activated and final results 12-15 months later. The goal of the trial is to demonstrate that previously treated HER2-negative metastatic breast cancer patients who have hyperactive HER2 and c-Met signaling tumors, as identified by the CELsignia test, respond to treatment with Tabrecta in combination with Nerlynx.

Companion Diagnostics Industry

According to the Centers for Disease Control and Prevention, cancer was the second-leading cause of death in the United States in 2020, responsible for nearly one of every four deaths. There are many types of cancer treatment options, including surgery, radiation therapy, chemotherapy, immunotherapy, hormone therapy, stem cell transplant, and targeted therapy. Targeted therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecular targets involved in the progression of cancer. Targeted therapies differ from standard chemotherapy drugs in that they are often cytostatic (block tumor cell proliferation) rather than cytotoxic (kill tumor cells). According to the National Cancer Institute, there are currently more than 90 approved targeted oncology therapies, some of which cost more than $100,000 per treatment course.

Diagnostic tests to detect single biomarkers are now widely used by pathologists to determine the molecular sub-type of a cancer. When a molecular biomarker test is used to support the choice of therapy to prescribe, it is often referred to as a "companion diagnostic." Increasing numbers of targeted therapeutics are prescribed based on the results from a companion diagnostic test to detect the presence of a molecular biomarker. Only patients testing positive for the biomarker are eligible to receive the associated therapy.

Companion diagnostics are becoming increasingly important to the pharmaceutical industry. The use of companion diagnostics to better match patients to effective treatments positively impacts clinical outcomes and lowers expenditures on drugs that do not benefit patients. Stratifying the eligible patient population to include only likely responders is particularly important when the percentage of likely responders is only a fraction of the total cancer population. In these circumstances, narrowing the eligible patient population is often necessary to meet the clinical endpoint targets required to receive FDA drug approval.

CELsignia Testing Opportunities

We expect to generate recurring companion diagnostic testing revenues once a CELsignia companion diagnostic-linked drug therapy is approved for patient use. On average, we believe that the lifetime value of providing the companion diagnostic test will significantly exceed the revenue generated from the companion diagnostic development program. We expect to offer each CELsignia test to patients at prices ranging from $4,000–$7,000, depending on the number of pathways evaluated. No tests directly comparable to the CELsignia tests are available today to offer reference points for pricing purposes. Pricing for several proprietary complex genomic tests, however, fall within this range and we believe this provides guidance on the amount insurance companies are willing to pay for highly informative tests that guide patient care.

Our CELsignia Platform

We have made significant investments in research and development of our CELsignia platform. To measure dynamic cellular activity, we internally developed two distinct but complementary technologies, which now comprise our CELsignia platform:

- our proprietary cell microenvironment; and
- our method to quantify dynamic patient cell signaling dysfunction.

We utilize our CELsignia platform to create CELsignia tests that measure specific signaling pathway activity in various tumor types.

Cell microenvironment. Previous research has shown that cancer cells extracted from a patient's tumor share the molecular features of the primary cancers from which they were derived and could provide an *ex vivo* (outside the patient) model of a patient's tumor. The technology around tumor cell extraction from individual patients and culturing techniques, however, has largely remained undeveloped. For instance, we are not aware of any competing diagnostic tests that use live patient tumor cells to measure dynamic cell signaling activity. Studies on the topic have historically highlighted the challenges of deriving a viable patient tumor cell sample from an individual patient tumor specimen.

We have developed a cell microenvironment to extract and expand viable tumor cells from fresh human tumor tissue, which meets the three critical clinical parameters a patient-derived tumor cell sample would need to satisfy in order to meet the regulatory and clinical requirements for a diagnostic test measuring signaling activity:

- **The patient cell sample tested must reflect the starting tumor's composition.** If samples do not reflect the original tumor's composition, test results derived from that sample may not be representative of the patient's tumor.
- **The sample must be available for testing in less than 21 days.** Clinicians generally require test results in cases of complex diseases such as cancer within two to three weeks so they can begin treatment of their patient as soon as the initial symptoms are evaluated or a preliminary diagnosis is made.

- **At least 90% of the tumor specimens obtained from a patient must yield testable samples.** Clinicians will only order tests that require a patient specimen when they are highly likely to receive a test result.

Dynamic patient cell signaling quantification. The second component of our CELsignia platform involves methods to quantify specific dynamic signal transduction events in patient derived tumor cells. The complexity of signal transduction processes is immense, and the permutations of the pathway variables are practically unquantifiable. Current analytical methods to assess these variables use cell fragments. Point-in-time measurements are limited to assessment of the compositional status (e.g., mutation), concentration level (e.g., protein amount), or activation status (e.g., phosphorylation) of a finite number of signaling pathway components. A key insight underlying our technology was our observation that, no matter how sophisticated or detailed, a point-in-time molecular profile would only provide a snapshot. These methods could not provide a complete, dynamic assessment of the signaling activity driving a patient's cancer. These point-in-time molecular analyses would, in many cases, only provide a weak correlation to the presence of the signaling pathway dysfunction driving a patient's cancer. Instead, we concluded that a complete diagnosis of cancer and an assessment of a patient's response to treating their disease requires measurement of the underlying activity of signaling pathways in live patient tumor cells.

To measure live real-time dynamic cell signaling activity, we utilize an impedance biosensor instrument. An impedance biosensor is an analytical platform that converts changes in cellular activity to a measurable electrical signal. When cells are stimulated and change their function, the accompanying changes alter the electrical signal that is measured. The output value is quantified over time and used to determine a Signaling Function Score. To determine the activity of a specific signaling pathway, an activating agent specific to a pathway receptor is used to turn on the pathway and a corresponding inhibitory agent specific to the pathway receptor is used to turn signaling off. When signaling pathways are stimulated in this manner, a change in the electrical signal occurs and Signaling Function Score recorded. By relying on the principle of detecting signaling pathway activity, we believe we can develop tests for a range of disease types and targeted therapies that affect various cellular pathways.

CELsignia Multi-Pathway Activity Test

Our CELsignia MP Test is a qualitative LDT that measures HER2, c-Met, and PI3K signaling activity in breast and ovarian tumor cells obtained from patients previously diagnosed with cancer to determine whether or not the patients have one of the following cancer sub-types:

1. Abnormal HER2 signaling driven cancer

2. Abnormal c-Met and HER2 signaling driven cancer

3. Abnormal PI3K-involved signaling driven cancer

CELsignia's Commercialization Strategy

Our commercial activities will target three complementary groups at various phases of the development of our CELsignia tests.

- **Pharmaceutical companies.** For each CELsignia test we develop to diagnose a new cancer sub-type, we intend to identify the matching targeted therapies, either currently approved or in the investigational phase, and the manufacturer of those therapies. We intend to initiate discussions and seek to reach development agreements with each of these pharmaceutical companies when we have verified the prevalence of the cancer sub-type and completed successful animal studies.

- **Medical and surgical oncologists.** We plan to initially target key opinion leaders (KOLs) in each cancer type once we have completed the analytical validation of a CELsignia test. This will allow us to build awareness and credibility for the CELsignia test as we are generating clinical validation data. When a new drug indication is received that requires use of a CELsignia companion diagnostic to identify eligible patients, we will coordinate the pharmaceutical company's go-to-market activities with our own. This coordination will allow us to significantly leverage the pharmaceutical company's sales, marketing, and reimbursement activities, unlike traditional molecular diagnostic companies.

- **Payors.** When a new drug indication is received that requires use of a CELsignia companion diagnostic to identify eligible patients, we expect to coordinate the pharmaceutical company's reimbursement activities with our own.

Our CELsignia tests are laboratory developed tests, or LDTs, and subject to regulation under the Clinical Laboratory Improvement Amendments, or CLIA. We completed the analytical validation of our first CELsignia test and received CLIA certification in 2016. Our current focus is to field clinical trials with leading cancer centers in collaboration with pharmaceutical companies to demonstrate that cancer patients diagnosed with an abnormal signaling pathway by a CELsignia test respond efficaciously to treatment with a matching targeted therapy. Once favorable efficacy data is available, we expect to generate revenues from CELsignia tests performed in conjunction with the clinical trials a pharmaceutical company will field during the registrational phase of our partners' drug approval process. We also expect that the agreements we enter into with the pharmaceutical companies partnering with us on these registrational trials will include milestone payments at initiation and completion of trials and perhaps at various other negotiated points during the trials. We expect to generate revenue from the sale of CELsignia tests ordered by physicians upon the approval of our pharmaceutical company's matching drug, as a companion diagnostic. A key requirement for success of these partnerships will be clinical trial results that demonstrate the advantages of using a CELsignia test as a companion diagnostic.

We intend to position our unique and highly differentiated tests as practice changing advancements in patient care. To inform key stakeholders of the value of our solution in order to drive adoption and reimbursement, we expect to employ the following diverse commercialization strategies over time:

- leverage our pharmaceutical partnership and their go-to-market initiatives for the drug with which our companion diagnostic is partnered;
- collaborate with oncology thought leaders, KOLs, and leading institutions on clinical research, publications, and product development;
- build an experienced, oncology-focused sales force in the United States and international distribution channels that are supported by dedicated company personnel;
- integrate into the everyday practice of clinicians through our medical affairs and client services efforts;
- publish important medical and scientific data in peer-reviewed journals and present at major industry conferences, conduct clinical trials; and
- work with patient advocacy groups, leading cancer philanthropic organizations, and medical societies to drive awareness of CELsignia tests and the importance of incorporating functional cellular analysis into cancer treatment.

Through these efforts, we will seek to promote our CELsignia test's unique capabilities throughout the oncology community—from patients, to the physicians treating them, to the third-party payors for these treatments and to biopharmaceutical companies developing new treatments—all with the goal of facilitating better-informed treatment decisions for the greatest number of patients.

A CELsignia test would be launched upon the approval of a pharmaceutical company's matching drug as a companion diagnostic. We would expect physicians, typically a medical or surgical oncologist, to order our tests in conjunction with the roll-out of the pharmaceutical company's matching drug. The physician will prescribe a CELsignia test and coordinate provision of a patient specimen from a biopsy or surgical procedure. The fresh tissue would then be shipped overnight directly to our laboratory where we would use our proprietary methods to extract diseased cell samples from the patient's tissue and perform the CELsignia tests ordered. Test results would typically be available in 10 to 14 days after receipt of the patient specimen. For each patient sample analyzed, a Signaling Function Score would be calculated quantitatively and converted into a final qualitative result: abnormal or normal. For patients found to have an abnormal signaling pathway, clinicians would use the results of the CELsignia test as a guide to select a targeted drug that inhibits the abnormal signaling activity identified.

Pricing and Reimbursement

The principal groups that we expect to pay us in the future for our CELsignia tests include:

- commercial third-party payors;
- government payors, including Medicare and state Medicaid plans;
- biopharmaceutical customers;
- hospitals, cancer centers, and other institutions; and
- patients.

Adequate reimbursement will be an important factor in achieving broad clinical adoption of our CELsignia tests. At the same time, we believe broad clinical adoption will help drive favorable reimbursement decisions. To achieve broad reimbursement coverage with commercial third-party payors and government payors, including Medicare and Medicaid, we plan to demonstrate the economic and clinical value of our CELsignia tests to payors by employing a multi-pronged strategy:

- **Set a high bar for analytical validation.** We expect to present data on the characterization of new cancer sub-types by CELsignia tests at conferences and will seek to publish the results in peer-reviewed journals.

- **Meet the evidence standards necessary to be consistent with leading clinical guidelines.** We believe inclusion in leading clinical practice guidelines plays a critical role in payers' coverage decisions. We plan to conduct clinical validation and clinical utility studies that are consistent with the requirements of the widely recognized National Comprehensive Cancer Network clinical practice guidelines.

- **Execute an internal managed care policy and claims adjudication function as part of our core business operations.** We plan to make obtaining adequate and widespread reimbursement a critical component of our business operations. We expect to hire a team of in-house claims processing and reimbursement specialists who will work with patients and payors to navigate the claims process and obtain maximum reimbursement.

- **Cultivate a network of KOLs.** KOLs are able to influence clinical practice by publishing research and determining whether new tests should be integrated into practice guidelines. We expect to collaborate with KOLs early in the development process to ensure our clinical studies are designed and executed in a way that clearly demonstrates the benefits of our tests to physicians and payers.

- **Compile a growing library of peer-reviewed studies that demonstrate the test is effective.** We will seek to publish peer-reviewed articles and review papers to help support our efforts to obtain widespread adoption and reimbursement of our CELsignia tests. In each disease area we pursue, we intend to conduct studies in order to develop similar supporting literature.

- **Reduce expenditures.** We intend to build economic models to measure the financial benefits of using our CELsignia test in guiding patient treatment and minimizing the use of drugs that will not likely have a positive impact. We plan to use the data we gather through the use of these models as we meet with commercial third-party payors and government payors.

- **Exploit efforts by commercial third-party and government payors to contain healthcare costs.** A major cost reduction opportunity is to reduce expenditures for drug courses that provide no patient benefit. Our technology will enable physicians to prescribe therapies that have significantly higher response rates than has been the case with targeted therapies to date. Since this will lower the drug cost per responsive patient, we believe widespread use of our CELsignia tests is consistent with payors goals of delivering health care more cost effectively.

CELsignia's Competition

At present, we are not aware of any other companies that offer diagnostic tests that use a patient's live tumor cells to identify the signaling pathway driving a patient's cancer. There are several companies focused on developing genomic or proteomic analyses of a patient's diseased cells. Initial efforts identified protein targets or genetic mutations, oftentimes referred to as "biomarkers," that are associated with a disease process to enable development of drugs more closely tailored to specific patient populations.

As tools for human genome analysis have become less expensive, a number of companies have also recently launched more complex genomic test panels and gene expression signatures tests. These tests rely on a static measurement of molecular properties and mathematical analysis to identify statistically significant correlations between the selected molecular properties and a clinical condition or outcome of populations of patients with the "same" disease.

These genetic tests often have limited predictive success because they only identify some, but not all, of, the molecular and cellular conditions required for a drug therapy to function in a patient. They may identify the presence of the genes associated with a disease, but they cannot determine how the gene products function in the context of a particular individual.

Providers of genomic or proteomic tests include diagnostic kit manufacturers, hospitals, and independent laboratories. We do not plan to develop tests where a molecular biomarker can identify drug responsive patients, so our current tests will not compete directly against the tests provided by these other companies.

Diagnostics competitors that have molecular method-based tests include, but are not limited to, Foundation Medicine, Caris Life Sciences, NeoGenomics, LabCorp, Quest, Nanostring, Paradigm, Biocept, Exosome Diagnostics, Guardant Health, Roche Diagnostics, Qiagen, Myriad, and Genomic Health.

Principal Suppliers for CELsignia

We purchase commercially available reagents and instruments from a variety of suppliers. Our principal reagent suppliers include Bio-Techne Corporation, Selleck Chemicals, Sigma-Aldrich, and VWR International. Our principal instrument suppliers include Agilent Technologies, Integra Biosciences, Invitrogen, and Thermo Fisher Scientific. These items are purchased on a purchase order basis pursuant to the applicable supplier's standard terms and conditions. The items purchased from these suppliers are standard products sold widely to the biotechnology industry. All items purchased are typically available within several days after an order is placed.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, manufacturing and process discoveries and other know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing our proprietary rights. We plan to protect our proprietary positions using a variety of methods, which include protecting current U.S. and foreign patents related to proprietary technology, inventions and improvements and prosecuting additional U.S. and foreign patents that we determine are important to the development and implementation of our business. For example, we, our licensors, or our collaborators currently have, or are pursuing, patents covering the composition of matter for our drug product candidates and we plan to generally pursue patent protection covering methods-of-use for one or more clinical programs. We also rely on trade secrets, trademarks, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position.

Gedatolisib Patents

We entered into the Gedatolisib License Agreement with Pfizer in April 2021, pursuant to which we acquired exclusive worldwide rights under Pfizer patents and know-how to develop, manufacture and commercialize gedatolisib. We have exclusive licenses under the Gedatolisib License Agreement to patent rights in the U.S. and numerous foreign jurisdictions relating to gedatolisib. The patent rights in-licensed under the Gedatolisib License Agreement include 11 granted patents in the U.S. and more than 290 patents granted in foreign jurisdictions including Australia, Canada, China, France, Germany, Spain, United Kingdom and Japan. A U.S. patent covering gedatolisib as a composition of matter has a statutory expiration date in December 2029 and a U.S. composition of matter patent that covers the lactic acid form of gedatolisib that is currently in clinical development expires in December 2035, in each case, not including patent term adjustment or any patent term extension, and relevant foreign counterparts.

CELsignia Patents

With respect to CELsignia, we have three issued U.S. patents, five issued international patents, five pending U.S. patent applications, 23 pending non-U.S. patent applications, and one pending PCT patent application, as well as numerous corresponding non-U.S. patent applications covering our diagnostic approach using cell signaling analysis in living patient cells to guide treatment of patients with targeted therapies. The earliest expiration date of patents is 2033. In addition, we have developed significant proprietary know-how and trade secrets for the various cell sample preparation and cellular analysis methods we have developed.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and partners. These agreements generally provide that all confidential information developed or made known during the course of an individual or entity's relationship with us must be kept confidential during and after the relationship. These agreements also generally provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties.

Government Regulation

Approval of Gedatolisib and Other Drug Products in the United States

Government authorities in the U.S. at the federal, state and local level and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products, such as gedatolisib. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority and submitted for review and approved by the regulatory authority.

Overview of FDA Approval Process

In the U.S., pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending New Drug Applications, or NDAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Pharmaceutical product development for a new product or certain changes to an approved product in the U.S. typically involves preclinical laboratory and animal tests, the submission to the FDA of an investigational new drug applicable, or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

The clinical stage of development involves the administration of the investigational product to healthy volunteers or disease-affected patients under the supervision of qualified investigators, generally physicians not employed by, or under control of, the trial sponsor, in accordance with Good Clinical Practices, or GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of an investigational new drug applicable, or IND. Furthermore, each clinical trial must be reviewed and approved by an Institutional Review Board, or IRB, for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Information about most clinical trials must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in some cases for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs. Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.

- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.

- Phase 3 clinical trials generally involve a larger number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

A registrational trial is a clinical trial that adequately meets regulatory agency requirements for the evaluation of a drug candidate’s efficacy and safety such that it can be used to justify the approval of the drug. Generally, registrational trials are Phase 3 trials but may be Phase 2 trials if the trial design provides a reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow up. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of a Biologics License Application, or BLA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. The FDA or the sponsor may suspend or terminate a clinical trial at any time, or the FDA may impose other sanctions on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the requirements of the IRB or if the drug has been associated with unexpected serious harm to patients. There are also requirements related to registration and reporting of certain clinical trials and completed clinical trial results to public registries.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product’s pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, currently $2,875,842 for Fiscal Year 2021, and the manufacturer and/or sponsor under an approved NDA are also subject to annual program fees for eligible products, which are currently $336,432 for Fiscal Year 2021.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of new drug applications. Most such applications for standard review drug products are reviewed within ten to twelve months; most applications for priority review drugs are reviewed in six to eight months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with cGMP is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

U.S. Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA cannot receive any Abbreviated New Drug Application, or ANDA, seeking approval of a generic version of that drug. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which FDA cannot approve an ANDA for a generic drug that includes the change. An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension for one patent. The allowable patent term extension is calculated as half of the drug's testing phase—the time between IND and NDA submission—and all of the review phase—the time between NDA submission and approval up to a maximum of five years. The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years from approval.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the U.S. Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Fast Track Designation and Accelerated Approval

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment, and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for Fast Track Designation within 60 days of receipt of the sponsor's request.

Under the Fast Track program and the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

In addition to other benefits such as the ability to use surrogate endpoints and engage in more frequent interactions with the FDA, the FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the Fast Track Designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Therapy Designation

Breakthrough Therapy Designation by the FDA provides more extensive development consultation opportunities with FDA senior staff, allows for the rolling review of the drug's application for approval and indicates that the product could be eligible for priority review if supported by clinical data at the time of application submission for drugs that are intended to treat a serious or life-threatening disease or condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Under the breakthrough therapy program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a breakthrough therapy concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for Breakthrough Therapy Designation within 60 days of receipt of the sponsor's request.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Approval of Gedatolisib and Other Drug Products in the European Union

Overview

In the EU, our product candidates also may be subject to extensive regulatory requirements. As in the U.S., medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the U.S., the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls.

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on GCP, and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific trial site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an IMPD, or the Common Technical Document, with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents. All suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the competent national authority and the Ethics Committee of the Member State where they occurred.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 was adopted. Currently, the regulation is anticipated not to come into effect before December 2021. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

To obtain a marketing authorization of a drug in the EU, we may submit Marketing Authorization Applications, or MAA, either under the so-called centralized or national authorization procedures.

Centralized Procedure

The centralized procedure provides for the grant of a single marketing authorization following a favorable opinion by the European Medicines Agency, or EMA, that is valid in all EU Member States, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, advanced therapy medicines (such as gene-therapy, somatic cell-therapy or tissue-engineered medicines) and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions and viral diseases. The centralized procedure is optional for products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee of Medicinal Products for Human Use, or the CHMP. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop-clocks.

National Authorization Procedures

There are also two other possible routes to authorize medicinal products in several EU countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EU country of medicinal products that have not yet been authorized in any EU country and that do not fall within the mandatory scope of the centralized procedure.

- Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one EU Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EU countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

Under the above described procedures, before granting an MAA, the EMA or the competent authorities of the Member States of the European Economic Area, or EEA, make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

EU Regulatory Exclusivity

In the EU, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The 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 held to bring a significant clinical benefit in comparison with existing therapies.

Drug Approval-Related Regulations – Rest of the World

For other countries outside of the EU and the U.S., such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from jurisdiction to jurisdiction. Additionally, the clinical trials must be conducted in accordance with cGCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Regulations of CELsignia Tests

CLIA and CMS for Diagnostic

The Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, regulates all clinical laboratory testing (except research) performed on humans in the United States through CLIA. All clinical laboratories that perform clinical lab services on human specimens for the purpose of providing information on the diagnosis, prevention or treatment of disease must receive CLIA certification. This covers approximately 175,000 laboratories as of 2017. Laboratories must obtain CLIA certification and demonstrate compliance with CLIA requirements as confirmed by an inspection by CMS. We received our CLIA certification in 2016. We also had our laboratory certified by the College of American Pathologies, or CAP, in 2016, an organization recognized by CMS as a third-party reviewer of clinical laboratories. Several states, including, among others, New York and California, require licensure of out-of-state labs that receive specimens from the state and compliance with the state's individual laboratory regulations.

