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

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 8, 2021

Celcuity Inc.

(Exact name of Registrant as Specified in its Charter)

Delaware	**001-38207**	**82-2863566**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

16305 36th Avenue North; Suite 100
Minneapolis, Minnesota 55446
(Address of Principal Executive Offices and Zip Code)

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

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

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. ☒

Item 1.01 Entry into a Material Definitive Agreement.

License Agreement

On April 8, 2021, Celcuity Inc. (the "Company") entered into a license agreement (the "License Agreement") with Pfizer, Inc. ("Pfizer"), pursuant to which the Company acquired exclusive (including as to Pfizer) worldwide sublicensable rights 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. Pursuant to the License Agreement, the Company is obligated to use commercially reasonable efforts to develop and seek regulatory approval for at least one product in the United States and if regulatory approval is obtained, to commercialize such product in the United States and at least one international major market.

The Company paid Pfizer a $5.0 million upfront fee upon execution of the License Agreement and, pursuant to an Equity Grant Agreement, issued to Pfizer $5.0 million of shares of the Company's common stock. The number of shares to be issued will be calculated by dividing $5.0 million by the closing price of a share of the Company's common stock on the Nasdaq Capital Market on the effective date of the License Agreement. 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 $330.0 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.

The descriptions of the License Agreement and the Equity Grant Agreement contained herein do not purport to be complete and are qualified in their entirety by reference to the complete text of the License Agreement, which will be filed as an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ending June 30, 2021 and the Equity Grant Agreement, which is filed as Exhibit 4.1 attached hereto.

Loan and Security Agreement

Also, 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"), as collateral agent and the Lenders listed on Schedule 1.1 thereto, pursuant to which Innovatus, as a Lender, has agreed to make certain term loans to the Company in the aggregate principal amount of up to $25.0 million (the "Term Loans").

Funding of the first $15.0 million tranche occured on April 8, 2021. The Company will be eligible to draw on a second tranche of $5.0 million upon achievement of certain milestones, including meeting the primary end points of either the FACT-1 or FACT-2 clinical trials and receipt of unrestricted net cash proceeds of at least $50.0 million from the issuance and sale of the Company's equity securities. The Company will be eligible to draw on a third tranche of $5.0 million upon the achievement of certain additional milestones, including commencement of certain Phase 3 clinical trials and the receipt of unrestricted net cash proceeds of at least $75.0 million from the issuance and sale of the Company's equity securities.

Innovatus 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")

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 Loan Agreement is secured by all assets of the Company. Proceeds will be used for working capital purposes and to fund the Company's general business requirements. The Loan Agreement contains customary representations and warranties and covenants, subject to customary carve outs, and includes financial covenants related to liquidity and trailing twelve months revenue.

In connection with each funding of the Term Loans, the Company is required to issue to Innovatus a warrant (the "Warrants") to purchase a number of shares of the Company's common 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) 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 or (ii) the closing price on the last trading day immediately preceding the execution of the Loan Agreement. For the second and third tranches only the exercise price will be based on the lower of (i) the exercise price for the first tranche or (ii) 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 relevant Term Loan funding. The Warrants may be exercised on a cashless basis and are exercisable through the 10th anniversary of the applicable funding date. The number of shares of common stock for which each Warrant is exercisable and the associated exercise price are subject to certain proportional adjustments as set forth in such Warrant.

The descriptions of the Loan Agreement and the Warrants contained herein do not purport to be complete and are qualified in their entirety by reference to the complete text of the Loan Agreement, which will be filed as an exhibit to the Company's Quarterly Report on Form 10-Q for the quarter ending June 30, 2021 and the form of Warrant filed as Exhibit 4.2 attached hereto.

Item 2.03 Creation of a Direct Financial Obligation or an Obligation under an Off-Balance Sheet Arrangement of a Registrant.

The information set forth under *Loan and Security Agreement* in Item 1.01 above is incorporated herein by reference.

Item 3.02 Unregistered Sales of Equity Securities.