If our laboratory is out of compliance with CLIA requirements, we may be subject to sanctions such as suspension, limitation or revocation of our CLIA certificate, as well as directed plan of correction, state on-site monitoring, civil money penalties, civil injunctive suit or criminal penalties. We must maintain CLIA compliance and certification to be eligible to bill for services provided to Medicare and Medicaid beneficiaries. If we were to be found out of compliance with CLIA program requirements and subjected to sanction, our business could be harmed. Failure to comply with state licensure laws, if applicable, could subject us to additional sanctions imposed by state licensing authorities.

FDA for Diagnostics

FDA approval or clearance is not currently required for CELsignia tests offered as a stand-alone LDT test. If we are partnered with a drug company to launch a CELsignia test as a companion diagnostic for a new drug indication, we would be required to obtain premarket approval, or PMA, in conjunction with the pharmaceutical company seeking a new drug approval for the matching therapy. Historically, the FDA has exercised enforcement discretion with respect to tests performed solely in a central laboratory, like the CELsignia tests or LDTs. The FDA has not required laboratories that furnish only LDTs to comply with the agency's requirements for medical devices (e.g., establishment registration, device listing, quality systems regulations, premarket clearance or premarket approval, and post-market controls).

Although the FDA proposed regulations that would apply to LDTs, the FDA decided that, at present, those regulations are not moving forward towards approval and implementation. In mid-2014, the FDA published a draft Guidance Document describing a proposed approach for a regulatory framework for LDTs that would have resulted in most of the high-value LDT tests marketed today eventually being required to obtain 510(k) clearances or PMAs. If implemented, this regulatory framework would require most hospital clinical labs to abandon a number of tests they perform or to pursue regulatory clearances or approvals to perform them. These proposals met significant resistance from Congress, the hospital industry, and independent clinical laboratories. The FDA indicated in late 2016 that it does not intend to finalize the draft Guidance Document at this time. However, the FDA continues to discuss potential regulatory approaches to LDTs.

Pricing and Reimbursement of our Product Candidates

Significant uncertainty exists as to the coverage and reimbursement status of any products we sell or may sell. Sales of any of our products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as Medicare and Medicaid, commercial health insurers, managed care organizations or pharmaceutical companies. The process for determining whether a third-party payor will provide coverage for a test sometimes is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product. Third-party payors may limit coverage to specific testing products on an approved list, which might not include all of the tests available for a particular indication.

In order to obtain coverage and reimbursement for any product, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the test. Whether or not we conduct such studies, our products may not be considered medically necessary or cost-effective. A third-party payor's decision to provide coverage for a test does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of tests and drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of testing products, drug products and medical services and questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available products or treatments, they may not cover our products or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls and restrictions on reimbursement. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for our testing products or drugs that require use of our testing products and could adversely affect our net revenue and results.

Pricing and reimbursement schemes vary widely from country to country. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular test to currently available tests. The downward pressure on healthcare costs in general, particularly prescription drugs and testing products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for testing products may not allow favorable reimbursement and pricing arrangements for any of our products.

Coverage policies, third-party reimbursement rates and pricing regulation may change at any time.

Other Healthcare Laws

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the U.S. in addition to the FDA, including CMS, the HHS Office of Inspector General and HHS Office for Civil Rights, other divisions of the HHS and the Department of Justice.

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our current and future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our drug and diagnostic products. In the U.S., these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

The U.S. federal Anti-Kickback Statute, or AKS, prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. The AKS has been interpreted to apply to arrangements between pharmaceutical and medical device manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other hand. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the AKS. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Moreover, a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. On November 20, 2020, the Office of Inspector General, or OIG finalized further modifications to the AKS. Under the final rule, OIG added safe harbor protections under the AKS for certain coordinated care and value-based arrangements among clinicians, providers, and others. The final rule (with some exceptions) became effective January 19, 2021. We continue to evaluate what effect, if any, this rule will have on our business.

In addition, under a federal law directed at “self-referral,” commonly known as the “Stark Law,” there are prohibitions, with certain exceptions, on referrals for certain designated health services, including laboratory services, that are covered by the Medicare and Medicaid programs by physicians who personally, or through a family member, have an investment or ownership interest in, or a compensation arrangement with, an entity performing the tests. The prohibition also extends to payment for any testing referred in violation of the Stark Law. A person who engages in a scheme to circumvent the Stark Law’s referral prohibition may be fined up to $100,000 for each such arrangement or scheme. In addition, any person who presents or causes to be presented a claim to the Medicare or Medicaid programs in violation of the Stark Law is subject to civil monetary penalties of up to $15,000 per bill submission, an assessment of up to three times the amount claimed and possible exclusion from participation in federal governmental payor programs. Bills submitted in violation of the Stark Law may not be paid by Medicare or Medicaid, and any person collecting any amounts with respect to any such prohibited bill is obligated to refund such amounts. Many states have comparable laws that are not limited to Medicare and Medicaid referrals.

Furthermore, we could be held liable under the federal False Claims Act, which imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things, knowingly presenting, or causing to be presented to federal programs (including Medicare and Medicaid) claims for items or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. This could apply even if we are not submitting claims directly to payors as would be the case with drug products. The government may deem manufacturers of such products to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Several biopharmaceutical, medical device and other healthcare companies have been prosecuted under federal false claims and civil monetary penalty laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved (e.g., or off-label), and thus non-covered, uses. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Our future marketing and activities relating to the reporting of wholesaler or estimated retail prices for our products, if approved, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our product candidates, are subject to scrutiny under these laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the AKS, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The Affordable Care Act, or the ACA, imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties. Covered manufacturers must submit reports by the 90th day of each subsequent calendar year and the reported information is publicly made available on a searchable website.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the Final HIPAA Omnibus Rule published on January 25, 2013, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity, although it is unclear that we would be considered a "business associate" in the normal course of our business. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern 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 requirements, thus complicating compliance efforts. See "European Data Collection" below for a discussion of data privacy and security enactments of the EU.

For example, California's Consumer Privacy Act, or CCPA, went into effect in January 2020, and the California Attorney General has since promulgated final regulations. The law provides broad rights to California consumers with respect to the collection and use of their personal information and imposes data protection obligations on certain businesses. While the CCPA does not apply to protected health information that is subject to HIPAA or personal information collected, used or disclosed in research, as defined by federal law, the CCPA may still affect our business activities. Moreover, on November 3, 2020, California voters passed the California Privacy Rights Act, or CPRA, under a ballot initiative. The CPRA amends the existing CCPA to include new consumer rights and additional data protection obligations. The new data protection requirements under the CPRA apply to information collected on or after January 1, 2022. With the promulgation of final regulations, the California State Attorney General has commenced enforcement actions against CCPA violators. The uncertainty surrounding the implementation of CCPA and the amendments under the CPRA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. The California law further expands the need for privacy and process enhancements and commitment of resources in support of compliance. Moreover, more than ten states have proposed bills in the last year with provisions similar to the CCPA and CPRA. It is likely that other states will pass laws similar to the CCPA and the CPRA in the near future and a federal data protection law may also be on the horizon.

Similar state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services. Such laws are generally broad and are enforced by various state agencies and private actions. Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance, and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing.

In order to sell products, we must also comply with state laws, including those that require the registration of manufacturers and wholesale distributors of drug and biological products. These include, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

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

European Data Collection

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

Current and Future Legislation

In the U.S. and other jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or any collaborators, may receive.

The ACA, for example, revised the methodology by which rebates owed by manufacturers for covered outpatient drugs are calculated under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of covered drugs dispensed to individuals enrolled in Medicaid managed care organizations and subjected manufacturers to new annual fees for certain branded prescription drugs. As the price of our test may be included in the reimbursement rates for certain drugs, this could significantly impact our pricing. Even if favorable coverage and reimbursement status is attained for one or more products, less favorable coverage policies and reimbursement rates may be implemented in the future.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, various portions of the ACA are currently undergoing legal and constitutional challenges in the U.S. Supreme Court, and the Trump Administration issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Additionally, Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. In December 2018, the CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of the federal district court litigation regarding the method CMS uses to determine this risk adjustment. Since then, the ACA risk adjustment program payment parameters have been updated annually. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business, especially given the new Biden Administration.

Additionally, other federal health reform measures have been proposed and adopted in the U.S. since the ACA was enacted:

- The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027, unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, and subsequent legislation, these Medicare sequester reductions are suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. Proposed legislation, if passed, would extend this suspension until the end of the pandemic.

- The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny over the manner in which companies set prices for their products, which have resulted in several recent Congressional inquiries and proposed and enacted bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and patient programs, and reform government program reimbursement methodologies for products. In addition, the U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost containment programs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs to limit the growth of government paid healthcare costs.

Individual states in the U.S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Congress and the Biden administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Individual states in the U.S. have also been increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Other Regulatory Requirements

Our operations use small amounts of hazardous materials in research and development and generate regulated medical waste in the normal course of performing our CELsignia tests. This subjects us to a variety of federal, state and local environmental and safety laws and regulations. Some of the regulations under the current regulatory structure provide for strict liability, holding a party potentially liable without regard to fault or negligence. We could be held liable for damages and fines as a result of our, or others', business operations should contamination of the environment or individual exposure to hazardous substances occur. We cannot predict how changes in laws or development of new regulations will affect our business operations or the cost of compliance.

Impact of COVID-19 on our Business

Health and Safety

To help protect the health and safety of our employees, suppliers and collaborators, we took proactive, aggressive action from the earliest signs of the outbreak. We enacted rigorous safety measures in our laboratory and administrative offices, including implementing social distancing protocols, allowing working from home for those employees that do not need to be physically present in a lab to perform their work, suspending travel, implementing temperature checks at the entrances to our facilities, extensively and frequently disinfecting our workspaces and providing masks to those employees who must be physically present. We expect to continue with these measures until the COVID-19 pandemic is better contained and we may take further actions as government authorities require or recommend or as we determine to be in the best interests of our employees, suppliers, and collaborators.

Clinical Trials and Collaborations

As a result of the COVID-19 pandemic, governmental authorities have implemented and are continuing to implement numerous and constantly evolving measures to try to contain the virus, such as travel bans and restrictions, limits on gatherings, quarantines, shelter-in-place orders, and business shutdowns. As we continue to advance our clinical trial collaborations, we are in close contact with our current clinical sponsors, and principal investigators, as well as prospective pharmaceutical company and clinical collaborators, to assess the ongoing impact of COVID-19 on our trial enrollment timelines and collaboration discussions. In light of the COVID-19 pandemic, the focus of healthcare providers and hospitals on fighting the virus, and consistent with the FDA's updated industry guidance for conducting clinical trials issued on March 18, 2020, we are experiencing delays in the enrollment of patients in our ongoing clinical trials. We now expect interim results from the FACT-1 and FACT-2 trials to be delayed until the first half of 2023 and final results approximately nine months later. As the impact of COVID-19 on our industry becomes clearer, we may need to reassess the timing of our anticipated clinical milestones. Prospective clinical trial collaborations with pharmaceutical companies and sponsors may also be delayed but the impact on the timing of finalizing agreements is not yet known.

Research and Development

While our facility currently remains operational, the evolving measures to try to contain the virus have impacted and may further impact our workforce and operations, as well as those of our vendors and suppliers. Although there is uncertainty related to the anticipated impact of the recent COVID-19 outbreak on our future results, we believe our existing balance of cash and cash equivalents will be sufficient to meet our cash needs arising in the ordinary course of business for at least the next twelve months. We continue to monitor the rapidly evolving situation and guidance from federal, state and local public health authorities and may take additional actions based on their recommendations. In these circumstances, there may be developments outside our control requiring us to adjust our operating plan.

Corporate History

We were organized as a Minnesota limited liability company in 2011 and commenced operations in 2012. On September 15, 2017, we converted from a Minnesota limited liability company into a Delaware corporation and changed our name from Celcuity LLC to Celcuity Inc.

Employees and Labor Relations

As of December 31, 2021, we had 39 full-time employees, most of which were engaged in research and development activities. None of our employees are currently represented by a labor union or covered by a collective bargaining agreement and we believe that our relations with our employees are good. During 2021, our voluntary turnover rate was approximately 10%.

ITEM 1A. Risk Factors

Risk factors that could cause actual results to differ from our expectations and that could negatively impact our financial condition and results of operations are discussed below and elsewhere in this Annual Report. Additional risks and uncertainties not presently known to us or that are currently not believed to be significant to our business may also affect our actual results and could harm our business, financial condition and results of operations. If any of the risks or uncertainties described below or any additional risks and uncertainties actually occur, our business, results of operations and financial condition could be materially and adversely affected.

Risks Relating to Our Business

We have a limited operating history and we may never generate revenue or profit.

We are a clinical-stage biotechnology company that commenced activities in January 2012. We only have a limited operating history and our business plan has not been tested. Since inception, we have had no revenue and have incurred significant operating losses. We have financed our operations primarily through equity and debt offerings. To generate revenue and become and remain profitable, we must continue to pursue our integrated companion diagnostic (CDx) and therapeutic (Rx) strategy that leverages our CELsignia CDx platform. To do so, we need to successfully complete our five existing clinical trial collaborations, continue to develop other CELsignia tests for other cancer sub-types, cultivate partnerships with pharmaceutical companies, and develop and commercialize gedatolisib pursuant to our license agreement with Pfizer. We must also build operational and financial infrastructure to support commercial operations, train and manage employees, and market and sell our CELsignia tests (as a companion diagnostic and/or as a stand-alone test) and, once fully developed and commercialized, our anticipated drug products.

We may never succeed in any of these activities and, even if we do, we may never generate revenue that is sufficient to achieve profitability. We expect to continue to incur significant expenses and operating losses for the foreseeable future, and the net losses we incur may fluctuate significantly from quarter to quarter. Our failure to become and remain profitable would decrease our value and could impair our ability to raise capital, maintain or expand our research and development efforts, expand our business, or continue our operations.

Our inability to raise additional capital on acceptable terms in the future may limit our ability to develop and commercialize our integrated therapeutic (Rx) and companion diagnostic (CDx) strategy.

We may require additional capital to finance capital expenditures and operating expenses over the next several years as we launch our integrated therapeutic and companion diagnostic strategy and expand our infrastructure, commercial operations and research and development activities. We may seek to raise additional capital through equity offerings, debt financings, collaborations or licensing arrangements. Additional funding may not be available to us on acceptable terms, or at all. If we raise funds by issuing equity securities, dilution to our stockholders could result. Any equity securities issued may also provide for rights, preferences or privileges senior to those of holders of our existing securities. The incurrence of additional indebtedness or the issuance of certain equity securities could result in increased fixed payment obligations and could also include restrictive covenants, such as limitations on our ability to incur additional debt or issue additional equity, limitations on our ability to acquire or license intellectual property rights, and other operating restrictions that could adversely affect our ability to conduct our business. In the event that we enter into collaborations or licensing arrangements to raise capital, we may be required to accept unfavorable terms. If we are not able to secure additional funding when needed, we may have to delay, reduce the scope of or eliminate one or more research and development programs or selling and marketing initiatives. In addition, we may have to work with a partner on one or more of our products or market development programs, which could lower the economic value of those programs to our company.

We will be dependent on our ability to attract and retain key personnel.

Our operations will be materially dependent upon the services of our officers and key employees, including Brian F. Sullivan, our Chief Executive Officer, and Dr. Lance G. Laing, our Chief Science Officer. Successful implementation of our business plan will also require the services of other consultants and additional personnel. We cannot assure you that we will be able to attract and retain such persons as employees, independent contractors, consultants or otherwise. If we are not able to attract individuals with the skills required for our business, or if we lose the services of either Mr. Sullivan or Dr. Laing, we may be unable to successfully implement our business plan.

The COVID-19 pandemic may materially and adversely impact our business, including ongoing clinical trials.

The outbreak of COVID-19 and government measures taken in response have had a significant impact on the global economy, with healthcare systems particularly affected. In response to the COVID-19 outbreak, public health measures have been implemented across much of the United States, Europe and Asia, including in the locations of our offices, clinical trial sites, and partners. Due to these public health measures, we are allowing employees who do not need to be physically present in the lab to perform their work at home. Our increased reliance on employees working from home may negatively impact productivity, or disrupt, delay or otherwise adversely impact our business.

As a result of the COVID-19 outbreak and related public health measures, we have and may in the future experience disruptions that could materially and adversely impact our clinical trials, business, financial condition and results of operations. Potential disruptions include but are not limited to:

- delays or difficulties in enrolling patients in clinical trials and obtaining the results of completed clinical trials;
- increased rates of patients withdrawing from clinical trials following enrollment as a result of quarantine or concerns about COVID-19;
- diversion of healthcare resources away from the conduct of clinical trials;
- delays in prospective clinical trial collaborations with pharmaceutical companies and sponsors;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- limitations on our ability to recruit and hire key personnel due to our inability to meet with candidates because of travel restrictions; and
- limitations on employee resources that would otherwise be focused on the conduct of clinical trials and research as a result of focus addressing COVID-19 mitigation and loss of productivity from remote work.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the outbreak impacts our business will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the magnitude of the pandemic, the duration of social distancing in the United States and other countries, business closures or business disruptions, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Beyond the direct effect of the pandemic, mitigation efforts have had broad economic effects. The extent of the scope and duration of these economic effects cannot currently be predicted, although they are likely to be significant for the near future. The economic impact of COVID-19 will affect us in a variety of ways, including without limitation making our stock price more volatile, making it more difficult to raise additional capital through offerings of equity or debt securities, and reducing the availability of bank loans. As a result, we may face difficulties raising capital and capital raising efforts may be on terms than are less favorable than would have been previously available.

All of the effects of COVID-19 described herein are expected to apply to any future recurrences of COVID-19 and any other pandemics that may occur in the future.

Risks Related to Our Drug Product, Gedatolisib

Our future strategy is dependent on the success of our initial drug product, gedatolisib, as well as other drug products we may develop. If we are unable to successfully complete clinical development of, obtain regulatory approval for or commercialize our drug products, or if we experience delays in doing so, our business will be materially harmed.

To date, we have not yet completed any registrational clinical trials or the development of any drug products. Our future success and ability to generate revenue from our drug products, which we do not expect will occur for several years, if ever, is dependent on our ability to successfully develop, obtain regulatory approval for and commercialize one or more drug products. We may not have the financial resources to continue development of, or to modify existing or enter into new collaborations for, a drug product if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, our drug products, including:

- our inability to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our drug products are safe and effective;
- insufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- negative or inconclusive results from our preclinical studies, clinical trials or the clinical trials of others for drug products similar to ours, leading to a decision or requirement to conduct additional preclinical studies or clinical trials or abandon a program;
- product-related adverse events experienced by subjects in our clinical trials or by individuals using drugs or therapeutic biologics similar to our drug products;
- delays in submitting applications, or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign regulatory authorities regarding the scope or design of our clinical trials;
- poor effectiveness of our drug products during clinical trials;
- better than expected performance of control arms, such as placebo groups, which could lead to negative or inconclusive results from our clinical trials;
- delays in enrolling subjects in clinical trials;
- high drop-out rates of subjects from clinical trials;
- inadequate supply or quality of drug products or other materials necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial or manufacturing costs;
- unfavorable FDA or comparable regulatory authority inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our therapies in particular; or
- varying interpretations of data by the FDA and comparable foreign regulatory authorities.

The preliminary efficacy and safety data reported for the B2151009 Phase 1b clinical trial was provided to us by Pfizer and is subject to change once data cleansing and data verification activities are completed.

The preliminary efficacy and safety data reported for the B2151009 Phase 1b clinical trial was provided to us by Pfizer. Pfizer provided this data as of a data cutoff date of January 11, 2021, before Pfizer had cleaned the data, locked the clinical database, and completed preparation of a final Clinical Study Report. We have not independently reviewed or verified the data, which includes case report forms (CRF) for each patient and reconciliation with the data endpoints reported. We may discover, upon performing the study close out activities for B2151009, which includes reconciliation and adjudication of the endpoint reported data with the CRF, inconsistencies with the data as originally provided by Pfizer to us. As a result, the data presented as of the date hereof is subject to change once data cleaning and verification activities have been completed and other study close-out procedures are completed.

We were not involved in the early development of gedatolisib; therefore, we are dependent on third parties having accurately generated, collected, interpreted and reported data from certain preclinical and clinical trials gedatolisib.

We had no involvement with or control over the initial preclinical and clinical development of gedatolisib. We are dependent on third parties having conducted their research and development in accordance with the applicable protocols and legal, regulatory and scientific standards; having accurately reported the results of all preclinical studies and clinical trials conducted with respect to such drug product; and having correctly collected and interpreted the data from these trials. If these activities were not compliant, accurate or correct, the clinical development, regulatory approval or commercialization of our drug product will be adversely affected.

As an organization, we have never successfully completed any registrational clinical trials, and we may be unable to do so for any drug candidates we may develop.

We will need to successfully complete registrational clinical trials in order to obtain the approval of the FDA or comparable foreign regulatory authorities to market our drug products. Carrying out clinical trials, including later-stage registrational clinical trials, is a complicated process. As an organization, we have not previously completed any registrational clinical trials. In order to do so, we will need to build and expand our clinical development and regulatory capabilities, and we may be unable to recruit and train qualified personnel. We also expect to continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to submission and approval of our drug products. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approval of any drug products that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our drug products.

If we encounter difficulties enrolling patients in any of our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the patient eligibility and exclusion criteria defined in the protocol;
- the size of the patient population required for analysis of the clinical trial's primary endpoints;
- the proximity of patients to clinical trial sites;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience, and the ability of these investigators to identify and enroll suitable patients;
- perception of the safety profile of our drug products;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

To obtain the requisite regulatory approvals to commercialize any drug products, we must demonstrate through extensive preclinical studies and clinical trials that such drug product is safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing.

Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. Additionally, we are conducting and plan to conduct some open-label trials, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in those trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Where a randomized, placebo-controlled clinical trial is designed to allow enrolled subjects to cross-over to the treatment arm, there may be a risk of inadvertent unblinding of subjects prior to cross-over, which may limit the clinical meaningfulness of those data and may require the conduct of additional clinical trials. As such, the results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

Successful completion of clinical trials is a prerequisite to submitting a new drug application, or NDA, to the FDA and similar marketing applications to comparable foreign regulatory authorities for each drug product and, consequently, the ultimate approval and commercial marketing of any drug products. We may experience delays in initiating or completing clinical trials and preparing for regulatory submissions. We also may experience numerous unforeseen events during, or as a result of, any future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our current product candidates or any future product candidates. Our costs will increase if we experience delays in clinical testing or marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be reassigned or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition and results of operations significantly.

The successful development of biopharmaceuticals is highly uncertain.

Successful development of biopharmaceuticals is highly uncertain and is dependent on numerous factors, many of which are beyond our control. Product candidates that appear promising in the early phases of development may fail to reach the market for several reasons including, among other things, that clinical trial results may show the product candidates to be less effective than expected or to have unacceptable side effects or toxicities; we may fail to receive the necessary regulatory approvals or there may be a delay in receiving such approvals; or the proprietary rights of others and their competing products and technologies that may prevent our product candidates from being commercialized.

The length of time necessary to complete clinical trials and to submit an application for marketing approval for a final decision by a regulatory authority varies significantly from one drug product to the next and from one country to the next and may be difficult to predict. Even if we are successful in obtaining marketing approval, commercial success of any approved products will also depend in large part on the availability of coverage and adequate reimbursement from third-party payors, including government payors such as the Medicare and Medicaid programs and managed care organizations in the U.S. or country specific governmental organizations in foreign countries, which may be affected by existing and future healthcare reform measures designed to reduce the cost of healthcare. Third-party payors could require us to conduct additional studies, including post-marketing studies related to the cost effectiveness of a product, to qualify for reimbursement, which could be costly and divert our resources. If government and other healthcare payors were not to provide coverage and adequate reimbursement for our products once approved, market acceptance and commercial success would be reduced.

In addition, if any of our drug products receive marketing approval, we will be subject to significant post-approval regulatory obligations. In addition, there is always the risk that we, a regulatory authority or a third party might identify previously unknown problems with a product post-approval, such as adverse events of unanticipated severity or frequency. Compliance with these requirements is costly, and any failure to comply or other issues with our drug products post-approval could adversely affect our business, financial condition and results of operations.

We face significant competition from other biopharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly as they develop novel approaches to treating disease indications that our product candidates are also focused on treating. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel therapeutics or to in-license novel therapeutics that could make the product candidates that we develop obsolete. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaboration partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, tolerability, reliability, convenience of use, price and reimbursement.

Even if we obtain regulatory approval of drug products, the availability and price of our competitors' products could limit the demand and the price 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.

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

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

- efficacy and potential advantages compared to other treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- convenience and ease of administration compared to other treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party coverage, market access and adequate reimbursement; and
- the prevalence and severity of any side effects.

Risks Related to Intellectual Property for Gedatolisib

We depend on intellectual property licensed from third parties, including from Pfizer for our lead product candidate, and termination of this license could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others. All patents covering gedatolisib and any combination therapies using our product candidates are licensed from third parties. Any termination of a product license could result in the loss of significant rights and would cause material adverse harm to our ability to commercialize our product candidates.

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

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of licensed technology in relation to our development and commercialization of our product candidates and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed 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.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we own, as we are for intellectual property that we license. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could materially suffer.

If we fail to comply with our obligations under our patent license with Pfizer, we could lose license rights that are important to our business.

We are a party to a license agreement with Pfizer pursuant to which we in-license key patents for our gedatolisib. This license imposes various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, Pfizer may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property. We may have limited control over the maintenance and prosecution of these in-licensed rights, activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

We may not be successful in obtaining or maintaining necessary rights to develop any future product candidates on acceptable terms.

Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which could harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

Risks Related to Government Regulation for Gedatolisib

We may not obtain the necessary regulatory approvals to commercialize our product candidate.

We will need FDA approval to commercialize our product candidate in the U.S. In order to obtain FDA approval, we must submit to the FDA a new drug application, or NDA, demonstrating that the drug product is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as pre-clinical studies, as well as human tests, which are referred to as clinical trials. Satisfaction of the FDA's regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the drug product and requires substantial resources for research, development and testing. We cannot predict whether our research and clinical approaches will result in a drug that the FDA considers safe for humans and effective for indicated uses. The FDA has substantial discretion in the drug approval process and may require us to conduct additional pre-clinical and clinical testing or to perform post-marketing studies. The approval process may also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals may delay commercialization of, and our ability to derive product revenues from, our drug product; impose costly procedures on us; or diminish any competitive advantages that we may otherwise enjoy. Even if we comply with all FDA requests, the FDA may ultimately reject our NDA. We cannot be sure that we will ever obtain regulatory clearance for our drug product. Failure to obtain FDA approval of our drug product will severely undermine our business by reducing our number of salable products and, therefore, corresponding product revenues.

The FDA or comparable foreign regulatory authorities may disagree with our regulatory plan for our product candidates.

The general approach for FDA approval of a new drug is dispositive data from one or more well-controlled Phase 3 clinical trials of the product candidate in the relevant patient population. Phase 3 clinical trials typically involve a large number of patients, have significant costs and take years to complete.

Our clinical trial results may not support approval of our product candidates. In addition, our product candidates could fail to receive regulatory approval, or regulatory approval could be delayed, for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the dosing regimen, design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our product candidates are safe and effective for any of their proposed indications;
- we may encounter safety or efficacy problems caused by the COVID-19 pandemic;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of an NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the U.S. or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Breakthrough Therapy Designation or Fast Track Designation from the FDA may not actually lead to a faster development or regulatory review or approval process.

We have received Fast Track Designation and may seek Breakthrough Therapy Designation for our product candidates. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe one of our product candidates is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if a product candidate qualifies as a breakthrough therapy, the FDA may later decide that the product no longer meets the conditions for qualification and rescind the Breakthrough Therapy Designation.

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

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, a comparable foreign regulatory authority must also approve the manufacturing, marketing and promotion of the product candidate in those countries.

Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the U.S., including additional preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the U.S. have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we receive regulatory approval of any product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies and submission of safety, efficacy and other post-marketing information, including both federal and state requirements in the U.S. and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may 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 candidate. Certain endpoint data we hope to include in any approved product labeling also may not make it into such labeling, including exploratory or secondary endpoint data such as patient-reported outcome measures. The FDA may impose consent decrees or withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-marketing studies or clinical trials to assess new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The policies of the FDA and comparable foreign regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Risks Related to Our CELsignia Tests

Our success with CELsignia is heavily dependent on the success of our first CELsignia trials.

Our business strategy is focused on attracting pharmaceutical company partnerships that provide revenue from the sale of CELsignia tests during clinical trials, from milestone payments during clinical trials, from sales of our CELsignia tests as companion diagnostics or stand-alone tests thereafter, and, potentially, from royalties on the incremental drug revenues our tests enable. Our ability to obtain such partnerships and generate such revenue depends in part on the ability of our first CELsignia tests to demonstrate the potential incremental opportunity available for pharmaceutical companies. We do not expect to receive the first interim results for our prospective clinical trials for the CELsignia HER2 Pathway Activity Test until the first half of 2023 and with final results expected approximately nine months later. Success of the clinical trials using the CELsignia HER2 Pathway Activity Test or CELsignia Multi-Pathway Activity Test will depend on many factors, such as successfully enrolling patients, meeting trial endpoint goals, and completing the trial in a timely manner. Our ability to complete the trial could be delayed or prevented for several reasons that are out of our control, such as the FDA withdrawing its authorization and approval to perform the study, NSABP, West Cancer Center, Massachusetts General Hospital, MD Anderson Cancer Center, or University of Rochester determining that the human and/or toxicology test results do not support continuing the trial, or participants having adverse reactions or side-effects to the drugs administered in the study. If we are unable to demonstrate that the CELsignia HER2 Pathway Activity Test or CELsignia Multi-Pathway Activity Test is suitable as a companion diagnostic for the targeted therapy, we will likely not be able to generate future revenue from our CELsignia HER2 Pathway Activity Test or CELsignia Multi-Pathway Activity test and may not be able to attract other pharmaceutical companies to partner with us for the development and commercialization of other CELsignia tests. Further, potential pharmaceutical company partners may delay negotiating development agreements until results of the first clinical trial using our CELsignia HER2 Pathway Activity Test trial are available. Even if the ultimate outcome of the first clinical trial using a CELsignia HER2 Pathway Activity Test trial is positive, any delays could materially and adversely affect our business.

We may not be successful in finding pharmaceutical company partners for continuing development of additional CELsignia tests.

We intend to develop strategic partnerships with pharmaceutical companies for developing additional CELsignia tests. Many of the potential partners are global, multi-billion-dollar pharmaceutical companies with sophisticated research and development organizations and multiple priorities. We may not be successful in our efforts to establish such a strategic partnership or other alternative arrangements for our CELsignia tests because, among other things, our research and development pipeline may be insufficient, such tests may be deemed to be at too early of a stage of development for collaborative effort, or third parties may not view such tests as having the requisite potential to demonstrate efficacy. In addition, we may be restricted under collaboration agreements from entering into future agreements with other partners. Even if we are able to find suitable partners, we may not be successful in negotiating development agreements with such partners that provide revenue from the sale of our CELsignia tests, from milestone payments, and/or from royalties on the incremental drug revenues that our tests enable. If we are unable to reach agreements with suitable strategic partners on a timely basis, on acceptable terms or at all, we may have to curtail the development of additional CELsignia tests, our expected revenue opportunities may be significantly smaller than expected and our business may fail.

While our CELsignia HER2 Pathway Activity Test and CELsignia Multi-Pathway Activity Test are commercially ready, we have not attempted to market these to physicians or their patients as stand-alone tests and have no ability to determine if these tests or any of our other tests will be commercially viable.

While our CELsignia HER2 Pathway Activity Test and CELsignia Multi-Pathway Activity Test are analytically validated, conducted in our CLIA certified and CAP accredited laboratory, and currently ready for commercial use as an LDT, we have not attempted to market them to physicians or their patients. Furthermore, we have commenced only limited communications with KOLs to build awareness and credibility of our CELsignia diagnostic platform and CELsignia tests. Accordingly, we have no ability to determine whether our CELsignia HER2 Pathway Activity Test, CELsignia Multi-Pathway Activity Test or any other future CELsignia tests, will be commercially viable as stand-alone tests. We may never be successful in generating revenue from our CELsignia tests as stand-alone tests, and if we are unable to build pharmaceutical partnerships that enable us to market the CELsignia HER2 Pathway Activity Test, the CELsignia Multi-Pathway Activity Test, and other tests as companion diagnostic tests, we may never generate any revenue and our business may fail.

Developing our CELsignia tests involves a lengthy and complex process that may not be successful.

Our CELsignia tests may take several years to develop from the time they are discovered to the time they are available for patient use, if ever. In order to develop additional CELsignia tests into commercially ready products, we need to successfully complete a variety of activities, including, among others, conducting substantial research and development, conducting extensive analytical testing, and maintaining our CLIA certified and CAP accredited laboratory. In addition, our business strategy is focused on our CELsignia tests being sold as companion diagnostics. This will require obtaining and maintaining partnerships with pharmaceutical companies and successfully completing clinical studies that demonstrate the suitability of the applicable CELsignia test as a companion diagnostic for their targeted therapies.

These activities will require us to expend significant resources. Based on comparable companies in this industry, few research and development projects result in commercially viable products, and success in early clinical studies often is not replicated in later studies. At any point, we may abandon development of a product candidate for several reasons, such as a clinical validation study failing to demonstrate the prospectively defined endpoints of the study. We may also be required to expend considerable resources repeating clinical studies, which would adversely affect the timing for generating potential revenue from a new product and our ability to invest in other products in our pipeline.

Clinical trials are expensive and complex with uncertain outcomes, which may prevent or delay commercialization of our CELsignia tests.

For our CELsignia tests to become a companion diagnostic for a matching targeted therapy, we must conduct clinical trials to demonstrate that patients who have an abnormal signaling pathway, as identified by our CELsignia tests, respond to treatment with a matching targeted therapy. Clinical testing is expensive, is difficult to design and implement, and can take many years to complete, and its outcome is inherently uncertain. As a company, we have limited experience in conducting or participating in clinical trials. We cannot be certain that any future clinical trials will conclusively demonstrate that any CELsignia test is effective as a companion diagnostic. If our trials do not yield positive results, we may be unable to maintain the pharmaceutical company partnerships we build or find additional partners, we may not be able to successfully commercialize our CELsignia tests or generate any revenue, our business may fail, and you may lose part or all of your investment.

We cannot be certain that our existing clinical trial or future clinical trials, if any, will begin or be completed on time, if at all. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to commercialize our CELsignia tests, such as:

- delay or failure in reaching agreement on acceptable clinical trial contracts or clinical trial protocols with planned trial sites and/or strategic partners;
- delay or failure in reaching agreement with the FDA or a comparable foreign regulatory authority on a trial design, in obtaining authorization from such authorities to commence the trial, and/or in complying with conditions or other requirements imposed by such regulatory authorities with respect to the trial;
- delay or failure in recruiting and enrolling suitable subjects to participate in one or more clinical trials, or in such participants completing a trial or returning for follow-up during or after the trial;
- clinical sites, investigators or other third-parties deviating from the trial protocol, failing to conduct the trial in accordance with regulatory and contractual requirements, and/or dropping out of a trial;
- regulatory imposition of a clinical hold for any of our clinical trials, where a clinical hold in a trial in one indication would result in a clinical hold for clinical trials in other indications; and
- changes in governmental regulations or administrative actions.

Significant nonclinical or clinical trial delays could prevent us from maintaining and/or developing new pharmaceutical company partnerships. Delays could also shorten any periods during which we may have the exclusive right to commercialize our CELsignia tests or allow our competitors to bring products to market before we do. As such, any delays could impair our ability to successfully commercialize our CELsignia tests and may materially and adversely affect our business, financial condition, results of operations and prospects.

Even if our CELsignia tests achieve positive clinical trial results, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our potential CELsignia tests, including our first CELsignia HER2 Pathway Activity Test and CELsignia Multi-Pathway Activity Test, achieve positive clinical trial results, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success. For example, conventional genomic- or proteomic-based analyses are commonly used today to diagnose cancer and prescribe cancer medications, and physicians may continue to rely on these diagnostic tests instead of adopting the use of a CELsignia test. The degree of market acceptance of our CELsignia tests will depend on a number of factors, including:

- their efficacy and other potential advantages compared to alternative diagnostic tests;
- our ability to offer them for sale at competitive prices;
- their convenience and ease of obtaining patient specimens compared to alternative diagnostics;
- the willingness of the target patient population to try new diagnostics and of physicians to initiate such diagnostics;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for our diagnostic tests; and
- our ability to partner with pharmaceutical companies to develop companion diagnostic programs for the new cancer sub-types we discover.

If our CELsignia tests do not achieve an adequate level of acceptance, we may never generate significant product revenues and we may not become profitable.

Our CELsignia related business, operational and financial goals may not be attainable if the market opportunities for our CELsignia tests or our pharmaceutical company partners are smaller than we expect. Our internal research and estimates on market opportunities have not been verified by independent sources, and we have not independently verified market and industry data from third-parties that we have relied on.

The total market opportunities that we believe exist are based on a variety of assumptions and estimates, including the number of potential companion diagnostic programs we will be able to successfully pursue, the amount of potential milestone payments that we could receive in companion diagnostic programs, the number of patients we will test in clinical trials, the price we will be able to charge for our tests and the total annual number of cancer patients with undiagnosed abnormal cell signaling. In addition, we have relied on third-party publications, research, surveys and studies for information related to determining market opportunities, including without limitation, information on the number of cancer patients and those receiving various forms of treatment, the cost of drug therapy, the amount of revenue generated from various types of drug therapy, the objective response rates of drug therapies, the number of deaths caused by cancer and the expected growth in cancer drug therapy and diagnostic markets. Our internal research and estimates on market opportunities have not been verified by independent sources, and we have not independently verified market and industry data from third-parties that we have relied on. Any or all of our assumptions and/or estimates may prove to be incorrect for several reasons, such as inaccurate reports or information that we have relied on, potential patients or providers not being amenable to using our CELsignia platform for diagnostic testing or such patients becoming difficult to identify and access, limited reimbursement for companion diagnostics, pricing pressure due to availability of alternative diagnostic tests, or an inability of the CELsignia tests' companion drugs to obtain the necessary regulatory approvals for new indications. If any or all of our assumptions and estimates prove inaccurate, we and our companion diagnostic pharmaceutical partners may not attain our business, operational and financial goals.

The expected selling price range of our CELsignia tests is an estimate. We have not yet sold any such tests and the actual price we are able to charge may be substantially lower than our expected price range.

We have estimated the selling price range of our CELsignia tests based on the pricing of other diagnostic tests currently available and assumptions regarding the efficacy and market acceptance of our tests. We have not yet sold our CELsignia tests and cannot be certain of the actual price we may be able to charge. The availability and price of our competitors' products could limit the demand and the price we are able to charge. We may not achieve our business plan if acceptance is inhibited by price competition, if pharmaceutical companies refuse to pay our expected prices for CELsignia tests in clinical trials, if physicians are reluctant to switch from other diagnostic tests to our CELsignia tests or if physicians switch to other new products or choose to reserve our CELsignia tests for use in limited circumstances. Furthermore, reductions in the reimbursement rate of third-party payors have occurred and may occur in the future. Each of these factors could cause our selling price to be substantially lower than expected, and we may fail to generate revenue or become profitable.

The insurance coverage and reimbursement status of new diagnostic products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for CELsignia tests could limit our ability to market those CELsignia tests and decrease our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive diagnostic tests and treatments. Sales of any of our potential CELsignia tests will depend substantially, both in the United States and internationally, on the extent to which the costs of our CELsignia tests will be paid by health maintenance, managed care, and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. Reimbursement by a payor may depend on a number of factors, including a payor's determination that the CELsignia tests are neither experimental nor investigational, appropriate for the specific patient, cost-effective, supported by peer-reviewed publications, and included in clinical practice guidelines.

If reimbursement is not available, or is available only to a limited amount, we may not be able to successfully commercialize our CELsignia tests at expected levels, or potentially at all. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our research and development investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved diagnostic products. In the United States, the principal decisions about reimbursement for new diagnostic products and services are typically made by CMS. CMS decides whether and to what extent a new product or service will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. As such, a significant portion of our potential revenue depends on CMS approving coverage and reimbursement of our CELsignia tests.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of diagnostic tests such as our potential CELsignia tests. In many countries, particularly the countries of the European Union, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time. To obtain reimbursement or pricing approval in some countries, we may be required to demonstrate the cost-effectiveness of our CELsignia tests relative to other available diagnostic tests. The prices of products under such systems may be substantially lower than in the United States. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our CELsignia tests. Accordingly, in markets outside the United States, the reimbursement for our potential CELsignia tests may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profit.

Moreover, increasing efforts by governmental and third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our potential CELsignia tests. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. We expect to experience pricing pressures in connection with the sale of any CELsignia tests due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes.

We may encounter difficulties in commercializing and marketing our CELsignia products, including in hiring and retaining a qualified sales force.

In order to commercialize any CELsignia test, we must build marketing, sales, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. For each CELsignia test we develop, we intend to pursue development agreements with the pharmaceutical companies that provide matching targeted therapies. Once we have completed the analytical validation of a CELsignia test, we plan to target KOLs to build product awareness. Once we have clinical validation data available, we expect to expand our sales and marketing efforts to target the broader market and coordinate our go-to-market activities with those of our partner pharmaceutical companies. These activities will be expensive and time consuming and will require significant attention of our executive officers to manage. In particular, there is intense competition for qualified sales personnel and our inability to hire or retain an adequate number of sales representatives could limit our ability to maintain or expand our business and increase sales. Furthermore, there is no guarantee that any new drug indications will require our CELsignia tests as a companion diagnostic or that any pharmaceutical company will effectively coordinate sales and marketing activities with us. Any failure or delay in these activities, including if we are unable to develop our marketing and sales networks or if our sales personnel do not perform as expected, would adversely impact the commercialization our CELsignia platform, and our business, financial condition, results of operations and prospects may be materially and adversely affected.

We face significant competition from other diagnostic companies and our operating results will suffer if we fail to compete effectively.

The diagnostic testing industry is intensely competitive. We have competitors both in the United States and abroad, including universities and other research institutions and providers of diagnostics that focus on developing genomic or proteomic analyses of a patient's diseased cells or theranostic tests to predict specific patient responses to a drug therapy. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and well-established marketing and sales forces. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, products or services that are more effective or less costly than the CELsignia tests that we are currently developing or that we may develop. In addition, established medical technology, biotechnology and/or pharmaceutical companies may invest heavily to accelerate discovery and development of diagnostic tests that could make our CELsignia tests less competitive.

Our ability to compete successfully will depend largely on our ability to:

- discover and develop CELsignia tests for cancer sub-types that are superior to other products in the market;
- demonstrate compelling advantages in the efficacy and convenience of our CELsignia tests on a cost competitive basis;
- attract qualified scientific, product development and commercial personnel;
- obtain and maintain patent and other proprietary protection as necessary for our CELsignia platform;
- obtain required U.S. and international regulatory approvals;
- successfully collaborate with research institutions and pharmaceutical companies in the discovery, development and commercialization of our current and future CELsignia tests; and
- successfully expand our operations and build a sales force to support commercialization.

If our sole laboratory facility becomes inoperable, we will be unable to perform our tests and our business will be harmed.

We do not have redundant laboratory facilities. We perform all of our diagnostic services in our laboratory located in Minneapolis, Minnesota. Our facility and the equipment we use to perform our tests would be costly to replace and could require substantial lead time to repair or replace. The facility may be harmed or rendered inoperable by physical damage from fire, floods, tornadoes, power loss, telecommunications failures, break-ins and similar events, which may render it difficult or impossible for us to perform our tests for some period of time. The inability to perform our tests may result in the loss of customers or harm our reputation, and we may be unable to regain those customers in the future. Although we possess insurance for damage to our property and the disruption of our business, this insurance may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, or at all.

In order to rely on a third party to perform our tests, we could only use another facility with established state licensure and CLIA accreditation under the scope of which our potential CELsignia tests could be performed following validation and other required procedures. We cannot assure you that we would be able to find another CLIA-certified facility willing to adopt CELsignia tests and comply with the required procedures, or that this laboratory would be willing to perform the tests for us on commercially reasonable terms.

Our instrument or reagent suppliers may fail to meet our quality requirements for the items we purchase or fail to provide a continuous supply of the items we utilize to perform our CELsignia tests.

We utilize highly specialized reagents and instruments to perform our CELsignia tests. We may be unable to find suitable replacement reagents and instruments on a timely basis, if at all. Interruption in the supply of these items or degradation in their quality could delay analytical and clinical studies, and/or render us unable to deliver CELsignia tests. This would interrupt sales and adversely affect our business, results of operations and financial condition.

Performance issues or price increases by our shipping carriers could adversely affect our business, results of operations and financial condition, and harm our reputation and ability to provide our CELsignia tests on a timely basis.

Expedited, reliable shipping is essential to our operations. Should our shipping carrier encounter delivery performance issues such as loss, damage or destruction of a sample, such occurrences may damage our reputation and lead to decreased demand for our services and increased cost and expense to our business. In addition, any significant increase in shipping rates could adversely affect our operating margins and results of operations. Similarly, strikes, severe weather, natural disasters or other service interruptions by delivery services we use would adversely affect our ability to receive and process patient samples on a timely basis. There are only a few providers of overnight nationwide transport services, and there can be no assurance that we will be able to maintain arrangements with providers on acceptable terms, if at all.