The information set forth under Item 1.01 above regarding the issuance of equity to Pfizer under the License Agreement, the Conversion Right, and the Warrants is incorporated herein by reference. The issuance of shares of the Company's common stock pursuant to the License Agreement, the Conversion Right, and the Warrants will be made in reliance on the exemption from registration contained in Section 4(a)(2) of the Securities Act of 1933, as amended, and Rule 506 of Regulation D thereunder.

Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

In connection with the execution of the license agreement, each of Brian Sullivan, our President and Chief Executive Officer, Lance Laing, our Chief Science Officer, and Vicky Hahne, our Chief Financial Officer, earned a milestone bonus under the Company's milestone-based incentive pay program, payable in the form of stock options. These bonuses were consistent with the previously disclosed executive bonus program, except for Ms. Hahne's bonus. She received a one-time increase to the stock option that would otherwise be issued from a fair market value of $51,000 to a fair market value of $71,000.

Item 8.01 Other Events

On April 8, 2021, the Company issued a press release announcing the License Agreement and a press release announcing certain business updates, including the Loan Agreement. These press releases are attached as Exhibit 99.1 and Exhibit 99.2, respectively, hereto and are incorporated herein by reference.

To reflect the addition of the License Agreement to the Company's business, the Company is providing supplements to its Business Description and Risk Factors as presented in the Annual Report on Form 10-K for the year ended December 31, 2020. The supplemental business description is attached hereto as Exhibit 99.3 and the supplemental risk factors are attached hereto as Exhibit 99.4, each of which is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

4.1	Equity Grant Agreement, dated April 8, 2021 between the Company and Pfizer, Inc.
4.2	Form of Warrant
99.1	Press Release dated April 8, 2021 regarding the License Agreement.
99.2	Press Release dated April 8, 2021 certain business updates, including the Loan Agreement.
99.3	Supplemental Business Description.
99.4	Supplemental Risk Factors.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: April 8, 2021

CELCUITY INC.

By: /s/ Brian F. Sullivan
Brian F. Sullivan
Chief Executive Officer

Exhibit 4.1

EQUITY GRANT AGREEMENT

This Equity Grant Agreement (this "Agreement") is made effective as of the 7 day of April, 2021 (the "Effective Date"), by and between Celcuity Inc., a Delaware corporation (the "Company"), and Pfizer Inc., a Delaware corporation (the "Investor").

WHEREAS, the Company and the Investor are entering into a License Agreement dated the Effective Date (the "License Agreement") under which the Company is licensing certain technology from the Investor;

WHEREAS, the Company and the Investor are executing and delivering this Agreement in reliance upon the exemption from securities registration afforded by Section 4(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"), and Rule 506 of Regulation D as promulgated by the United States Securities and Exchange Commission (the "Commission") under the Securities Act; and

WHEREAS, the License Agreement provides that, among other things, the Company will issue to the Investor shares of common stock, par value $0.001 per share (the "Common Stock"), of the Company upon the terms and conditions stated in this Agreement.

NOW, THEREFORE, in consideration of the mutual covenants set forth herein, and for other good and valuable consideration, the receipt and sufficiency of which is acknowledged, and intending to be legally bound hereby, the parties hereto agree as follows:

1. Issuance of Shares.

1.1. Shares;Number of Shares. In consideration of the licenses and rights granted to the Company under the License Agreement, and subject to the terms and conditions of this Agreement and in reliance on the representations and warranties of the Investor set forth herein, the Company hereby agrees to issue to the Investor, and the Investor hereby agrees to acquire from the Company, such number of shares of the Company's Common Stock (the "Shares") equivalent in monetary value on an aggregate basis to five million U.S. dollars ($5,000,000.00), where the number of shares of Company's Common Stock issued to Investor shall be calculated by dividing five million U.S. dollars ($5,000,000.00) by the closing price of a share of the Company's Common Stock on the NASDAQ Capital Market on the Effective Date, rounded to the nearest whole share.