Our CELsignia tests represent a novel approach to companion diagnostics, which could result in heightened regulatory scrutiny, delays in clinical development, or delays in our ability to commercialize any products.

Our unique and proprietary CELsignia technology is the first cancer diagnostic platform we are aware of that can detect the underlying signaling dysfunction driving a patient's cancer. Because this is a novel approach to companion diagnostics, there can be no assurance as to the length of a clinical trial period, the number of patients the FDA or another applicable regulatory authority will require to be enrolled in the trials in order to establish the safety and efficacy of our CELsignia tests and the companion drugs, or that the data generated in these trials will be acceptable to the FDA or another applicable regulatory authority to support marketing approval of new indications for the companion drugs. This could delay or prohibit our clinical trials and/or commercialization of our CELsignia tests.

If the FDA were to begin regulating our tests, we could incur substantial costs and delays associated with trying to obtain premarket clearance or approval.

Most LDTs are not currently subject to FDA regulation, although reagents, instruments, software or components provided by third parties and used to perform LDTs may be subject to regulation. We believe that the CELsignia tests are LDTs, which is a term that describes tests that are designed and performed within a single laboratory. As a result, we believe the CELsignia tests are not currently subject to regulation by the FDA in accordance with the FDA's current policy of exercising enforcement discretion regarding LDTs.

Historically, the FDA has not required laboratories that furnish only LDTs to comply with the agency's requirements for medical devices (e.g., establishment registration, device listing, quality systems regulations, premarket clearance or premarket approval, and post-market controls). In mid-2014, the FDA published a draft Guidance Document describing a proposed approach for a regulatory framework for LDTs, but in late 2016, the FDA indicated it did not intend to finalize the LDT Guidance Document at that time. It is not clear when or if the FDA will seek to alter the current LDT regulatory framework in the future. We cannot provide any assurance that FDA regulation, including premarket review, will not be required in the future for our tests, whether through additional guidance issued by the FDA, new enforcement policies adopted by the FDA or new legislation enacted by Congress. We cannot predict with certainty the timing or content of future legislation enacted or guidance issued regarding LDTs, or how it will affect our business.

If premarket review is required by the FDA at a future date or if we decide to voluntarily pursue FDA premarket review of our CELsignia tests, there can be no assurance that our CELsignia tests or any tests we may develop in the future will be cleared or approved by the FDA on a timely basis, if at all, nor can there be assurance that labeling claims will be consistent with our current claims or adequate to support continued adoption of and reimbursement for our CELsignia tests. If our CELsignia tests are allowed to remain on the market but there is uncertainty in the marketplace about our tests, if they are labeled investigational by the FDA, or if labeling claims the FDA allows us to make are more limited than we expect, reimbursement may be adversely affected and we may not be able to sell our CELsignia tests. Compliance with FDA regulations would increase the cost of conducting our business and subject us to heightened regulation and scrutiny by the FDA and penalties for failure to comply with these requirements.

If we fail to obtain required federal and state laboratory licenses, we could lose the ability to perform our tests.

Clinical laboratory tests, including our CELsignia tests, are regulated under CLIA. CLIA is a federal law that regulates clinical laboratories that perform testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention or treatment of disease. CLIA regulations mandate specific standards for laboratories in the areas of personnel qualifications, administration, and participation in proficiency testing, patient test management and quality assurance. CLIA certification is also required in order for us to be eligible to bill state and federal healthcare programs, as well as many private third-party payers, for any tests we launch. We will also be required to maintain state licenses in certain states to conduct testing in our laboratories. While we currently have CLIA certification for our Minnesota laboratory, failure to maintain this certification would adversely affect our ability to launch our CELsignia tests.

CELsignia Risks Related to Intellectual Property

If we are unable to obtain and maintain intellectual property protection for our CELsignia technology, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and diagnostic tests similar or identical to ours, and our ability to successfully commercialize our technology and diagnostic tests may be impaired.

Our ability to compete successfully will depend in part on our ability to obtain and enforce patent protection for our products, preserve our trade secrets and operate without infringing the proprietary rights of third parties. We have applied for patents that protect our technology. Our patent portfolio includes three issued U.S. patents, five issued international patents, five pending U.S. patent applications, 23 pending non-U.S. patent applications, one pending international PCT patent application, and numerous corresponding non-U.S. patent applications. Each patent and patent application covers methods of use. However, we cannot assure you that our intellectual property position will not be challenged or that all patents for which we have applied will be granted. The validity and breadth of claims in patents involve complex legal and factual questions and, therefore, may be highly uncertain. Uncertainties and risks that we face include the following:

- our pending or future patent applications may not result in the issuance of patents;
- the scope of any existing or future patent protection may not exclude competitors or provide competitive advantages to us;
- our patents may not be held valid if subsequently challenged;
- other parties may claim that our products and designs infringe the proprietary rights of others, and even if we are successful in defending our patents and proprietary rights, such litigation may be costly; and
- other parties may develop similar products, duplicate our products, or design around our patents.

The patent prosecution process is expensive and time-consuming, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner, or in all jurisdictions. We may choose not to seek patent protection for certain innovations and may choose not to pursue patent protection in certain jurisdictions, and under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope. It is also possible that we will fail to identify patentable aspects of our discovery and nonclinical development output before it is too late to obtain patent protection.

The patent position of companies like ours is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. The U.S. Patent and Trademark Office, or U.S. PTO, has not established a consistent policy regarding the breadth of claims that it will allow in medical technology patents. In addition, the laws of foreign jurisdictions may not protect our rights to the same extent as the laws of the United States. For example, India and China do not allow patents for methods of treating the human body. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or CELsignia tests, in whole or in part, or which effectively prevent others from commercializing competitive technologies and diagnostic tests. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. PTO or patent offices in foreign jurisdictions, or become involved in opposition, derivation, reexamination, inter parties review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology and compete directly with us, without payment to us, or result in our inability to commercialize CELsignia platform without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to develop or commercialize current or future CELsignia tests.

Even if our owned patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and product candidates, or limit the duration of the patent protection of our technology and potential diagnostic tests. Given the amount of time required for the development, testing and regulatory review of new diagnostic tests, patents protecting such tests might expire before or shortly after such candidates are commercialized. As a result, our owned patent portfolio may not provide us with sufficient rights to exclude others from commercializing diagnostic tests similar or identical to ours.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

The commercial success of CELsignia tests depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our CELsignia tests and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the medical technology, biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our CELsignia platform, including interference or derivation proceedings before the U.S. PTO and similar bodies in other jurisdictions. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our CELsignia platform and CELsignia tests. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our CELsignia platform or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we are not able to prevent disclosure of our trade secrets and other proprietary information, the value of our CELsignia platform could be significantly diminished.

We rely on trade secret protection to protect our interests in proprietary know-how and in processes for which patents are difficult to obtain or enforce. We may not be able to protect our trade secrets adequately. We have a policy of requiring our consultants, advisors and strategic partners to enter into confidentiality agreements and our employees to enter into invention, non-disclosure and non-compete agreements. However, no assurance can be given that we have entered into appropriate agreements with all parties that have had access to our trade secrets, know-how or other proprietary information. There is also no assurance that such agreements will provide meaningful protection of our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure of information. Furthermore, we cannot provide assurance that any of our employees, consultants, contract personnel, or strategic partners, either accidentally or through willful misconduct, will not cause serious damage to our programs and/or our strategy, for example by disclosing important trade secrets, know-how or proprietary information to our competitors. It is also possible that our trade secrets, know-how or other proprietary information could be obtained by third parties as a result of breaches of our physical or electronic security systems. Any disclosure of confidential data into the public domain or to third parties could allow our competitors to learn our trade secrets and use the information in competition against us. In addition, others may independently discover our trade secrets and proprietary information. Any action to enforce our rights is likely to be time consuming and expensive, and may ultimately be unsuccessful, or may result in a remedy that is not commercially valuable. These risks are accentuated in foreign countries where laws or law enforcement practices may not protect proprietary rights as fully as in the United States. Any unauthorized disclosure of our trade secrets or proprietary information could harm our competitive position.

Other Risks Related to Government Regulation for Our Business

Failure to comply with the HIPAA security and privacy regulations may increase our operational costs.

A portion of the data that we obtain and handle for or on behalf of our clients is considered protected health information, or PHI, subject to HIPAA. Under HIPAA and our contractual agreements with our HIPAA-covered entity health plan customers, we are considered a "business associate" to those customers, and are required to maintain the privacy and security of PHI in accordance with HIPAA and the terms of our business associate agreements with our clients, including by implementing HIPAA-required administrative, technical and physical safeguards. We are also required to maintain similar business associate agreements with our subcontractors that have access to PHI of our customers in rendering services to us or on our behalf. We will incur significant costs to establish and maintain these safeguards and, if additional safeguards are required to comply with HIPAA regulations or our clients' requirements, our costs could increase further, which would negatively affect our operating results. Furthermore, we cannot guarantee that such safeguards have been and will continue to be adequate under applicable laws. If we have failed, or fail in the future, to maintain adequate safeguards, or we or our agents or subcontractors use or disclose PHI in a manner prohibited or not permitted by HIPAA, our subcontractor business associate agreements, or our business associate agreements with our customers, or if the privacy or security of PHI that we obtain and handle is otherwise compromised, we could be subject to significant liabilities and consequences.

We will also need to expend a considerable amount of resources complying with other federal, state and foreign laws and regulations. If we are unable to comply or have not complied with such laws, we could face substantial penalties or other adverse actions.

Our operations are subject, directly or indirectly, to other federal, state and foreign laws and regulations that are complex and their application to our specific products, services and relationships may not be clear and may be applied to our business in ways that we do not anticipate. Compliance with laws and regulations will require us to expend considerable resources implementing internal policies and procedures for compliance and ongoing monitoring and will require significant attention of our management team. This will be challenging as an early-stage company with limited financial resources and human capital. These laws include, for example:

- Title XI of the Social Security Act, commonly referred to as the federal Anti-Kickback Statute, which prohibits the knowing and willful offer, payment, solicitation or receipt of remuneration, directly or indirectly, in cash or in kind, in return for or to reward the referral of patients or arranging for the referral of patients, or in return for the recommendation, arrangement, purchase, lease or order of items or services that are covered, in whole or in part, by a federal healthcare program such as Medicare or Medicaid;
- The civil False Claims Act, that forbids the knowing submission or "causing the submission" of false or fraudulent information or the failure to disclose information in connection with the submission and payment of claims for reimbursement to Medicare, Medicaid, federal healthcare programs or private health plans;
- The federal Physician Self-referral Law, commonly known as the Stark Law, which prohibits physicians from referring Medicare or Medicaid patients to providers of "designated health services" with whom the physician or a member of the physician's immediate family has an ownership interest or compensation arrangement, unless a statutory or regulatory exception applies, and similar state equivalents that may apply regardless of payor; and
- The U.S. Foreign Corrupt Practices Act of 1977, as amended, or FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, and the USA PATRIOT Act, which among other things, prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector.

Many states and foreign governments have adopted similar laws and regulations. Violations of law could subject us to civil or criminal penalties, monetary fines, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations. We could also be required to change or terminate some portions of operations or business or could be disqualified from providing services to healthcare providers doing business with government programs.

Risks Related to Our Reliance on Third Parties

We will rely on third parties to conduct certain aspects of our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for, or commercialize, any potential product candidates.

We will depend upon third parties to conduct certain aspects of our preclinical studies and depend on third parties, including independent investigators, to conduct our clinical trials, under agreements with universities, medical institutions, contract research organizations, or CROs, strategic partners and others. We expect to negotiate budgets and contracts with such third parties, which may result in delays to our development timelines and increased costs.

We continue to build our infrastructure and hire personnel necessary to execute our operational plans. We will rely especially heavily on third parties over the course of our clinical trials, and, as a result, may have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of clinical trial sponsors, clinical investigators and clinical trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP requirements and may require a large number of patients.

Our failure or any failure by these third parties to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be adversely affected if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting aspects of our preclinical studies or our clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our preclinical studies and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the preclinical or clinical data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements or for other reasons, our development timelines, including clinical development timelines, may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed or precluded entirely.

The pharmaceutical companies that we partner with may not be successful in receiving regulatory approval for drug indications or may not commercialize their companion therapies for our expected companion diagnostic programs.

While we intend to provide our pharmaceutical company partners with new patient populations for such partners' existing or investigational targeted therapies, there can be no assurances that such partners will be able to obtain regulatory approval for new indications to treat these patient populations or otherwise be successful in commercializing these new therapies. The pharmaceutical companies we partner with:

- may not meet clinical trial endpoint targets in evaluating efficacy of a targeted therapy in the patient population;
- may encounter regulatory or production difficulties that could constrain the supply of the companion therapies;
- may have difficulties gaining acceptance of the use of the companion therapies in the clinical community;
- may not pursue commercialization of any companion therapies;
- may elect not to continue or renew commercialization programs based on changes in their strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- may not commit sufficient resources to the marketing and distribution of such companion therapies; or
- may terminate their relationship with us.

Any of these factors could adversely affect our commercialization strategy, business, results of operations and financial condition.

Our reliance on third parties to formulate and manufacture our drug product will expose us to a number of risks that may delay the development, regulatory approval and commercialization of our drug product or result in higher product costs.

We have no direct experience in drug formulation or manufacturing and do not intend to establish our own manufacturing facilities. We lack the resources and expertise to formulate or manufacture our own product candidates. Instead, we will contract with one or more manufacturers to manufacture, supply, store and distribute drug supplies for our clinical trials. If our drug product receives FDA approval, we will rely on one or more third-party contractors to manufacture our drugs. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to risks that, among other things, we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must approve any replacement contractor; our third-party manufacturers might be unable to formulate and manufacture our drugs in the volume and of the quality required to meet our clinical and/or commercial needs, if any; our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products; and our contract manufacturers may fail to comply with good manufacturing practice and other government regulations and corresponding foreign standards. Each of these risks could delay our clinical trials, the approval, if any, of our product candidates by the FDA, or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenues.

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

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The U.S. PTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Depending on future actions by the U.S. Congress, the federal courts, and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. In addition, there may be patent law reforms in foreign jurisdictions that could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents in those foreign jurisdictions.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Our current and future employees may have been previously employed at universities or other biotechnology, diagnostic technology or pharmaceutical companies, including our competitors or potential competitors and strategic partners. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or 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 prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Any lawsuits relating to infringement of intellectual property rights necessary to defend ourselves or enforce our rights will be costly and time consuming and could be unsuccessful.

Because competition in our industry is intense, competitors may infringe or otherwise violate our issued patents, patents of our licensors or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming, and could distract our technical and management personnel from their normal responsibilities. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could be significant. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure.

Risks Relating to Our Common Stock

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors will be responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any of these provisions of our charter documents or Delaware law could, under certain circumstances, depress the market price of our common stock.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock or could subject us to securities litigation.

Our stock price may be extremely volatile. The stock market in general and the market for smaller medical technology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell our common stock at or above the price they paid for such stock. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of planned clinical trials of our CELsignia HER2 Pathway Activity Test, CELsignia Multi-Pathway Activity Test or other CELsignia tests may develop in the future;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our CELsignia tests or clinical development programs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- operating results that fail to meet expectations of securities analysts that cover our company;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical, biotechnology and medical technology sectors;
- sales of our stock by us, our insiders and our other stockholders;
- general economic and market conditions; and
- the other factors described in this “Risk Factors” section.

Additionally, companies that have experienced volatility in the market price of their stock have been subject to an increased incidence of securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management’s attention from other business concerns, which could seriously harm our business.

If securities or industry analysts do not publish research or reports about our business, or publish negative reports about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us or provide favorable coverage. If one or more of the analysts who cover us downgrade our stock or change their opinion of our stock, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting of Section 404(b) of the Sarbanes-Oxley Act;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this report. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the continued listing requirements of The Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our ongoing legal and financial compliance costs and will make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. Depending upon our filer status, if we cease to be an emerging growth company, we could also be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm as required by Section 404(b). While we, as of December 31, 2021, concluded that our internal control over financial reporting was effective, we may need to dedicate additional internal resources and engage outside consultants to maintain compliance with Section 404 in the future. Any material weaknesses that we may identify in the future could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

ITEM 1B. Unresolved Staff Comments

None.

ITEM 2. Properties

We currently lease and occupy approximately 16,000 square feet in Minneapolis, Minnesota, which includes our clinical laboratory and offices. The amended lease expires in April 2023 and is renewable with the right to extend the term for one additional year and provides for monthly rent, real estate taxes and operating expenses. We believe that this leased space is adequate to meet current and anticipated future requirements and that additional or substitute space will be available as needed to accommodate any expansions that our operations require.

ITEM 3. Legal Proceedings

From time to time we may be involved in disputes or litigation relating to claims arising out of our operations. We are not currently a party to any legal proceedings that could reasonably be expected to have a material adverse effect on our business, financial condition and results of operations.

ITEM 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Price Information

Our common stock has been listed on The Nasdaq Capital Market under the symbol "CELC" since September 20, 2017.

As of March 15, 2022, there were approximately 43 holders of record of our common stock. The actual number of holders of common stock is greater than this number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain our future earnings, if any, to finance the operation and expansion of our business. We do not expect to pay cash dividends on our common stock in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, outstanding indebtedness and plans for expansion and restrictions imposed by lenders, if any.

Recent Sales of Unregistered Securities

The information required by this Item is incorporated herein by reference from Item 3.02 of the Company's Current Report on Form 8-K filed with the SEC on April 8, 2021.

Issuer Purchases of Equity Securities

None.

Equity Compensation Plan Information

The information required by this Item concerning equity compensation plans is incorporated herein by reference from Part III, Item 11 of this Annual Report.

Use of Proceeds from Registered Securities

On September 22, 2017, we issued and sold 2,760,000 shares of our common stock in the IPO at a public offering price of $9.50 per share, for aggregate gross proceeds of $26.2 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-220128), which was declared effective by the SEC on September 19, 2017. Craig-Hallum Capital Group LLC acted as the sole manager for the offering. The offering terminated on September 22, 2017.

The net offering proceeds to us, after deducting underwriting discounts of approximately $1.8 million and offering expenses paid by us totaling approximately $1.1 million, were approximately $23.3 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

At December 31, 2021, the net proceeds were used in furtherance of our planned use of proceeds, which includes funding additional research and development for discovery of new cancer sub-types and development and validation of new CELsignia tests; clinical trials to support clinical claims; development of operational processes and capital expenditures; and working capital and other general corporate purposes. As of December 31, 2021, all proceeds from the IPO have been utilized.

ITEM 6. Reserved.

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

You should read the following discussion and analysis of our financial condition and results of operations together in conjunction with our financial statements and the related notes included elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and expected financial results, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" discussed in Item 1A of Part I of this Annual Report.

OVERVIEW

We are a clinical-stage biotechnology company seeking to extend the lives of cancer patients by pursing an integrated therapeutic (Rx) and companion diagnostic (CDx) strategy. Our therapeutic efforts are focused on developing potential first-in-class or best-in-class molecularly targeted therapies that address the same cancer driver a CELsignia companion diagnostic can identify. CELsignia is uniquely able to analyze live patient tumor cells to identify new groups of cancer patients likely to benefit from targeted therapies. This enables a CELsignia CDx to support advancement of new indications for already approved targeted therapies. We believe this integrated Rx and CDx strategy will maximize the impact our drug development efforts have on the treatment landscape for cancer patients.

The first drug candidate we are developing internally is gedatolisib, a potent, well-tolerated, small molecule dual inhibitor, administered intravenously, that selectively targets all class I isoforms of PI3K and mammalian target of rapamycin (mTOR). In April 2021, we obtained exclusive global development and commercialization rights to gedatolisib under a license agreement with Pfizer, Inc. We believe gedatolisib's unique mechanism of action, favorable pharmacokinetic properties, and intravenous formulation offer distinct advantages over currently approved and investigational therapies that target PI3K or mTOR alone or together.

- **Overcomes limitations of therapies that only inhibit a single class I PI3K isoform or only one mTOR kinase complex**

  Gedatolisib is a pan-class I isoform PI3K inhibitor with low nanomolar potency for the p110α, p110β, p110γ, and p110δ isoforms. Each isoform is known to preferentially affect different signal transduction events that involve tumor cell survival, depending upon the aberrations associated with the linked pathway. When a therapy only inhibits a single class I isoforms (e.g., alpelisib, a PI3K-α inhibitor) or only one mTOR kinase complex (e.g., everolimus, an mTORC1 inhibitor), numerous feedforward and feedback loops between the PI3K isoforms and mTOR cross-activates the uninhibited sub-units. This, in turn, induces compensatory resistance that reduces the efficacy of isoform specific PI3K or single mTOR kinase complex inhibitors. Inhibiting all four PI3K isoforms and both mTOR complexes, as gedatolisib does, thus prevents the confounding effect of isoform interaction that may occur with isoform-specific PI3K inhibitors and the confounding interaction between PI3K isoforms and mTOR.

- **Better tolerated by patients than oral PI3K and mTOR drugs.**

  Gedatolisib is administered intravenously (IV) on a four-week cycle of three weeks-on, one week-off, in contrast to the orally administered pan-PI3K or dual PI3K/mTOR inhibitors that are no longer being clinically developed. Oral pan-PI3K or PI3K/mTOR inhibitors have repeatably been found to induce significant side effects that were not well tolerated by patients. This typically leads to a high proportion of patients requiring dose reductions or treatment discontinuation. The challenging toxicity profile of these drug candidates ultimately played a significant role in the decisions to halt their development, despite showing promising efficacy. By contrast, gedatolisib stabilizes at lower concentration levels in plasma compared to orally administered PI3K inhibitors, resulting in less toxicity, while maintaining concentrations sufficient to inhibit PI3K/mTOR signaling.

  Isoform-specific PI3K inhibitors administered orally were developed to reduce toxicities in patients. While the range of toxicities associated with isoform-specific inhibitors is narrower than oral pan-PI3K or PI3K/mTOR inhibitors, administering them orally on a continuous basis still leads to challenging toxicities. The experience with an FDA approved oral p110-α specific inhibitor, Piqray, illustrates the challenge. In its Phase 3 pivotal trial Piqray was found to induce a Grade 3 or 4 adverse event (AE) related to hyperglycemia in 39% of patients evaluated. In addition, 26% of patients discontinued alpelisib due to treatment related adverse events. By contrast, in the 103-patient dose expansion portion of the Phase 1b clinical trial with gedatolisib, only 7% of patients experienced Grade 3 or 4 hyperglycemia and less than 10% discontinued treatment.

As of December 31, 2021, 492 patients with solid tumors have received gedatolisib in eight clinical trials sponsored by Pfizer. Of the 492 patients, 129 were treated with gedatolisib as a single agent in three clinical trials. The remaining 363 patients received gedatolisib in combination with other anti-cancer agents in five clinical trials. Additional patients received gedatolisib in combination with other anti-cancer agents in nine investigator sponsored clinical trials.

A Phase 1b trial (B2151009) evaluating patients with HR+/HER2- metastatic breast cancer was initiated in 2016 and subsequently enrolled 138 patients. Twelve patients from this study continue to receive study treatment, as of December 31, 2021, ten of whom have received study treatment for more than three years. The B2151009 clinical was an open label, multiple arm Phase 1b study that evaluated gedatolisib in combination with palbociclib (CDK4/6 inhibitor) and fulvestrant or letrozole in patients with HR+/HER2- advanced breast cancer. Thirty-five patients were enrolled in two dose escalation arms to evaluate the safety and tolerability and to determine the maximum tolerated dose (MTD) of gedatolisib when used in combination with the standard doses of palbociclib and endocrine therapy (letrozole or fulvestrant). The MTD was determined to be 180 mg administered intravenously once weekly. A total of 103 patients were subsequently enrolled in one of four expansion arms (A, B, C, D).

High objective overall response rates were observed in all four expansion arms and were comparable in each arm for PIK3CA WT and PIK3CA MT patients. In treatment-naïve patients (Arm A), ORR was 85%. In patients who received prior hormonal therapy alone or in combination with a CDK4/6 inhibitor (Arms B, C, and D), ORR ranged from 32% to 77%. Each arm achieved its primary endpoint target, which was reporting higher ORR in the study arm than ORR from either the PALOMA-2 (ORR=55%) study that evaluated palbociclib plus letrozole for Arm A or the PALOMA-3 study (ORR=25%) that evaluated palbociclib plus fulvestrant for Arms B, C, and D. For all enrolled patients, a clinical benefit rate (CBR) of ≥79% was observed. Median progression-free survival (PFS) was 31.1 months for patients receiving first-line treatment (Arm A) and 12.9 months for patients who received a prior CDK4/6 inhibitor and were treated in the study with the Phase 3 dosing schedule (Arm D).

Gedatolisib combined with palbociclib and endocrine therapy demonstrated a favorable safety profile with manageable toxicity. The majority of treatment emergent adverse events were Grade 1 and 2. The most frequently observed adverse events included stomatitis/mucosal inflammation, the majority of which were Grade 1 and 2. The most common Grade 4 AEs were neutropenia and neutrophil count decrease, which were assessed as related to treatment with palbociclib. No grade 5 events were reported in this study.

We are preparing to initiate VIKTORIA-1, a Phase 3, open-label, randomized clinical trial to evaluate the efficacy and safety of two regimens in adults with HR+/HER2- advanced breast cancer whose disease has progressed after prior CDK4/6 therapy in combination with an aromatase inhibitor: 1) gedatolisib in combination with palbociclib and fulvestrant; and 2) gedatolisib in combination with fulvestrant. We expect to initiate the VIKTORIA-1 study in the first half of 2022.

The clinical trial will enable separate evaluation of subjects according to their PIK3CA status. Subjects who meet eligibility criteria and are PIK3CA WT will be randomly assigned (1:1:1) to receive a regimen of either gedatolisib, palbociclib, and fulvestrant (Arm A), gedatolisib and fulvestrant (Arm B), or fulvestrant (Arm C). Subjects who meet eligibility criteria and are PIK3CA MT will be randomly assigned (1:1) to receive a regimen of either gedatolisib, palbociclib, and fulvestrant (Arm D) or alpelisib and fulvestrant (Arm E).

On January 13, 2022, gedatolisib was granted Fast Track designation for the treatment of patients with ER+/HER2- metastatic breast cancer after progression on CDK4/6 therapy. Fast Track designation is granted by the FDA for products that are intended for the treatment of serious or life-threatening disease or conditions and which demonstrate the potential to address an unmet medical need. The designation offers the opportunity for frequent interactions with the FDA to discuss the drug’s development plan and to ensure collection of appropriate data needed to support drug approval, as well as eligibility for rolling submission of a New Drug Application.

Our proprietary CELsignia diagnostic platform is the only commercially ready technology we are aware of that uses a patient’s living tumor cells to identify the specific abnormal cellular process driving a patient’s cancer and the targeted therapy that best treats it. This enables us to identify patients whose tumors may respond to a targeted therapy, even though they lack a previously associated molecular mutation. By identifying cancer patients whose tumors lack an associated genetic mutation but have abnormal cellular activity a matching targeted therapeutic is designed to inhibit, CELsignia CDx can expand the markets for a number of already approved targeted therapies. Our current CDx identifies breast and ovarian cancer patients whose tumors have cancer drivers potentially responsive to treatment with human epidermal growth factor receptor 2-negative (HER2), mesenchymal-epithelial transition factor (c-MET), or phosphatidylinositol 3-kinases (PI3K) targeted therapeutics. While U.S. Food and Drug Administration (“FDA”) approval or clearance is not currently required for CELsignia tests offered as a stand-alone laboratory developed test, if we are partnered with a drug company to launch a CELsignia test as a companion diagnostic for a new drug indication, we would be required to obtain premarket approval, or PMA, in conjunction with the pharmaceutical company seeking a new drug approval for the matching therapy.

We are supporting the advancement of new potential indications for four different targeted therapies, controlled by other pharmaceutical companies, that would rely on a CELsignia CDx to select patients. Five Phase 2 trials are underway to evaluate the efficacy and safety of these therapies in CELsignia selected patients. These patients are not currently eligible to receive these drugs and are not identifiable with a molecular test.

Supporting the development of a potential first-in-class targeted therapy for breast cancer, like gedatolisib, with our CELsignia platform is a natural extension of our strategy to use our CELsignia CDx to enable new indications for other companies' targeted therapies. By combining companion diagnostics designed to enable proprietary new drug indications with targeted therapies that treat signaling dysregulation our CDx identifies, we believe we are uniquely positioned to improve the standard-of-care for many early and late-stage breast cancer patients. Our goal is to play a key role in the multiple treatment approaches required to treat breast cancer patients at various stages of their disease. With each program, we are:

- Leveraging the proprietary insights CELsignia provides into live patient tumor cell function
- Using a CELsignia CDx to identify new patients likely to respond to the paired targeted therapy
- Developing a new targeted therapeutic option for breast cancer patients
- Maximizing the probability of getting regulatory approval to market the targeted therapy indication

We have not generated any revenue from sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not and have never been profitable and have incurred losses in each period since we began operations in 2012. For the years ended December 31, 2021 and 2020, we reported a net loss of approximately $29.6 million and $9.5 million, respectively. As of December 31, 2021, our cash and cash equivalents were approximately $84.3 million, and we had an accumulated deficit of approximately $55.9 million.

Impact of COVID-19 on our Business

A novel strain of coronavirus (COVID-19) was first identified in Wuhan, China in December 2019, and subsequently declared a pandemic by the World Health Organization. The impact of the COVID-19 pandemic on our business is discussed in further detail below:

Health and Safety

To help protect the health and safety of our employees, suppliers and collaborators, we took proactive, aggressive action from the earliest signs of the outbreak. We enacted rigorous safety measures in our laboratory and administrative offices, including implementing social distancing protocols, allowing working from home for those employees that do not need to be physically present in a lab to perform their work, suspending travel, implementing temperature checks at the entrances to our facilities, extensively and frequently disinfecting our workspaces and providing masks to those employees who must be physically present. We expect to continue with these measures until the COVID-19 pandemic is contained and we may take further actions as government authorities require or recommend or as we determine to be in the best interests of our employees, suppliers, and collaborators.

Clinical Trials and Collaborations

As a result of the COVID-19 pandemic, governmental authorities have implemented and are continuing to implement numerous and constantly evolving measures to try to contain the virus, such as travel bans and restrictions, limits on gatherings, quarantines, shelter-in-place orders, and business shutdowns. As we continue to advance our clinical trial collaborations, we are in close contact with our current clinical sponsors, and principal investigators, as well as prospective pharmaceutical company and clinical collaborators, to assess the impact of COVID-19 on our trial enrollment timelines and collaboration discussions. In light of the COVID-19 pandemic, the focus of healthcare providers and hospitals on fighting the virus, and consistent with the FDA's updated industry guidance for conducting clinical trials issued on March 18, 2020, we are experiencing delays in the enrollment of patients in our ongoing clinical trials. We now expect interim results from the FACT-1 and FACT-2 trials to be delayed until the first half of 2023 and final results approximately nine months later. As the impact of COVID-19 on our industry becomes clearer, we may need to reassess the timing of our anticipated clinical milestones. Prospective clinical trial collaborations with pharmaceutical companies and sponsors may also be delayed but the impact on the timing of finalizing agreements is not yet known.

Research and Development

While our facility currently remains operational, the evolving measures to try to contain the virus have impacted and may further impact our workforce and operations, as well as those of our vendors and suppliers. Our laboratory remains operational as of this date, but, in response to the COVID-19 pandemic, we have implemented protective policies that reduce the number of research and development staff operating in our laboratory at any one time. While governmental measures may be modified or extended, we expect that our research and development and clinical laboratory will remain operational. However, in light of the focus of healthcare providers and hospitals on fighting the virus, several of the clinical sites that provide us tumor tissue for research have halted this service, reducing the number of new tumor tissue specimens we would typically expect to receive. These various constraints may slow or diminish our research and development activities. In addition, cancer research-related industry meetings, such as the American Association for Cancer Research (AACR), were delayed for several months. Our submissions to present research results at these meetings were accepted, but the release of the results was postponed in conjunction with the delayed meeting schedules.

Liquidity

Although there is uncertainty related to the anticipated impact of the recent COVID-19 outbreak on our future results, we believe our existing balance of cash and cash equivalents will be sufficient to meet our cash needs arising in the ordinary course of business for at least the next twelve months. We continue to monitor the rapidly evolving situation and guidance from federal, state and local public health authorities and may take additional actions based on their recommendations. In these circumstances, there may be developments outside our control requiring us to adjust our operating plan. In addition, see Item 1A of Part I of this Annual Report for additional information on risks associated with pandemics in general and COVID-19 specifically and how those risks may impact our business and operations.

RESULTS OF OPERATIONS

Components of Operating Results

Revenue

To date, we have not generated any revenue. Initially, our ability to generate revenue will depend primarily upon our ability to obtain partnership agreements with pharmaceutical companies to provide companion diagnostics for such pharmaceutical partners' existing or investigational targeted therapies. We expect these partnerships to generate significant revenue from the sale of tests to identify patients eligible for clinical trials, from milestone payments, and, potentially, from royalties on the incremental drug revenues our tests enable. Once a new drug indication is received that requires use of our companion diagnostic to identify eligible patients, we expect to generate revenues from sales of tests to treating physicians. With the execution of the Pfizer license agreement in April 2021, whereby we acquired exclusive world-wide licensing rights to develop and commercialize gedatolisib, we expect to conduct clinical trials to support potential regulatory approval to market gedatolisib. If we obtain regulatory approvals to market gedatolisib, we expect to generate revenue from sales of the drug for the treatment of breast cancer patients.

Research and Development

Since our inception, we have primarily focused on research and development of our CELsignia platform, development and validation of our CELsignia tests, and research related to the discovery of new cancer sub-types. Beginning in April 2021, we are also focusing on development of gedatolisib, a PI3K/mTOR targeted therapy. Research and development expenses primarily include:

- employee-related expenses related to our research and development activities, including salaries, benefits, recruiting, travel and stock-based compensation expenses;
- laboratory supplies;
- consulting fees paid to third parties;
- clinical trial costs;
- manufacturing validation costs for gedatolisib
- facilities expenses; and
- legal costs associated with patent applications.

Internal and external research and development costs are expensed as they are incurred. As we initiate a Phase 3 clinical trial for gedatolisib and continue to expand clinical trials to evaluate efficacy of targeted therapies in cancer patients selected with one of our CELsignia tests, the proportion of research and development expenses allocated to external spending will grow at a faster rate than expenses allocated to internal expenses.

General and Administrative

General and administrative expenses consist primarily of salaries, benefits and stock-based compensation related to our executive, finance and support functions. Other general and administrative expenses include professional fees for auditing, tax, and legal services associated with being a public company, director and officer insurance and travel expenses for our general and administrative personnel.

Sales and Marketing

Sales and marketing expenses consist primarily of professional and consulting fees related to these functions. To date, we have incurred immaterial sales and marketing expenses as we continue to focus primarily on the development of our first drug, gedatolisib, development of our CELsignia platform and corresponding CELsignia tests. We expect to begin to incur increased selling and marketing expenses in anticipation of regulatory approval to market gedatolisib and the commercialization of our first CELsignia tests. These increased expenses are expected to include payroll-related costs as we add employees in the commercial departments, costs related to the initiation and operation of our sales and distribution network and marketing related costs.

Interest Expense

Interest expense is primarily due to a loan agreement and finance lease obligations.

Interest Income

Interest income consists of interest income earned on our cash and cash equivalents.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

	Years Ended December 31,		Increase (Decrease)	
	2021	**2020**	**$**	**Percent Change**
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 25,758,006	$ 7,683,522	$ 18,074,484	235%
General and administrative	2,597,909	1,872,642	725,267	39
Total operating expenses	28,355,915	9,556,164	18,799,751	197
Loss from operations	(28,355,915)	(9,556,164)	(18,799,751)	197
Other income (expense)				
Interest expense	(1,262,350)	(120)	(1,262,230)	n/a
Interest income	13,262	82,109	(68,847)	(84)
Loss on sale of fixed assets	(263)	-	(263)	n/a
Other income (expense), net	(1,249,351)	81,989	(1,331,341)	n/a
Net loss before income taxes	(29,605,266)	(9,474,175)	(20,131,091)	212
Income tax benefits	-	-	-	-
Net loss	$ (29,605,266)	$ (9,474,175)	$ (20,131,091)	212%

Research and Development

For the year ended December 31, 2021, our research and development expenses were approximately $25.8 million, representing an increase of approximately $18.1 million, or 235%, compared to the same period in 2020. The increase primarily resulted from a $10.0 million upfront license fee related to the execution of the Pfizer license agreement, which included $5.0 million of non-cash expense for the issuance of common stock. The remaining $8.1 million increase primarily resulted from expenses related to the support and development of gedatolisib. Employee related expenses, including consulting fees, accounted for a $3.4 million increase. The increase of $3.4 million included an increase of $0.6 million in non-cash stock-based compensation. The remaining increase of $4.7 million is related to clinical trials, costs associated with the transfer of the gedatolisib-related activities from Pfizer to Celcuity and patent legal fees.

Conducting a significant amount of research and development is central to our business model. We plan to increase our research and development expenses for the foreseeable future as we seek to develop gedatolisib, discover new cancer sub-types, and develop and validate additional CELsignia tests to diagnose such sub-types. We also expect to incur increased expenses to support companion diagnostic business development activities with pharmaceutical companies as we develop additional CELsignia tests and initiate a clinical trial for gedatolisib.

General and Administrative

For the year ended December 31, 2021, our total general and administrative expenses were $2.6 million, representing an increase of approximately $0.7 million, or 39%, compared to the same period in 2020. The increase primarily resulted from a $0.4 million increase in compensation related expenses, including approximately $0.3 million of non-cash stock-based compensation. In addition, other general and administrative expenses increased $0.3 million primarily due to professional fees associated with being a public company and director and officer insurance.

We anticipate that our general and administrative expenses will increase in future periods, reflecting both increased costs in connection with the potential future commercialization of gedatolisib and CELsignia tests, an expanding infrastructure, and increased professional fees associated with being a public company.

Interest Expense

For the year ended December 31, 2021, interest expense was $1.3 million and represents an increase of $1.3 million compared to the same period in 2020. The increase is due to the loan agreement that was executed in April 2021 and includes $0.6 million of non-cash interest expense.

Interest Income

For the year ended December 31, 2021, interest income decreased approximately $0.1 million compared to the same period in 2020. The decrease was primarily the result of lower market interest rates.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception, we have incurred losses and cumulative negative cash flows from operations. Through December 31, 2021, we raised capital of approximately $13.7 million and $7.5 million through private placements of common equity and unsecured convertible notes, respectively. On September 22, 2017, we closed on the IPO of our common stock, which generated approximately $23.3 million of additional cash after taking into account underwriting discounts and commissions and offering expenses. On June 5, 2020, we entered into an At Market Issuance Sales Agreement with B. Riley, FBR, Inc (the "ATM Agreement"). The ATM Agreement allowed us to sell shares of common stock up to an aggregate offering price of $10.0 million. Through December 31, 2021, we generated approximately $0.1 million of additional cash through sales pursuant to the ATM Agreement, after taking into account commissions and offering expenses. On February 26, 2021, we completed a follow-on offering of our common stock, which generated approximately $25.8 million of additional cash after taking into account underwriting discounts and offering expenses. In conjunction with the follow-on offering, the ATM Agreement was terminated. On April 8, 2021, we entered into a loan agreement with Innovatus Life Sciences Lending Fund I, LP ("Innovatus"), whereby Innovatus agreed to loan up to $25 million in three tranches consisting of (i) a $15.0 million non-contingent term A loan that was funded on April 8, 2021, (ii) a $5 million term B loan to be funded upon our request no later than March 31, 2022, and (iii) a $5 million term C loan to be funded upon our request no later than March 31, 2023. Funding of the term B and C loan is subject to our ability to achieve certain milestones. Net proceeds generated from the loan agreement were $14.4 million. On July 1, 2021, we completed a follow-on offering of our common stock, which generated approximately $52.8 million of additional cash after taking into account underwriting discounts of and offering expenses.

Cash from these capital raising activities has been our primary source of funds for our operations since inception. As of December 31, 2021, our cash and cash equivalents were approximately $84.3 million, and we had an accumulated deficit of approximately $55.9 million.

In February of 2022, we entered into an Open Market Sale Agreement[SM] with Jefferies LLC, as agent ("Jefferies"), pursuant to which we may offer and sell, from time to time, through Jefferies, shares of our common stock having an aggregate offering price of up to $50,000,000. We will pay Jefferies a commission equal to 3.0% of the aggregate gross proceeds from each sale of such shares. To date, we have not yet made any sales under this arrangement.

We expect that our research and development and general and administrative expenses will increase as we continue development of gedatolisib, development and validation of our CELsignia platform and additional CELsignia tests, conduct research related to the discovery of new cancer sub-types, conduct clinical trials, and pursue other business development activities. We will also start to incur sales and marketing expenses as we commercialize our CELsignia tests and gedatolisib. We expect to use cash on hand to fund our research and development expenses, capital expenditures, working capital, sales and marketing expenses, and general corporate expenses, as well as for the increased costs associated with being a public company.

Based on our current business plan, we believe that our current cash on hand will provide sufficient cash to finance operations and pay obligations when due for at least the next twelve months.

We may seek to raise additional capital to expand our business, pursue strategic investments, and take advantage of financing or other opportunities that we believe to be in the best interests of the Company and our stockholders. Additional capital may be raised through the sale of common or preferred equity or convertible debt securities, entry into debt facilities or other third-party funding arrangements. The sale of equity and convertible debt securities may result in dilution to our stockholders and those securities may have rights senior to those of our common shares. Agreements entered into in connection with such capital raising activities could contain covenants that would restrict our operations or require us to relinquish certain rights. Additional capital may not be available on reasonable terms, or at all.

Cash Flows

The following table sets forth the primary sources and uses of cash for the years ended December 31:

	2021	2020
Net cash provided by (used in):		
Operating activities	$ (20,311,940)	$ (7,145,689)
Investing activities	(81,398)	(89,371)
Financing activities	93,041,808	137,969
Net increase (decrease) in cash and cash equivalents	$ 72,648,470	$ (7,097,091)

Operating Activities

Net cash used in operating activities was approximately $20.3 million for the year ended December 31, 2021 and consisted primarily of a net loss of approximately $29.6 million, offset by non-cash expense items of approximately $8.5 million and working capital changes of $0.8 million. Non-cash expense items of approximately $8.5 million primarily consisted of $5.0 million for issuance of common stock related to a license agreement, $2.6 million of stock-based compensation expense, non-cash interest expense of $0.6 million and depreciation expense of $0.3 million. The approximately $0.8 million of working capital changes was primarily due to an increase in accounts payable, slightly offset by an increase in prepaid assets.

Net cash used in operating activities was approximately $7.1 million for the year ended December 31, 2020 and consisted primarily of a net loss of approximately $9.5 million, adjusted for non-cash items of approximately $2.2 million and working capital changes of approximately $0.2 million. Non-cash expense items of approximately $2.2 million consisted of stock-based compensation expense of approximately $1.8 million and of depreciation of approximately $0.4 million. The working capital change was primarily due to approximately $0.2 million in accrued expenses.

Investing Activities

Net cash used in investing activities for the years ended December 31, 2021 and December 31, 2020 were flat at approximately $0.1 million and consisted of purchases of property and equipment.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was approximately $93.0 million. The $93.0 million primarily consisted of net proceeds from the sale of shares of our common stock through two follow-on offerings totaling $78.5 million and $14.4 million from net proceeds related to the closing of a loan agreement. The remaining $0.1 million was the result of proceeds from the exercise of common stock warrants and employee stock options and proceeds from employee stock purchases.

Net cash provided by financing activities for the year ended December 31, 2020 was approximately $0.1 million and primarily reflects net proceeds from the sale of shares of our common stock through the ATM Agreement and employee stock purchases.

RECENT ACCOUNTING PRONOUNCEMENTS

From time-to-time new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB, or other standard setting bodies and adopted by us as of the specified effective date. Unless otherwise discussed in Note 2 to our financial statements included elsewhere in this Annual Report, we believe that the impact of recently issued standards that are not yet effective will not have a material impact on our financial position or results of operations upon adoption.

CRITICAL ACCOUNTING POLICIES AND USE OF ESTIMATES

Our management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or Generally Accepted Accounted Principles ("U.S. GAAP"). The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances; the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates.

Our significant accounting policies are more fully described in Note 2 to our financial statements included elsewhere in this Annual Report. Of our significant accounting policies, we believe that the following are the most critical:

Stock-Based Compensation

Our stock-based compensation consists of common stock options and restricted stock issued to certain employees and nonemployees and our Employee Stock Purchase Plan ("ESPP"). We recognize compensation expense based on an estimated grant date fair value using the Black-Scholes option-pricing method. We have elected to account for forfeitures as they occur.