1.2. Closing; Delivery of Shares. The issuance of the Shares shall take place on the Effective Date, remotely via the exchange of documents and signatures, or at such other time, date and place as the Company and the Investor mutually agree upon in writing (which time and place are designated as the "Closing"). On or before the Closing, the Company will cause the transfer agent for the Common Stock (the "Transfer Agent") to issue the Shares to the Investor and to hold the Shares in book-entry form for the account of the Investor. The book entry for the Shares will be subject to a stop transfer order reflecting such the transfer restrictions referred to in Sections 4.5 and 4.6 of this Agreement. At the Closing, the Company will deliver to Investor a copy of Company's irrevocable instructions to its Transfer Agent for the Common Stock instructing such Transfer Agent to register the issuance of the Shares to the Investor via book-entry.

2. Conditions to Closing.

2.1. Conditions to the Investor's Obligations. The obligation of the Investor to acquire the Shares at the Closing is subject to the fulfillment to the reasonable satisfaction of the Investor on or prior to the Closing of each of the following conditions, any of which may be waived by the Investor:

(a) Each of the representations and warranties of the Company contained in Section 3 shall be true and correct in all material respects or, if subject to materiality or Material Adverse Effect (as defined in Section 3.1), shall be true and correct in all respects, at and as of the Closing (except for such representations and warranties that are made as of a specific date, which shall be true and correct in all material respects or, if subject to materiality or Material Adverse Effect, shall be true and correct in all respects as of such date), as though such representation or warranty were made as of such date.

(b) The Company shall have performed in all material respects all obligations and covenants herein or in the License Agreement required to be performed by it on or prior to the Closing.

(c) The Company shall have delivered or caused to be delivered an irrevocable instruction letter to the Company's Transfer Agent instructing the Transfer Agent to issue the Shares to the Investor in book-entry form for the account of the Investor.

(d) No judgment, writ, order, injunction, award or decree of or by any court, or judge, justice or magistrate, including any bankruptcy court or judge, or any order of or by any governmental authority, shall have been issued, and no action or proceeding shall have been instituted by any governmental authority, enjoining or preventing the consummation of the transactions contemplated hereby or in the License Agreement.

(e) No stop order or suspension of trading shall have been imposed by the Commission or any other governmental or regulatory body with respect to public trading in the Common Stock.

(f) Since the Effective Date, there shall not have occurred any Material Adverse Effect, and no event shall have occurred or circumstance shall exist that, in combination with any other events or circumstances, could reasonably be expected to have or result in a Material Adverse Effect.

2.2. Conditions to the Company's Obligations. The Company's obligation to issue the Shares at the Closing is subject to the fulfillment to the reasonable satisfaction of the Company on or prior to the Closing of each of the following conditions, any of which may be waived by the Company:

(a) Each of the representations and warranties of the Investor contained in Section 4 shall be true and correct in all material respects at and as of the Closing, as though such representation or warranty were made as of such date.

(b) The License Agreement shall not have been terminated.

(c) No judgment, writ, order, injunction, award or decree of or by any court, or judge, justice or magistrate, including any bankruptcy court or judge, or any order of or by any governmental authority, shall have been issued, and no action or proceeding shall have been instituted by any governmental authority, enjoining or preventing the consummation of the transactions contemplated hereby or in the License Agreement.

(d) No stop order or suspension of trading shall have been imposed by the Commission or any other governmental or regulatory body with respect to public trading in the Common Stock.