The inputs for the Black-Scholes valuation model require management's significant assumptions. Prior to our IPO, the price per share of common stock was determined by our board based on recent prices of common stock sold in private offerings. Subsequent to the IPO, the price per share of common stock is determined by using the closing market price on the Nasdaq Capital Market on the grant date. The risk-free interest rates are based on the rate for U.S. Treasury securities at the date of grant with maturity dates approximately equal to the expected life at the grant date. The expected life was based on the simplified method in accordance with SEC Staff Accounting Bulletin Nos. 107 and 110. The expected volatility was estimated based on historical volatility information of peer companies that are publicly available in combination with our calculated volatility since being publicly traded.

All assumptions used to calculate the grant date fair value of nonemployee options are generally consistent with the assumptions used for options granted to employees. In the event we terminate any of our consulting agreements, the unvested options issued in connection with such agreements would also be cancelled.

For grants of restricted stock, we record compensation expense based on the quoted fair value of the shares on the grant date over the requisite service period. Compensation expense for ESPP rights is recorded in line with each respective offering period.

Clinical Trial Costs

The Company records prepaid assets or accrued expenses for prepaid or estimated clinical trial costs conducted by third-party service providers, which includes the conduct of preclinical studies and clinical trials. These costs can be a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with service agreements with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its prepaid assets or accrued expenses. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollments may vary from the Company's estimates, resulting in an adjustment to expense in future periods. Changes in these estimates that result in material changes to the Company's prepaid assets or accrued expenses could materially affect the Company's results of operations.

ITEM 7A. Quantitative and Qualitative Disclosures About Market Risk

As a smaller reporting company, we are not required to provide disclosure pursuant to this item.

ITEM 8. Financial Statements and Supplementary Data

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and
Stockholders of Celcuity Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Celcuity, Inc. (the Company) as of December 31, 2021 and 2020, and the related statements of operations, changes in stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2021, and the related notes (collectively referred to as the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Boulay PLLP

We have served as the Company's auditor since 2017.
Minneapolis, Minnesota
March 23, 2022

PCAOB ID: 542

PART I. FINANCIAL INFORMATION

ITEM 1. Financial Statements

Celcuity Inc.
Balance Sheets

	December 31, 2021	December 31, 2020
Assets		
Current Assets:		
Cash and cash equivalents	$ 84,286,381	$ 11,637,911
Deposits	22,009	22,009
Deferred transaction costs	22,144	-
Payroll tax receivable	298,764	190,000
Prepaid assets	722,677	317,040
Total current assets	85,351,975	12,166,960
Property and equipment, net	312,444	558,876
Operating lease right-of-use assets	241,901	230,911
Total Assets	$ 85,906,320	$ 12,956,747
Liabilities and Stockholders' Equity:		
Current Liabilities:		
Accounts payable	$ 1,507,099	$ 217,377
Finance lease liabilities	5,850	5,810
Operating lease liabilities	189,858	187,518
Accrued expenses	802,893	774,612
Total current liabilities	2,505,700	1,185,317
Finance lease liabilities	2,449	8,299
Operating lease liabilities	61,771	60,861
Note payable, non-current	14,625,923	-
Total Liabilities	17,195,843	1,254,477
Stockholders' Equity:		
Preferred stock, $0.001 par value: 2,500,000 shares authorized; 0 shares issued and outstanding as of December 31, 2021 and December 31, 2020	-	-
Common stock, $0.001 par value: 25,000,000 shares authorized; 14,918,887 and 10,299,822 shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	14,919	10,300
Additional paid-in capital	124,622,405	38,013,551
Accumulated deficit	(55,926,847)	(26,321,581)
Total Stockholders' Equity	68,710,477	11,702,270
Total Liabilities and Stockholders' Equity	$ 85,906,320	$ 12,956,747

See accompanying notes to the financial statements

Celcuity Inc.
Statements of Operations

	Years Ended December 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 25,758,006	$ 7,683,522
General and administrative	2,597,909	1,872,642
Total operating expenses	28,355,915	9,556,164
Loss from operations	(28,355,915)	(9,556,164)
Other income (expense)		
Interest expense	(1,262,350)	(120)
Interest income	13,262	82,109
Loss on sale of fixed assets	(263)	-
Other income (expense), net	(1,249,351)	81,989
Net loss before income taxes	**(29,605,266)**	**(9,474,175)**
Income tax benefits	-	-
Net loss	**$ (29,605,266)**	**$ (9,474,175)**
Net loss per share, basic and diluted	$ (2.21)	$ (0.92)
Weighted average common shares outstanding, basic and diluted	13,382,553	10,266,884

See accompanying notes to the financial statements

Celcuity Inc.
Statements of Changes in Stockholders' Equity

	Common Stock		Additional Paid-In	Accumulated	
	Shares	Amount	Capital	Deficit	Total
Balance at December 31, 2019	10,253,988	$ 10,254	$ 36,134,723	$ (16,847,406)	$ 19,297,571
Stock-based compensation	15,686	16	1,763,863	-	1,763,879
Employee stock purchases	12,423	12	60,291	-	60,303
Issuance of common stock in an at-the-market ("ATM") offering	17,725	18	182,676	-	182,694
Issuance costs associated with ATM offering	-	-	(128,002)	-	(128,002)
Net loss	-	-	-	(9,474,175)	(9,474,175)
Balance at December 31, 2020	10,299,822	10,300	38,013,551	(26,321,581)	11,702,270
Stock-based compensation	2,964	3	2,609,932	-	2,609,935
Employee stock purchases	13,487	14	65,825	-	65,839
Exercise of common stock warrants	1,975	2	18,760	-	18,762
Exercise of common stock options, net of shares withheld for exercise price	27,051	27	63,393	-	63,420
Issuance of common stock upon closing of follow-on offerings, net of underwriting discounts and offering costs	4,221,100	4,221	78,526,363	-	78,530,584
Issuance of common stock in an at-the-market ("ATM") offering	3,082	3	38,959	-	38,962
Issuance costs associated with ATM offering	-	-	(3,868)	-	(3,868)
Issuance of common stock warrants, note payable	-	-	289,839	-	289,839
Issuance of common stock, licensing agreement	349,406	349	4,999,651	-	5,000,000
Net loss	-	-	-	(29,605,266)	(29,605,266)
Balance at December 31, 2021	14,918,887	$ 14,919	$ 124,622,405	$ (55,926,847)	$ 68,710,477

See accompanying notes to the financial statements

Celcuity Inc.
Statements of Cash Flows

	Years Ended December 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (29,605,266)	$ (9,474,175)
Adjustments to reconcile net loss to net cash used for operations:		
Depreciation	303,235	385,591
Stock-based compensation	2,609,935	1,763,879
Issuance of common stock, licensing agreement	5,000,000	-
Amortization of debt issuance costs and discount	267,821	-
PIK interest	300,001	-
Loss on sale of fixed assets	263	-
Changes in operating assets and liabilities:		
Payroll tax receivable	(108,764)	-
Prepaid assets and deposits	(405,637)	(42,440)
Accounts payable	1,305,932	52,971
Accrued expenses	28,280	190,293
Non-cash operating lease, net	(7,740)	(21,808)
Net cash used for operating activities	(20,311,940)	(7,145,689)
Cash flows from investing activities:		
Purchases of property and equipment	(81,898)	(89,371)
Proceeds from sale of property and equipment	500	-
Net cash used for investing activities	(81,398)	(89,371)
Cash flows from financing activities:		
Proceeds from exercise of common stock warrants	18,762	-
Proceeds from exercise of employee stock options	63,420	-
Proceeds from employee stock purchases	65,839	60,303
Proceeds from follow-on offering, net of underwriting discounts and offering costs	78,530,585	-
Proceeds from note payable, net of debt issuance costs and discount of $652,061	14,347,939	-
Gross proceeds from an ATM offering	38,962	182,694
Payments for secondary registration statement costs	(17,889)	(99,259)
Payments for finance leases	(5,810)	(5,769)
Net cash provided by financing activities	93,041,808	137,969
Net change in cash and cash equivalents	72,648,470	(7,097,091)
Cash and cash equivalents:		
Beginning of period	11,637,911	18,735,002
End of period	$ 84,286,381	$ 11,637,911
Supplemental disclosure of cash flow information:		
Interest paid	$ 694,528	$ 120
Supplemental disclosures of non-cash investing and financing activities:		
Registration statement costs included in accounts payable	$ 8,123	$ -
Property and equipment included in accounts payable	-	24,333
Issuance of common stock warrants and final fee recognized as discount to note payable	964,839	-

See accompanying notes to the financial statements

CELCUITY INC.
NOTES TO FINANCIAL STATEMENTS

1. Organization

Nature of Business

Celcuity Inc., a Delaware corporation (the "Company"), is a clinical-stage biotechnology company seeking to extend the lives of cancer patients by pursuing an integrated therapeutic and companion diagnostic strategy. The company's therapeutic efforts are focused on in-licensing and developing molecularly targeted therapies that address the same cancer driver its companion diagnostics can identify. Its CELsignia companion diagnostic platform is uniquely able to analyze live patient tumor cells to identify new groups of cancer patients likely to benefit from already approved targeted therapies. The Company was co-founded in 2012 by Brian F. Sullivan and Dr. Lance G. Laing and is based in Minnesota. The Company has not generated any revenues to date.

Follow-on Offering

On July 1, 2021, the Company completed a follow-on offering whereby it sold 2,250,000 shares of common stock at a public offering price of $25.00 per share. The aggregate gross proceeds from the sale of shares in the follow-on offering was approximately $56.3 million before deducting underwriting discounts of approximately $3.4 million and offering expenses of approximately $0.1 million.

On February 26, 2021, the Company completed a follow-on offering whereby it sold 1,971,100 shares of common stock (including 257,100 shares of common stock in connection with the full exercise of the underwriters' option to purchase additional shares) at a public offering price of $14.00 per share. The aggregate gross proceeds from the sale of shares in the follow-on offering, including the sale of shares pursuant to the full exercise of the underwriters' option to purchase additional shares, was approximately $27.6 million before deducting underwriting discounts of approximately $1.6 million and offering expenses of approximately $0.2 million.

2. Basis of Presentation, Summary of Significant Accounting Policies and Recent Accounting Pronouncements

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP") and pursuant to the rules and regulations of the Securities and Exchange Commission (the "SEC"). Operating results for the year ended December 31, 2021 are not necessarily indicative of results to be expected for any future year.

Accounting Estimates

Management uses estimates and assumptions in preparing these financial statements in accordance with U.S. GAAP. Those estimates and assumptions affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities, and the reported revenues and expenses. Actual results could differ from those estimates and the difference could be significant. Significant items subject to such estimates and assumptions include the valuation of stock-based compensation and prepaid or accrued clinical trial costs.

Cash and Cash Equivalents

The Company maintains its accounts at one financial institution. At times throughout the year, the Company's cash balances may exceed amounts insured by the Federal Deposit Insurance Corporation. At December 31, 2021 and December 31, 2020, the Company had $83,286,381 and $11,378,685, respectively, in money market funds that are considered cash equivalents and not insured by the Federal Deposit Insurance Corporation.

Property and Equipment

Property and equipment are stated at cost. Depreciation is provided over estimated useful lives using the straight-line method. Maintenance and repairs are expensed as incurred; major improvements and betterments are capitalized.

Estimated useful lives of property and equipment are as follows for the major classes of assets:

Asset Description	Estimated Lives
Furniture and Equipment	4-5
Leasehold Improvements	2-3

Long-Lived Assets

Long-lived assets, such as property and equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. If circumstances require a long-lived asset or asset group be tested for possible impairment, the Company first compares undiscounted cash flows expected to be generated by that asset or asset group to its carrying value. If the carrying value of the long-lived asset or asset group is not recoverable on an undiscounted cash flow basis, an impairment is recognized to the extent that the carrying value exceeds its fair value. Fair value is determined through various valuation techniques including discounted cash flow models, quoted market values, and third-party independent appraisals, as considered necessary.

Deferred Transaction Costs

Deferred transaction costs primarily consist of legal fees and SEC filing fees related to the Company's Registration Statement on Form S-3 filed on November 17, 2021 and declared effective by the SEC on November 26, 2021. The deferred transaction costs were capitalized as incurred and will be offset against the proceeds from future securities offered by the Company for a period up to three years. The deferred transaction costs will be reviewed periodically to assess the probability that future securities will be offered. In the event that no future offering will occur, any deferred transaction costs will be expensed. Total costs incurred were $22,144 and $0 for years ended December 31, 2021 and 2020, respectively.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. For all periods presented, there was no difference between net loss and comprehensive loss.

Risks and Uncertainties

The Company is subject to risks common to companies in the development stage including, but not limited to, dependency on the clinical and commercial success of its initial drug product, gedatolisib, the clinical and commercial success of its diagnostic tests, ability to obtain regulatory approval of its diagnostic tests, the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians and consumers, and significant competition.

Fair Value of Financial Instruments

The Company's accounting for fair value measurements of assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring or nonrecurring basis adheres to the Financial Accounting Standards Board ("FASB") fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements) and the lowest priority to measurements involving significant unobservable inputs (Level 3 measurements). The three levels of the fair value hierarchy are as follows:

- Level 1 Inputs: Unadjusted quoted prices in active markets for identical assets or liabilities accessible to the Company at the measurement date.
- Level 2 Inputs: Other than quoted prices included in Level 1 inputs that are observable for the asset or liability, either directly or indirectly, for substantially the full term of the asset or liability.
- Level 3 Inputs: Unobservable inputs for the asset or liability used to measure fair value to the extent that observable inputs are not available, thereby allowing for situations in which there is little, if any, market activity for the asset or liability at measurement date.

The level in the fair value hierarchy within which a fair value measurement in its entirety falls, is based on the lowest level input that is significant to the fair value measurement in its entirety.

The carrying values of cash equivalents, accounts payable, accrued expenses and other financial working capital items approximate fair value at December 31, 2021 and December 31, 2020, due to the short maturity nature of these items.

Income Taxes

The Company accounts for income taxes using the asset and liability method, as required by the accounting standard for income taxes. Under this method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, as well as net operating loss and tax credit carryforwards. Deferred taxes are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred taxes of a change in tax rates is recognized in results of operations in the period that includes the enactment date. The effects of any future changes in tax laws or rates have not been considered. The Company regularly reviews deferred tax assets to assess their potential realization and establish a valuation allowance for portions of such assets to reduce the carrying value if the Company does not consider it to be more likely than not that the deferred tax assets will be realized.

The Company recognizes the impact of an uncertain tax position in its financial statements if, in management's judgment, the position is more-likely-than-not sustainable upon audit based on the position's technical merits. This involves the identification of potential uncertain tax positions, the evaluation of applicable tax laws and an assessment of whether a liability for an uncertain tax position is necessary.

Stock-Based Compensation

The Company's stock-based compensation consists of stock options and restricted stock issued to certain employees and nonemployees of the Company and the Company's 2017 Employee Stock Purchase Plan. The Company recognizes compensation expense based on an estimated grant date fair value using the Black-Scholes option-pricing method. If the factors change and different assumptions are used, the Company's stock-based compensation expense could be materially different in the future. The Company recognizes stock-based compensation expense for these options on a straight-line basis over the requisite service period. The Company has elected to account for forfeitures as they occur.

Research and Development

Research and development costs are expensed as incurred. Research and development costs amounted to $25,758,006 for the year ended December 31, 2021 and $7,683,522 for the year ended December 31, 2020.

Clinical Trial Costs

The Company records prepaid assets or accrued expenses for prepaid or estimated clinical trial costs conducted by third-party service providers, which includes the conduct of preclinical studies and clinical trials. These costs can be a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with service agreements with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its prepaid assets or accrued expenses. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollments may vary from the Company's estimates, resulting in an adjustment to expense in future periods. Changes in these estimates that result in material changes to the Company's prepaid assets or accrued expenses could materially affect the Company's results of operations.

Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions.

Application of New or Revised Accounting Standards

Pursuant to the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"), a company constituting an "emerging growth company" is, among other things, entitled to rely upon certain reduced reporting requirements. The Company is an emerging growth company but has irrevocably elected not to take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards. As a result, the Company will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for public companies that are not emerging growth companies.

Recently Adopted Accounting Pronouncements

In December 2019, the FASB issued ASU No. 2019-12 "Income Taxes: Simplifying the Accounting for Income Taxes" intended to simplify the accounting for income taxes by eliminating certain exceptions related to the approach for intra-period tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside cost basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The standard is effective for annual periods beginning after December 15, 2020 and interim periods within, with early adoption permitted. Adoption of the standard requires certain changes to be made prospectively, with some changes to be made retrospectively. The Company adopted this standard on January 1, 2021 and it did not have a significant impact on the Company's consolidated financial statements and related disclosures.

In August 2020, the FASB issued ASU No. 2020-06, Debt -– Debt with Conversion and other Options (Subtopic 470-20) and Derivatives and Hedging -– Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity (""ASU 2020-06""), which simplifies accounting for convertible instruments by removing major separation models required under current U.S. GAAP. ASU 2020-06 removes certain settlement conditions that are required for equity contracts to qualify for derivative scope exceptions and also simplifies the diluted earnings per share calculation in certain areas. The standard is effective for public business entities, excluding entities eligible to be smaller reporting companies as defined by the SEC, for fiscal years and interim periods within those fiscal years beginning after December 15, 2021. For all other entities, the standard will be effective for fiscal years beginning after December 15, 2023. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, and adoption must be as of the beginning of the Company's annual fiscal year. The Company's early adoption of this accounting standard on April 8, 2021, in conjunction with the closing of a loan agreement, did not have an impact on the Company's financial statements and related disclosures.

3. Liquidity

Based on the Company's cash and cash equivalents on hand at December 31, 2021 of $84,286,381, the Company believes that its cash will be sufficient to fund the Company's current operating plan through at least the next 12 months from the issuance date of this Annual Report.

4. Net Loss Per Common Share

Basic and diluted net loss per common share is determined by dividing net loss attributable to common stockholders by the weighted-average common shares outstanding during the period. For all periods presented, the common shares underlying the options and warrants have been excluded from the calculation because their effect would be anti-dilutive. Therefore, the weighted-average shares outstanding used to calculate both basic and diluted loss per common share are the same.

For the years ended December 31, 2021 and 2020, potentially dilutive securities excluded from the computations of diluted weighted-average shares outstanding were options to purchase 1,315,321 and 849,949 shares of common stock, respectively, warrants to purchase 377,652 and 353,585 shares of common stock, respectively, and 2,964 and 15,686 shares of restricted common stock, respectively.

5. Payroll Tax Receivable

The payroll tax receivable was initially recorded in 2019. It is the result of the Company's utilization of research and development tax credits as authorized by the Path Act. The balance at December 31, 2021 was $298,764 and December 31, 2020 was $190,000.

6. Prepaid Assets

Prepaid assets consisted of the following at December 31:

	2021	2020
Current:		
Directors & officers' insurance	$ 313,958	$ 288,750
Prepaid research & development	338,760	-
Other	69,959	28,290
Total	$ 722,677	$ 317,040

7. Property and Equipment

Property and equipment consisted of the following at December 31:

	2021	2020
Leasehold improvements	$ 302,848	$ 302,848
Furniture and equipment	1,517,896	1,461,512
	1,820,744	1,764,360
Less: Accumulated depreciation	(1,508,300)	(1,205,484)
Total	$ 312,444	$ 558,876

Depreciation expense was $303,235 and $385,591 for the years ended December 31, 2021 and 2020, respectively.

8. Accrued Expenses

Accrued expenses consisted of the following at December 31:

	2021	2020
Accrued compensation	$ 438,477	$ 628,121
Employee Stock Purchase Plan	34,455	9,471
Clinical trial	138,788	-
Other	191,173	137,020
Total	$ 802,893	$ 774,612

9. Commitments

Operating and Finance Leases

The Company leases its corporate space in Minneapolis, Minnesota. In September 2017, the Company entered into a non-cancelable operating lease agreement for building space. The new lease commenced, and the Company moved to the facility in May 2018, in conjunction with the termination of its then existing lease. Rent expense is recorded on a straight-line basis over the lease term. In July 2020 the Company signed an amendment to extend this lease through April 30, 2022. The lease amendment provides for monthly rent, real estate taxes and operating expenses. As a result of the lease amendment, the Company recorded an incremental $197,211 in the operating right-of-use ("ROU") asset and lease liability. In July 2021, the Company signed the second amendment to extend this lease through April 30, 2023. This amendment provides for monthly rent, real estate taxes and operating expenses. The Company recorded an incremental $193,517 in the operating right-of-use ("ROU") asset and lease liability pertaining to this amendment. The second amendment also includes the option to extend the term for one additional year. The option to extend is at the Company's discretion and because the Company has not determined if the option to extend will be exercised, the extended lease term is not included in the ROU assets and lease liabilities. The Company regularly evaluates the renewal options and when it is reasonably certain of exercise, the Company will include the renewal period in its lease term.

In May 2018, the Company entered into a non-cancelable finance lease agreement for office equipment with a five-year term. The underlying assets are included in furniture and equipment. The lease contains a bargain purchase option at the end of the lease.

When an implicit rate is not provided, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of the lease payments.

Supplemental balance sheet information consisted of the following at December 31, 2021:

Operating Lease		
Right-of-use assets	$	241,901
Operating lease liability	$	251,629
Less: short term portion		(189,858)
Long term portion	$	61,771
Finance Lease		
Furniture and equipment	$	28,932
Less: Accumulated depreciation		(20,735)
Net book value of property and equipment under finance lease	$	8,197
Finance lease liability	$	8,299
Less: short term portion		(5,850)
Long term portion	$	2,449

Maturity analysis under lease agreements consisted of the following as of December 31, 2021:

		Operating Leases		Finance Leases
2022	$	201,099	$	7,255
2023		68,080		3,022
Total minimum lease payments		269,179		10,277
Less: Present value discount		(17,550)		(43)
Less amount representing services		-		(1,935)
Present value of net minimum lease payments	$	251,629	$	8,299

Weighted Average	Remaining Lease Term	Discount Rate
Operating lease	1.3 years	6.0%
Finance lease	1.4 years	1.0%

Lease costs for the years ended December 31:

	2021	2020
Operating lease cost	$ 185,379	$ 171,530
Finance lease cost:		
Amortization	5,786	5,786
Interest	79	119
Variable lease cost	79,477	85,265
Total lease cost	$ 270,721	$ 262,700

Supplemental cash flow information related to leases for the years ended December 30:

	2021	2020
Cash paid for amounts included in operating and finance leases:		
Operating cash outflow from operating leases	$ 274,297	$ 278,603
Operating cash outflow from finance leases	79	119
Financing cash outflow from finance leases	5,810	5,769
Total cash paid for amounts included in operating and finance leases	$ 280,186	$ 284,491

Clinical Research Studies

The Company enters into contracts in the normal course of business for clinical trials, preclinical studies, manufacturing and other services and products for operating purposes. The Company currently has five Phase 2 clinical trial agreements in place to evaluate targeted therapies selected with one of our CELsignia tests. The Company also has a license agreement in place with Pfizer to research, develop, manufacture and commercialize gedatolisib. In conjunction with the license agreement, the Company continued a Phase 1b study – B2151009 related to gedatolisib. These patients subsequently transitioned to an Expanded Access study – CELC-G-001. Timing of milestone payments related to the Phase 2 clinical trials are uncertain and the contracts generally provide for termination following a certain period after notice, therefore the Company believes that non-cancelable obligations under the agreements are not material. Contracts related to the Phase 1b study and the Expanded Access study are generally based on time and material.

10. Stockholders' Equity

On September 15, 2017, in connection with its IPO, Celcuity LLC filed a certificate of conversion, whereby Celcuity LLC effected a corporate conversion from a Minnesota limited liability company to a Delaware corporation and changed its name to Celcuity Inc. Pursuant to the conversion, units of membership interest in the limited liability company were converted into shares of common stock of the corporation at a conversion ratio of 40 units for one share of common stock. The Company had 257,604,208 units issued and outstanding as of September 15, 2017. After giving effect to the corporate conversion, the number of common shares outstanding as of such date was 6,440,139. As a result of the corporate conversion, accumulated deficit was reduced to zero on the date of the corporate conversion, and the corresponding amount was credited to additional paid-in capital. The corporate conversion was approved by members holding a majority of the outstanding units of Celcuity LLC, and in connection with such conversion, the Company filed a certificate of incorporation and adopted bylaws. The Company determined that the corporate conversion is equivalent to a change in the Company's capital structure.

On September 22, 2017, the Company completed its IPO whereby it sold 2,760,000 shares of common stock at a public offering price of $9.50 per share. The aggregate net proceeds received by the Company from the IPO were approximately $23.3 million, net of underwriting commissions of approximately $1.8 million and offering expenses of approximately $1.1 million. Upon the closing of the IPO, 10,082,050 shares of common stock were outstanding, which included 881,911 shares of common stock issued as a result of the conversion of the Company's convertible notes. Shares of the Company's common stock began trading on September 20, 2017 on The Nasdaq Capital Market under the symbol "CELC".

On May 11, 2018, the Company filed an amendment to its certificate of incorporation with the Secretary of State of the State of Delaware to decrease the number of authorized shares of its common stock and preferred stock. Pursuant to the Company's amended certificate of incorporation, the Company is authorized to issue up to 25,000,000 shares of common stock, $0.001 par value per share and 2,500,000 shares of preferred stock, $0.001 par value per share.

On June 5, 2020, the Company entered into an At Market Issuance Sales Agreement (the "ATM Agreement") with B. Riley FBR, Inc. (the "Agent"). Pursuant to the ATM Agreement, the Company was able to offer and sell from time to time, at its option, shares of common stock having an aggregate offering price of up to $10,000,000, par value $0.001 per share (the "Placement Shares"), through the Agent.

The Placement Shares were registered under the Securities Act of 1933, as amended, pursuant to the Registration Statement on Form S-3 (File No. 333-227466), which was originally filed with the SEC on September 21, 2018 and declared effective by the SEC on October 4, 2018, the base prospectus contained within the Registration Statement, and a prospectus supplement that was filed on June 5, 2020. Sales of the Company's common stock, if any, under this prospectus supplement were able to be made by any method deemed to be an "at the market offering" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended.

Pursuant to the ATM Agreement, the company sold 3,082 shares of common stock at an average selling price of $12.64 per share in the year ended December 31, 2021 and 17,725 shares of common stock at an average selling price of $10.31 per share in the year ended December 31, 2020.

On February 23, 2021, in conjunction with the Company's follow-on offering, the ATM Agreement was terminated.

On February 26, 2021, the Company completed a follow-on offering whereby it sold 1,971,100 shares of common stock (including 257,100 shares of common stock in connection with the full exercise of the underwriters' option to purchase additional shares) at a public offering price of $14.00 per share. The aggregate gross proceeds from the sale of shares in the follow-on offering, including the sale of shares pursuant to the full exercise of the underwriters' option to purchase additional shares, was approximately $27.6 million before deducting underwriting discounts of approximately $1.6 million and offering expenses of approximately $0.2 million.

On April 8, 2021, in conjunction with entering into a license agreement with Pfizer to research, develop, manufacture and commercialize gedatolisib, the Company issued to Pfizer $5.0 million of shares of the Company's common stock pursuant to an Equity Grant Agreement. The number of shares issued totaled 349,406 at a price of $14.31.

On July 1, 2021, the Company completed a follow-on offering whereby it sold 2,250,000 shares of common stock at a public offering price of $25.00 per share. The offering generated approximately $56.3 million before deducting underwriting discounts of approximately $3.4 million and offering expenses of approximately $0.1 million.

At December 31, 2021 and 2020, the Company had 14,918,887 and 10,299,822 shares of common stock outstanding, respectively.

Warrants

In connection with the 2016 private placement offering of units, the Company issued ten-year warrants to the placement agent of the private placement. The warrants allow the placement agent to purchase up to 55,249 shares of common stock at $7.56 per share. The warrants were immediately exercisable and expire on January 14, 2026 and May 2, 2026. These warrants are equity classified and the $330,607 fair value of the warrants is reflected as additional paid-in capital.

In connection with the private placement offering of convertible notes, the Company issued ten-year warrants to the placement agent to purchase 48,615 shares of common stock at a price of $8.42 per share. The warrants were immediately exercisable and expire on April 28, 2027 and May 17, 2027. These warrants are equity classified and the $286,999 fair value of the warrants is reflected as additional paid-in-capital.

In addition, the Company granted the purchasers of the convertible notes the right to receive a seven-year warrant to purchase 131,675 shares of common stock at an exercise price equal to the conversion price of the convertible notes. With the completion of the IPO on September 22, 2017, these warrants were issued. These warrants were immediately exercisable and expire on September 22, 2024. These warrants are equity classified and the $776,717 fair value of the warrants is reflected as additional paid-in-capital.

In connection with the IPO, the Company issued a five-year warrant to the underwriter. The warrant allows the underwriter to purchase up to 138,000 shares of common stock at $10.45 per share. This warrant was immediately exercisable and expires on September 19, 2022. This warrant is equity classified and the $784,111 fair value of the warrant is reflected as additional paid-in-capital.

In connection with entering into a loan and security agreement with Innovatus Life Sciences Lending Fund I, LP, the Company issued a warrant to Innovatus to purchase 26,042 shares of the Company's common stock at an exercise price of $14.40 per share. This warrant is equity classified and the $289,839 fair value of the warrant was reflected as additional debt discount.

At December 31, 2021 and 2020, the Company had warrants to purchase 377,652 and 353,585 shares of common stock outstanding, at a weighted average exercise price of $9.76 and $9.42, respectively. A total of 1,975 and 0 warrants were exercised in the years ended December 31, 2021 and 2020, respectively.

11. Stock-Based Compensation

2012 Equity Incentive Plan

The 2012 Equity Incentive Plan, as amended, was adopted by the Company's board and approved by the members of Celcuity LLC on August 10, 2012. The Company reserved a maximum of 625,000 shares of common stock for issuance under the 2012 Equity Incentive Plan. The 2012 Equity Incentive Plan provides for options, restricted stock awards, performance stock awards or stock bonuses. The exercise price of each option granted under the 2012 Equity Incentive Plan is not less than 100% of the fair market value of one share on the date of grant. The maximum permitted term of options granted under the 2012 Equity Incentive Plan is ten years. The Company's board administers the 2012 Equity Incentive Plan and determines the provisions of incentive awards, including eligible recipients, number of shares subject to an incentive award, exercise price, vesting schedule, duration of an incentive award and other restrictions an incentive award may be subject to. The 2012 Equity Incentive Plan was frozen on September 6, 2017 and any new awards will be issued under the terms of the 2017 Amended and Restated Stock Incentive Plan.

2017 Stock Incentive Plan

The 2017 Amended and Restated Stock Incentive Plan (the "2017 Plan") was adopted by the Company's board on September 6, 2017, became effective following the corporate conversion on September 15, 2017, and was approved by stockholders at the Company's annual stockholder meeting on May 10, 2018. The 2017 Plan was amended and approved by stockholders at the Company's annual stockholder meeting on May 14, 2020. The Company initially reserved a maximum of 750,000 shares of common stock for issuance under the 2017 Plan. The number of shares reserved for issuance was automatically increased by 102,998 and 102,540 shares on January 1, 2021 and 2020, respectively and will increase automatically on January 1 of each of 2022 through 2027 by the number of shares equal to 1.0% of the aggregate number of outstanding shares of Company common stock as of the immediately preceding December 31. However, the Company's board may reduce the amount of the increase in any particular year. At the Annual Meeting held on May 12, 2021, the stockholders approved a one-time, 500,000 increase to the number of shares reserved for issuance under the 2017 Plan. The 2017 Plan provides for options, restricted stock awards, stock appreciation rights, restricted stock units, performance awards and stock bonuses. The exercise price of each option granted under the 2017 Plan is not less than 100% of the fair market value of one share on the date of grant. The maximum permitted term of options granted under the 2017 Plan is ten years. The 2017 Plan is generally administered by the compensation committee of the Company's board, which has the authority to interpret the 2017 Plan, grant awards and make all other determinations necessary for the administration of the 2017 Plan.

The following table summarizes the activity for all stock options outstanding for the years ended December 31:

	2021		2020	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Options outstanding at beginning of year	849,949	$ 9.33	585,215	$ 14.37
Granted	538,567	16.09	277,986	7.17
Exercised	(44,828)	7.06	-	-
Forfeited	(28,367)	18.72	(13,252)	11.54
Balance at December 31:	1,315,321	$ 11.97	849,949	$ 9.33
Options exercisable at December 31:	592,141	$ 9.53	397,425	$ 10.35
Weighted Average Grant Date Fair Value for options granted during the period:		$ 14.93		$ 4.63

The following table summarizes additional information about stock options outstanding and exercisable at December 31, 2021:

Options Outstanding				Options Exercisable		
Options Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Aggregate Intrinsic Value	Options Exercisable	Weighted Average Exercise Price	Aggregate Intrinsic Value
1,315,321	8.01	$ 11.97	$ 4,284,653	592,141	$ 9.53	3,188,333

The Company recognized stock-based compensation expense for stock options of $2,488,742 and $1,668,859 for the years ended December 31, 2021 and 2020, respectively. In December 2021, the Company modified the exercise price on 311,000 stock option awards to $13.44, the closing market price on the Nasdaq Capital Market on December 15, 2021. No director or officer awards were modified. The effect on stock-based compensation was $53,000 for the year ended December 31, 2021. The effect on stock-based compensation over the remaining service period will be approximately $344,000. In May 2020, the Company modified the exercise price on 203,750 stock option awards to $5.10, the closing market price on the Nasdaq Capital Market on May 14, 2020. No director or officer awards were modified. The effect on stock-based compensation was $46,000 and $83,000 for the years ended December 31, 2021 and 2020, respectively. The effect on stock-based compensation over the remaining service period will be approximately $85,000.

The Black-Scholes option-pricing model was used to estimate the fair value of equity-based awards with the following weighted-average assumptions for the years ended December 31:

	2021	2020
Risk-free interest rate	0.63% - 1.39%	0.35% - 1.66%
Expected volatility	76.6% - 76.9%	73.3% - 77.1%
Expected life (years)	5.0 to 6.11	5.5 to 6.1
Expected dividend yield	0%	0%

The inputs for the Black-Scholes valuation model require management's significant assumptions. Prior to the Company's initial public offering, the price per share of common stock was determined by the Company's board based on recent prices of common stock sold in private offerings. Subsequent to the initial public offering, the price per share of common stock is determined by using the closing market price on the Nasdaq Capital Market on the grant date. The risk-free interest rates are based on the rate for U.S. Treasury securities at the date of grant with maturity dates approximately equal to the expected life at the grant date. The expected life is based on the simplified method in accordance with the SEC Staff Accounting Bulletin Nos. 107 and 110. The expected volatility is estimated based on historical volatility information of peer companies that are publicly available in combination with the Company's calculated volatility since being publicly traded.

All assumptions used to calculate the grant date fair value of non-employee options are generally consistent with the assumptions used for options granted to employees. In the event the Company terminates any of its consulting agreements, the unvested options issued in connection with the agreements would also be cancelled.

The Company had 2,964 and 15,686 shares of restricted stock outstanding for the years ended December 31, 2021 and 2020, respectively, and 15,686 and 0 shares of restricted stock vested during the years ended December 31, 2021 and 2020, respectively. The Company recognized stock-based compensation expense for restricted stock of $80,150 and $52,727 for the years ended December 31, 2021 and 2020, respectively.

The total remaining shares available for grant under the Company's 2017 Plan as of December 31, 2021 was 288,756.

Total unrecognized compensation cost related to stock options and restricted stock is estimated to be recognized as follows:

2022	$ 3,202,846
2023	2,410,853
2024	1,932,745
2025	925,350
Total estimated compensation cost to be recognized	$ 8,471,794

2017 Employee Stock Purchase Plan

The Company's 2017 Employee Stock Purchase Plan (the "ESPP") was adopted by the Company's board on September 6, 2017 and approved by stockholders at the Company's annual stockholder meeting on May 10, 2018. The Company initially reserved a total of 100,000 shares for issuance under the ESPP. The number of shares reserved for issuance was automatically increased by 51,499 and 51,270 shares on January 1, 2021 and 2020, respectively and will increase automatically on each subsequent January 1 by the number of shares equal to 0.5% of the total outstanding number of shares of Company common stock as of the immediately preceding December 31. However, the Company's board may reduce the amount of the increase in any particular year. The total remaining shares available for issuance under the employee stock purchase plan as of December 31, 2021 is 150,223.

The ESPP provides participating employees with an opportunity to purchase shares of the Company's common stock at a discount through payroll deductions. The ESPP is available to all employees unless they are employed for less than 20 hours per week or own 5% or more of the total combined voting power or value of the Company's common stock. The ESPP is administered using overlapping 24 month offering periods, referred to as an Offering Period. Each Offering Period has four six-month purchase periods. A new Offering Period and purchase period begin every six months on May 1 and November 1 of each year. Participating employees may purchase common stock, on a voluntary after tax-basis, at a price equal to 85% of the fair market value of a share of common stock on either the offering date or the purchase date, whichever is lower. If the purchase date has a lower price, the employee will automatically be placed in the Offering Period beginning immediately after the purchase date. The Company recognized stock-based compensation expense related to the ESPP of $41,043 and $42,293 for the years ended December 31, 2021 and 2020, respectively.

The Company recognized total stock-based compensation expense as follows for the years ended December 31:

	2021	2020
Stock-based compensation expense in operating expenses:		
Research and development	$ 1,645,353	$ 1,055,094
General and administrative	964,582	708,785
Total	$ 2,609,935	$ 1,763,879

12. Debt

On April 8, 2021, the Company entered into a loan and security agreement (the "Loan Agreement") with Innovatus Life Sciences Lending Fund I, LP, a Delaware limited partnership ("Innovatus") in its capacity as Collateral Agent and sole Lender. The Lender agreed to loan up to $25 million in three tranches consisting of (i) a $15.0 million non-contingent term A loan that was funded on April 8, 2021, (ii) a $5 million term B loan to be funded upon request of the Company no later than March 31, 2022, and (iii) a $5 million term C loan to be funded upon request of the Company no later than March 31, 2023 (collectively the "Term Loans"). Funding of the term B and C loan is subject to the Company's ability to achieve certain milestones. The Innovatus Loan Agreement is secured by a lien covering substantially all assets of the Company.

The Loan Agreement also contains certain events of default, warranties and covenants of the Company. In connection with each funding of the Term Loans, the Company is required to issue Innovatus a warrant (the"Warrants") to purchase a number of shares of the Company's stock equal to 2.5% of the principal amount of the relevant Term Loan funded divided by the exercise price, which will be based on the lower of (i) $14.40 per share or (ii) the volume weighted price per share of the Company's stock for the five-trading day period ending on the last trading day immediately preceding the funding date of the Term B or Term C Loan, as applicable. The warrants may be exercised on a cashless basis and are immediately exercisable through the tenth anniversary of the applicable funding date. In connection with the first tranche of the Term Loans, the Company issued a warrant to Innovatus to purchase 26,042 shares of the Company's common stock at an exercise price of $14.40 per share. The Company evaluated the warrant under ASC 470, debt, and recognized an additional debt discount of approximately $0.3 million based on the relative fair value of the base instruments and warrants. The Company calculated the fair value of the warrant using the Black-Scholes model. The Company is also required to maintain a minimum cash balance in agreement with the term loans' default terms.

The Company is entitled to make interest-only payments for thirty-six months, or up to forty-eight months if certain conditions are met. The Term Loans will mature on the fifth anniversary of the initial funding date and will bear interest at a rate equal to sum of (a) the greater of (i) Prime Rate (as defined in the Loan Agreement) or (ii) 3.25%, plus (b) 5.70%. The effective interest rate is 11.36%. Additionally, the Company elected to make 2.7% of the interest rate as payable in kind, which shall accrue as principal monthly. The Company is obligated to pay the Lenders (i) a non-refundable facility fee in the amount of 1.00% of each term loan that is funded (the "Facility Fee"), and (ii) a final fee equal to 4.50% of the aggregate amount of the term loans funded (the "Final Fee"). In connection with the funding of the first tranche of the Term Loans, a final fee of approximately $0.7 million was recorded as additional principal and as a debt discount, and a facility fee of approximately $0.1 million was recorded as additional debt discount. The Company has the option to prepay the loan at any time following the first anniversary of the loan closing, with tiered prepayment fees ranging from 0 – 2% based on when the prepayment would occur.

Innovatus also has the right, at its election, after June 1, 2021 and until the third anniversary of the Loan Agreement, to convert up to 20% of the outstanding principal amount of all Terms Loans made under the Loan Agreement into shares of the Company's common stock at a price per share equal to the volume weighted average closing price of the Company's stock for the 5-trading day period ending on the last trading day immediately preceding the execution of the Loan Agreement (the "Conversion Right").

In connection with the Loan Agreement and the funding of the first tranche of the Term Loans, the Company incurred debt issuance costs of approximately $0.5 million. The debt issuance costs, and the debt discount are amortized to interest expense using the effective interest method over the life of the Term Loans. The carrying value of the debt approximates fair value as of December 31, 2021.

Long-term debt consisted of the following at December 31:

	2021
Note payable	$ 15,000,000
Add: PIK interest (added to principal)	300,001
Add: final fee	675,000
Less: unamortized debt issuance costs	(386,578)
Less: unamortized debt discount	(962,500)
Total long-term debt	$ 14,625,923

Future principal payments, including the final fee, are as follows:

	Years Ending December 31,
2024	$ 5,737,500
2025	7,650,001
2026	2,587,500
Total	$ 15,975,001

13. License Agreement

On April 8, 2021 the Company entered into a license agreement with Pfizer to research, develop, manufacture and commercialize gedatolisib, a potent, well-tolerated, reversible dual inhibitor that targets PI3K and mTOR, for the treatment, diagnosis and prevention of all diseases. The Company paid Pfizer $5.0 million in upfront fees and issued to Pfizer $5.0 million of shares of the Company's common stock pursuant to an Equity Grant Agreement. The upfront payment and the issuance of shares were expensed to research & development in full for the three months ending June 30, 2021.

The Company is also required to make milestone payments to Pfizer upon achievement of certain development and commercial milestone events, up to an aggregate of $335.0 million. Additionally, the Company will pay Pfizer tiered royalties on sales of gedatolisib at percentages ranging from the low to mid-teens, which may be subject to deductions for expiration of valid claims, amounts due under third-party licenses and generic competition. Unless earlier terminated, the license agreement will expire upon the expiration of all royalty obligations. The royalty period will expire on a country-by-country basis upon the later of (a) 12 years following the date of first commercial sale of such product in such country, (b) the expiration of all regulatory or data exclusivity in such country for such product or (c) the date upon which the manufacture, use, sale, offer for sale or importation of such product in such country would no longer infringe, but for the license granted in the license agreement, a valid claim of a licensed patent right.

The Company has the right to terminate the license agreement for convenience upon 90 days' prior written notice. Pfizer may not terminate the agreement for convenience. Either the Company or Pfizer may terminate the license agreement if the other party is in material breach and such breach is not cured within the specified cure period. In addition, either the Company or Pfizer may terminate the license agreement in the event of specified insolvency events involving the other party.

14. Income Taxes

Following the conversion of Celcuity LLC to Celcuity Inc. on September 15, 2017, Celcuity Inc. began filing federal and state returns where required. No income tax benefit was recorded for the years 2021 and 2020, due to net losses and recognition of a valuation allowance. The following table presents a reconciliation of the tax expense computed at the statutory federal rate and the Company's tax expense for the years ending December 31:

	2021	2020
Tax benefit at statutory federal rate	$ (6,217,000)	$ (1,990,000)
State income tax benefit, net of federal tax effect	(49,000)	(16,000)
Change in valuation allowance on deferred tax assets	6,330,000	2,159,000
Research and Development Credits	(222,000)	(450,000)
Other permanent items	158,000	297,000
Income tax benefits	$ -	$ -

On December 22, 2017 H.R. 1, commonly referred to as the Tax Cuts and Jobs Act, (the "Tax Act") was enacted. Among the significant changes to the U.S. Internal Revenue Code, the Tax Act lowered the U.S. federal corporate income tax rate ("Federal Tax Rate") from 35% to 21% effective January 1, 2018. The Act also made changes related to the use and limitation of net operating loss carryforwards generated in tax years beginning after December 31, 2017. For years beginning after December 31, 2017 net operating losses have an indefinite carryforward and the utilization of losses is limited to 80% of taxable income each year.

In response to the COVID-19 pandemic, the Coronavirus Aid, Relief and Economic Security Act ("CARES Act") was signed into law on March 27, 2020. The CARES Act lifts certain deduction limitations originally imposed by the Tax Act. Corporate taxpayers may carryback net operating losses originating during 2018 through 2020 for up to five years, which was not previously allowed under the Tax Act. The CARES Act also eliminates the 80% of taxable income limitation allowing corporate entities to fully utilize net operating loss carryforwards to offset taxable income in 2018, 2019 and 2020. The enactment of the CARES Act did not result in any material impact to the Company's income tax provision.

Deferred income taxes reflect the net effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's deferred tax assets relate primarily to its net operating loss carryforwards and other balance sheet basis differences. In accordance with ASC 740, "Income Taxes," the Company recorded a valuation allowance to fully offset the net deferred tax asset, because it is more likely than not that the Company will not realize future benefits associated with these deferred tax assets at December 31, 2021. The tax effects of temporary differences and carryforwards that give rise to significant portions of the deferred tax assets are as follows:

	2021	2020
Deferred tax assets (liabilities):		
Accrued expenses	$ 50,000	$ 79,000
Share-based compensation	796,000	528,000
Property and equipment	319,000	255,000
Right-of-use assets	(51,000)	(49,000)
Lease liability	53,000	53,000
Start-up expenditures	6,966,000	2,610,000
Net operating losses and tax credits	4,915,000	3,242,000
Valuation allowance	(13,048,000)	(6,718,000)
Net deferred tax assets (liabilities)	$ -	$ -

At December 31, 2021, the Company had federal and state net operating loss carryforwards of approximately $16.8 million and $0.3 million, respectively. The federal and state net operating loss carryforwards for 2017 will begin to expire in the year ending December 31, 2037. The federal net operating loss carryforwards starting in 2018 have no expiration. These deferred tax assets were subject to a full valuation allowance as of December 31, 2021 and December 31, 2020.

At December 31, 2021, the Company had federal and state research and development tax credit carryforwards resulting in deferred tax assets of approximately $0.7 million and $0.7 million, respectively. The federal and state credit carryforwards will begin to expire in the years ending December 31, 2037 and December 31, 2032, respectively. These deferred tax assets were subject to a full valuation allowance as of December 31, 2021 and December 31, 2020.

Under the provisions of Section 382 of the Internal Revenue Code of 1986, certain substantial changes in the Company's ownership, including a sale of the Company, or significant changes in ownership due to sales of equity, may limit in the future the amount of net operating loss carryforwards available to offset future taxable income.

The Company recognizes uncertain tax positions in accordance with ASC 740 on the basis of evaluating whether it is more-likely-than not that the tax positions will be sustained upon examination by tax authorities. For those tax positions that meet the more-likely-than not recognition threshold, we recognize the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement. As of December 31, 2021, and 2020, the Company has no significant uncertain tax positions. There are no unrecognized tax benefits included on the balance sheet that would, if recognized, impact the effective tax rate. The Company does not anticipate there will be a significant change in unrecognized tax benefits within the next 12 months.

Prior to the conversion, Celcuity was a limited liability company and therefore was taxed as a partnership for income tax purposes. Accordingly, no benefit for income taxes was recorded prior to the conversion.

For years prior to 2017, the Company is no longer subject to U.S. federal or state income tax examinations. The Company's policy is to recognize interest and penalties related to uncertain tax positions as a component of general and administrative expenses.

15. Subsequent Event

In February of 2022, we entered into an Open Market Sale Agreement^{SM} with Jefferies LLC, as agent ("Jefferies"), pursuant to which we may offer and sell, from time to time, through Jefferies, shares of our common stock having an aggregate offering price of up to $50,000,000. We will pay Jefferies a commission equal to 3.0% of the aggregate gross proceeds from each sale of such shares. To date, we have not yet made any sales under this arrangement.

ITEM 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None

ITEM 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective.

Management Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rule 13a-15(f) under the Securities Exchange Act of 1934. Management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2021 based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO – 2013") in Internal Control-Integrated Framework. Based on this assessment, our Chief Executive Officer and Chief Financial Officer concluded that our system of internal control over financial reporting was effective as of such date.

This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to our designation as an "emerging growth company," as defined in the JOBS Act.

Changes in Internal Control over Financial Reporting

There were no changes to our system of internal control over financial reporting during the three months ended December 31, 2021 and during the subsequent time period through the filing of this Annual Report that have materially affected, or are reasonably likely to materially affect, our system of controls over financial reporting.

ITEM 9B. Other Information

None.

PART III

ITEM 10. Directors, Executive Officers and Corporate Governance

Directors

Brian F. Sullivan, age 60, is our co-Founder and has served as Chairman of the Board and Chief Executive Officer since we commenced operations in 2012. Mr. Sullivan has over 25 years of experience founding and building successful, high growth technology companies. He was Chairman and CEO of SterilMed, a medical device reprocessing company, from 2003, when he led an investment group to acquire a majority interest, until its sale to Ethicon Endo-Surgery Inc., a Johnson & Johnson company, for $330 million in 2011. Previously, he was co-founder and Chief Executive Officer of Recovery Engineering, a filtration company, which he took public and subsequently sold to Procter & Gamble for $265 million in 1999. Since 2003, Mr. Sullivan has served on the board of directors of Entegris, Inc., a publicly-held company. Mr. Sullivan has received seven U.S. patents and has several pending. He graduated *magna cum laude* with distinction from Harvard College with an A.B. in economics. Among other attributes, skills, and qualifications, the board of directors believes Mr. Sullivan is uniquely qualified to serve as a director based on his extensive operational and business development experience, and his knowledge in building stockholder value, growing a company from inception and navigating significant corporate transactions and the public company process.

Lance G. Laing, Ph.D., age 60, is our co-Founder and has served as Chief Science Officer, Vice President, Secretary and Director since we commenced operations in 2012. Dr. Laing's career spans more than 15 years in drug discovery research and technology development. He received his doctorate in biophysics and biochemistry from The Johns Hopkins University and completed a National Institutes of Health post-doctoral fellowship at Washington University Medical School. He has received 19 U.S. patents and has an additional 24 U.S. patents pending. His drug discovery research career began at Scriptgen/Anadys Pharmaceuticals (purchased by Novartis), where he worked under Professor Peter Kim, who became President of Merck Research. He also was Director of Chemistry and Bioapplications and Director of Detection Product Development for two companies that each developed instruments similar to those Celcuity uses to perform the CELsignia tests. His work at these two instrument companies gave him unique expertise and experience in developing a variety of patented applications for these instruments. Most recently, he served as an executive director for an international drug discovery and development company. Among other attributes, skills, and qualifications, the board of directors believes Dr. Laing is uniquely qualified to serve as a director based on his significant research, medical and scientific expertise.

Richard E. Buller, M.D., Ph.D., age 72, was appointed to Celcuity's board of directors in December 2019. Dr. Buller has over 15 years of experience leading oncology clinical development and translational medicine departments at major pharmaceutical companies. He has participated in the development of 15 drugs and several companion diagnostics that received U.S. FDA approval. Dr. Buller most recently served as Head Oncology Clinical Development and Vice President of Translational Oncology at Pfizer, Inc, one of the world's largest pharmaceutical companies, until he retired in 2016. He had previously served as Vice President of Translational Medicine at Exelixis, a leading biopharmaceutical company, where he led efforts to study patients selected by molecular testing for inclusion in their phase 2 and phase 3 clinical trials. He began his pharmaceutical company career at GlaxoSmithKline as Director of the Oncology Medicine Development Center. Prior to his leadership positions in drug development, he was Professor of Gynecologic Oncology at the University of Iowa, where he led laboratory research focused on identifying genomic variants involved in ovarian cancer. He received his M.D. from the Baylor College of Medicine, where he also received his Ph.D. in cell biology. Among other attributes, skills, and qualifications, the board of directors believes Dr. Buller is uniquely qualified to serve as a director based on his oncology drug and diagnostic development expertise.

David F. Dalvey, age 63, has served as a member of Celcuity's board of directors since February 2014. Mr. Dalvey has more than 30 years of experience in the fields of corporate finance and venture capital, working primarily with growth-oriented technology and life-science businesses. He has over 10 years of corporate finance advisory experience with two national investment banks, completing over 150 individual transactions. He has been the General Partner of Brightstone Venture Capital, a venture capital management company, since September 2000. Brightstone is a 25-year old venture capital management company that has raised and managed ten venture partnerships. Previously, he held management positions with R.J. Steichen and Company, an investment bank, from 1995 to 2000, The Food Fund LP, a venture capital firm, from 1992 to 1995 and Wessels, Arnold & Henderson, an investment bank, from 1987 to 1992. Mr. Dalvey served on the board of directors for Navarre Corporation (now Speed Commerce, Inc.) from 2009 until November 2012, on the board of managers for Blue Rock Market Neutral Fund, a mutual fund registered under the Investment Company Act of 1940 from 2000 to 2014 and on the board of directors for Digitiliti, Inc. from July 2011 until October 2012. Mr. Dalvey has significant operational exposure as a board director or advisor to many other public and privately held growth businesses and has served on these companies' audit, strategic or governance committees, including companies such as HomeSpotter, Definity Health, AppTec Laboratories, CHF Solutions, BiteSquad, Agiliti, and Nature Vision. Mr. Dalvey received a B.S. in Business/Management Economics from University of Minnesota. Among other attributes, skills, and qualifications, the board of directors believes Mr. Dalvey is uniquely qualified to serve as a director based on his leadership experience in operating both public and private companies and his experience working in the investment community and with investment firms enable him to bring valuable insight and knowledge to our board of directors.

Leo T. Furcht, M.D., age 75, was appointed to Celcuity's board of directors in May 2019. Dr. Furcht is currently Allen-Pardee Professor of Cancer Biology and Head of the Department of Laboratory Medicine and Pathology at the University of Minnesota and a member of the Division of Molecular Pathology and Genomics. He served as Chairman of the Board of Directors for University of Minnesota Physicians, the Medical School practice plan with approximately 700 physicians, from 2004-2014. He was also the founding Director of the Biomedical Engineering Center from 1990-2001, where he led efforts to establish stem cell and molecular diagnostics expertise at the University of Minnesota. He has published more than 180 scientific papers and holds more than 30 patents in the fields of polypeptides, biomaterials, and adult stem cells. His business experience includes co-founding two medical technology companies, South Bay Medical, a medical device company that was acquired by Mentor Corporation, and Diascreen, a diagnostics company, which was later acquired by Chronimed. Among other attributes, skills, and qualifications, the board of directors believes Dr. Furcht is uniquely qualified to serve as a director based on his research in tumor cell behavior and extracellular matrix proteins, Head of the University of Minnesota's Department of Laboratory Medicine and Pathology, and his experience in several biotechnology start-ups.

Richard J. Nigon, age 74, is currently Senior Vice President of Cedar Point Capital, LLC., a private company that raises capital for early stage companies, where he has served since 2007. Mr. Nigon has also been a board member for Tactile Systems Technology since September 2012 and Northern Technologies International Corp. since February 2010, including its non-executive Chairman of the board of directors since November 2012. Mr. Nigon also serves as a director of several private companies. Mr. Nigon previously served as a board member for Vascular Solutions, Inc. from November 2000 to February 2017, when it was acquired by Teleflex, Incorporated and as a board member for Virtual Radiologic Corporation from May 2007 until it was acquired in July 2010. From February 2001 until December 2006, Mr. Nigon was a Director of Equity Corporate Finance for Miller Johnson Steichen Kinnard, a privately held investment firm, which was acquired in December 2006 by Stifel Nicolaus, a brokerage and investment banking firm. After that acquisition, Mr. Nigon became a Managing Director of Private Placements of Stifel Nicolaus until May 2007. From February 2000 to February 2001, Mr. Nigon served as the Chief Financial Officer of Dantis, Inc., a web hosting company. Prior to joining Dantis, Mr. Nigon was employed by Ernst & Young LLP from 1970 to 2000, where he served as a partner from 1981 to 2000. While at Ernst & Young, Mr. Nigon served as the Director of Ernst & Young's Twin Cities Entrepreneurial Services Group and was the coordinating partner on several publicly-traded companies in the consumer retailing and manufacturing sectors. Among other attributes, skills, and qualifications, the board of directors believes Mr. Nigon is qualified to serve as a director because of his extensive public accounting and auditing experience, including particular experience with emerging growth companies. The board of directors also believes that Mr. Nigon will bring to the board of directors a strong background in financial controls and reporting, financial management, financial analysis, SEC reporting requirements and mergers and acquisitions. His strategic planning expertise gained through his management and leadership roles at private investment firms also makes him well-suited to serve as a member of the board of directors.

Executive Officers

Information regarding our Chief Executive Officer, Brian F. Sullivan, and our Chief Science Officer, Lance G. Laing, PhD., is included above under the heading "Directors".

Vicky Hahne, age 55, joined as our Chief Financial Officer in July 2017. She has more than 20 years of financial leadership experience, including the most recent 10 years in the healthcare industry. Prior to joining Celcuity, Ms. Hahne served as Controller of Respiratory Technologies Inc., a medical device manufacturer, from 2015 to 2017. While at Respiratory Technologies, she played a key role in the due diligence process to sell the company to Koninklijke Philips. In 2014, she served as Controller for Ability Network Inc., a healthcare information technology company. From 2007 to 2012, Ms. Hahne served as Controller of Sterilmed Inc., a medical device reprocessing company, where she was significantly involved in the sale of the company to Johnson & Johnson. Prior to these roles, Ms. Hahne held several senior financial positions at SimonDelivers Inc., including Chief Financial Officer. Ms. Hahne has extensive experience in early stage, high growth companies with responsibilities including financial controls and stewardship, financial analysis, mergers and acquisitions, building infrastructure and systems. She received a B.S. degree in Finance and Accounting from Northern State University and received her CPA certificate in 1990.

Corporate Governance

Our board of directors has adopted a Code of Business Conduct and Ethics that applies to our directors, officers and employees. This code is available on the corporate governance section of our website (which is a subsection of the investor relations section of our website) at the following address: www.celcuity.com. We intend to disclose on our website any amendments or waivers to the Code of Business Conduct and Ethics that are required to be disclosed by SEC rules.

Additional information required by this Item 10 will be contained in our definitive proxy statement for our 2022 Annual Meeting of Stockholders (the "Definitive Proxy Statement") and is incorporated herein by reference.

ITEM 11. Executive Compensation

The information required by this Item 11 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

ITEM 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

ITEM 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

ITEM 14. Principal Accounting Fees and Services

The information required by this Item 14 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. Exhibits, Financial Statement Schedules.

FINANCIAL STATEMENTS

FINANCIAL STATEMENT SCHEDULES

None.

EXHIBITS

See Exhibit Index immediately following the signature page hereto, which is incorporated herein by reference.

ITEM 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: March 23, 2022

CELCUITY INC.

By */s/ Brian F. Sullivan*
Brian F. Sullivan
Chairman and Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Each person whose signature appears below constitutes and appoints Brian F. Sullivan and Vicky Hahne as the undersigned's true and lawful attorneys-in fact and agents, each acting alone, with full power of substitution and resubstitution, for the undersigned and in the undersigned's name, place and stead, in any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granted unto said attorneys-in-fact and agents, each acting alone, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as the undersigned might or could do in person, hereby ratifying and confirming all said attorneys-in-fact and agents, each acting alone, or his substitute or substitutes, may lawfully do or cause to be done by virtue thereof.

Signature	Title	Date
/s/ Brian F. Sullivan Brian F. Sullivan	Chairman and Chief Executive Officer (Principal Executive Officer)	March 23, 2022
/s/ Vicky Hahne Vicky Hahne	Chief Financial Officer (Principal Financial and Accounting Officer)	March 23, 2022
/s/ Lance G. Laing Lance G. Laing	Chief Science Officer, Vice President and Secretary, and Director	March 23, 2022
/s/ Richard E. Buller Richard E. Buller	Director	March 23, 2022
/s/ Dave F. Dalvey Dave F. Dalvey	Director	March 23, 2022
/s/ Leo T. Furcht Leo T. Furcht	Director	March 23, 2022
/s/ Richard J. Nigon Richard J. Nigon	Director	March 23, 2022

EXHIBIT INDEX
CELCUITY INC.
FORM 10-K

Exhibit No.	Description
2.1	Form of Plan of Conversion (incorporated by reference to Exhibit 2.1 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).
3.1	Certificate of Incorporation of the Company as amended (incorporated by reference to Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 9, 2018).
3.2	Bylaws of the Company (incorporated by reference to Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 13, 2017).
4.1	Specimen Certificate representing shares of common stock of Celcuity Inc. (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).
4.2	Description of Registered Securities (incorporated by reference to Exhibit 4.2 to the Company's Annual Report on Form 10-K filed with the SEC on March 13, 2020).
4.3	Form of Warrant to Purchase Units of Membership Interest issued by Celcuity LLC to Cedar Point Capital, LLC, as placement agent of membership units and unsecured convertible promissory notes of Celcuity LLC (incorporated by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1 filed with the SEC on August 23, 2017).
4.4	Form of Warrant to Purchase Shares of Common Stock issued by Celcuity Inc. in connection with the conversion of 1.25% Unsecured Convertible Promissory Notes (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed with the SEC on September 25, 2017).
4.5	Representative's Warrant to Purchase Common Stock (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on September 25, 2017).
4.6	Form of Warrant (incorporated by reference from Exhibit 4.2 to the Company's Current Report on Form 8-K filed with the SEC on April 8, 2021).
4.7	Equity Grant Agreement, dated April 8, 2021, between the Company and Pfizer, Inc. (incorporated by reference from Exhibit 4.1 to the Company's Current Report on Form 8-K filed with the SEC on April 8, 2021).
4.8	Loan and Security Agreement, dated as of April 8, 2021, by and between the Company and Innovatus Life Sciences Lending Fund I, LP. (incorporated by reference from Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 11, 2021).
10.1+	Celcuity Inc. 2017 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).
10.2+	Celcuity Inc. Amended and Restated 2017 Stock Incentive Plan (incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on May 15, 2020).
10.3+	Form of Stock Option Agreement pursuant to Celcuity Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).
10.4+	Form of Restricted Stock Agreement pursuant to Celcuity Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).
10.5+	Form of Restricted Stock Unit Agreement pursuant to Celcuity Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).

10.6+	Form of Stock Appreciation Rights Agreement pursuant to Celcuity Inc. 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).
10.7+	Celcuity LLC 2012 Equity Incentive Plan, adopted August 10, 2012, as amended by First Amendment to the Celcuity LLC 2012 Equity Incentive Plan, adopted November 12, 2015 (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 filed with the SEC on August 23, 2017).
10.8+	Form of Incentive Plan Unit Option Agreement pursuant to the Celcuity LLC 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 filed with the SEC on August 23, 2017).
10.9	Commercial Lease, dated September 28, 2017, between West Glen Development I, LLC and Celcuity, LLC (incorporated by reference to Exhibit 10.11 to the Company's Quarterly Report on Form 10-Q filed with the SEC on November 13, 2017).
10.10	Commercial Lease, First Amendment to Lease, dated July 28, 2020, between West Glen Development I, LLC and Celcuity Inc. (incorporated by reference from Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 10, 2020).
10.11	Commercial Lease, Second Amendment to Lease, dated July 19, 2021, between West Glen Development I, LLC and Celcuity Inc., incorporated by reference from Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 11, 2021.
10.12	Clinical Trial Agreement, dated May 8, 2017, between NSABP Foundation, Inc. and Celcuity LLC (incorporated by reference to Exhibit 10.13 to the Company's Registration Statement on Form S-1 filed with the SEC on August 23, 2017).
10.13	Clinical Trial Agreement, Amendment No. 1, between NSABP Foundation, Inc and Celcuity Inc., dated October 15, 2020. (incorporated by reference from Exhibit 10.15 to the Company's Annual Report on Form 10-K filed with the SEC on February 16, 2021).
10.14+	Confidentiality, Assignment of Inventions and Non-Competition Agreement, dated November 15, 2011, between Celcuity LLC and Brian F. Sullivan (incorporated by reference to Exhibit 10.14 to the Company's Registration Statement on Form S-1 filed with the SEC on August 23, 2017).
10.15+	Confidentiality, Assignment of Inventions and Non-Competition Agreement, dated November 15, 2011, between Celcuity LLC and Lance G. Laing (incorporated by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1 filed with the SEC on August 23, 2017).
10.16+	Confidentiality, Non-Compete and Proprietary Rights Agreement, dated May 17, 2017, between Celcuity LLC and Vicky Hahne (incorporated by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1 filed with the SEC on August 23, 2017).
10.17	Form of Indemnification Agreement between Celcuity Inc. and each of its officers and directors (incorporated by reference to Exhibit 10.17 to the Company's Registration Statement on Form S-1/A filed with the SEC on September 12, 2017).

10.18†	License Agreement, dated April 8, 2021, by and between the Company and Pfizer, Inc (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 11, 2021).
10.19†	Amendment to License Agreement, dated May 6, 2021, by and between the Company and Pfizer, Inc. (incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed with the SEC on August 11, 2021).
23.1*	Consent of Boulay PLLP.
24.1*	Power of Attorney (included on the signature page).
31.1*	Certification of principal executive officer required by Rule 13a-14(a).
31.2*	Certification of principal financial officer required by Rule 13a-14(a).
32.1**	Section 1350 Certification of principal executive officer.
32.2**	Section 1350 Certification of principal financial officer.
101	Financial statements from the Annual Report on Form 10-K of the Company for the year ended December 31, 2021, formatted, in Inline XBRL: (i) the Balance Sheets, (ii) the Statements of Operations, (iii) the Statements of Changes in Stockholders' Equity, (iv) the Statements of Cash Flows, and (v) the Notes to Financial Statements.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and included in Exhibit 101).

* Filed herewith.
** Furnished herewith.
\+ Management contract or compensatory plan.
† Certain portions have been omitted from this exhibit.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We have issued our report dated March 23, 2022, with respect to the financial statements included in the Annual Report of Celcuity Inc. on Form 10-K for the year ended December 31, 2021. We hereby consent to the incorporation by reference in the Registration Statements of Celcuity Inc. on Form S-8 (Reg. Nos. 333-221117, 333-238787, 333-253940 and 333-256500) and on Form S-3 (Reg. No. 333-227466, 333-254625 and 333-261155).

/s/ Boulay PLLP

Minneapolis, Minnesota
March 23, 2022

Exhibit 31.1

CERTIFICATION UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Brian F. Sullivan, certify that:

1. I have reviewed this annual report on Form 10-K of Celcuity Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of material fact or omit to state a material fact necessary to make the statement made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2022

By */s/ Brian F. Sullivan*
Brian F. Sullivan
Chairman and Chief Executive Officer

Exhibit 31.2

CERTIFICATION UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Vicky Hahne, certify that:

1. I have reviewed this annual report on Form 10-K of Celcuity Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of material fact or omit to state a material fact necessary to make the statement made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 23, 2022

By */s/ Vicky Hahne*
Vicky Hahne
Chief Financial Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the filing of the Annual Report on Form 10-K for the year ended December 31, 2021 (the "Report") by Celcuity Inc. ("Registrant"), I, Brian F. Sullivan, the Chief Executive Officer of the Company, certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to the best of my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

Date: March 23, 2022

By */s/ Brian F. Sullivan*
Brian F. Sullivan
Chairman and Chief Executive Officer

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the filing of the Annual Report on Form 10-K for the year ended December 31, 2021 (the "Report") by Celcuity Inc. ("Registrant"), I, Vicky Hahne, the Chief Financial Officer of the Company, certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to the best of my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

Date: March 23, 2022

By */s/ Vicky Hahne*
Vicky Hahne
Chief Financial Officer