3. Representations and Warranties of the Company. The Company hereby represents and warrants to the Investor that:

3.1. Organization, Good Standing and Qualification. The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware and has all requisite corporate power and authority to carry on its business as presently conducted or proposed to be conducted and to own or lease the properties and assets it now owns or holds under lease. The Company and its Subsidiaries are duly qualified to transact business and is in good standing in each jurisdiction in which the failure so to qualify would, individually or in the aggregate, have a material adverse effect upon the general affairs, business, management, properties, operations, condition (financial or otherwise) or results of operations of the Company or any of its Subsidiaries, taken as a whole ("Material Adverse Effect"). The Company has disclosed all of its subsidiaries required to be disclosed in an exhibit to its applicable SEC Reports (the "Subsidiaries"). The Company owns, directly or indirectly, all of the capital stock or other equity interests of each Subsidiary free and clear of any liens, and all of the issued and outstanding shares of capital stock of each Subsidiary are validly issued and are fully paid and, if applicable in the relevant jurisdiction, non-assessable, and free of preemptive and similar rights to subscribe for or purchase securities.

3.2. Capitalization;Valid Issuance of Shares. The authorized capital of the Company, as of the last business day immediately prior to the Effective Date, consists of: (i) 25,000,000 shares of Common Stock, of which (x) 12,287,896 shares were issued and outstanding, (y) 1,285,582 shares were reserved for future issuance pursuant to the Company's stock-based compensation plans, including 854,622 shares issuable upon the exercise of stock options outstanding as of such date, and (z) 352,400 shares issuable were upon the exercise of stock warrants outstanding as of such date, and (ii) 2,500,000 shares of preferred stock, par value $0.001 per share, none of which were issued and outstanding as of such date. The capital stock of the Company, including the Common Stock and the Shares to be issued pursuant to this Agreement, conforms to the description thereof in the SEC Reports. All of the issued and outstanding shares of capital stock of the Company are duly authorized and validly issued, fully paid and nonassessable, have been issued in compliance with all federal and state securities laws, were not issued in violation of or subject to any preemptive rights or other rights to subscribe for or purchase securities that have not been waived in writing, and the holders thereof are not subject to personal liability by reason of being such holders. The Shares to be issued hereunder by the Company have been duly authorized and, when issued and delivered in accordance with the terms of this Agreement, will have been validly issued and will be fully paid and nonassessable, will not be subject to preemptive rights or other similar rights of stockholders of the Company, and will be free and clear of all lien (except for restrictions on transfer imposed by applicable securities Laws or contained herein) and the holder thereof will not be subject to personal liability by reason of being such holder.

3.3. Authorization; No Conflicts; Authority. This Agreement has been duly authorized, executed and delivered by the Company, and constitutes a valid, legal and binding obligation of the Company, enforceable in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization or similar laws affecting the rights of creditors generally and subject to general principles of equity. The execution, delivery and performance of this Agreement and the consummation of the transactions herein contemplated will not (a) conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, or result in the creation or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to any indenture, mortgage, deed of trust, loan agreement or other material agreement or instrument to which the Company is a party or by which the Company is bound or to which any of the property or assets of the Company is subject, (b) result in any violation of the provisions of the Company's charter or bylaws or (c) result in the violation of any law or statute or any judgment, order, rule, regulation or decree of any court or arbitrator or federal, state, local or foreign governmental agency or regulatory authority having jurisdiction over the Company or any of its properties or assets (each, a "Governmental Authority"), except in the case of clauses (a) and (c) above as would not result in a Material Adverse Effect. No consent, approval, authorization or order of, or registration or filing with any Governmental Authority is required for the execution, delivery and performance of this Agreement or for the consummation of the transactions contemplated hereby, including the issuance of the Shares by the Company, except such as may be required under the Securities Act, the Nasdaq Stock Market Rules or state securities or blue sky laws; and the Company has full power and authority to enter into this Agreement and to consummate the transactions contemplated hereby, including the authorization and issuance of the Shares as contemplated by this Agreement.

3.4. Exchange Listing and Exchange Act Registration. The Common Stock is registered pursuant to Section 12(b) of the Securities Exchange Act of 1934, as amended ("Exchange Act") and is included for listing on the Nasdaq Capital Market and the Company has not taken any action designed to, or likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act or delisting the Common Stock from the Nasdaq Capital Market, and the Company has not received any notification that the Commission or the Nasdaq Capital Market is contemplating terminating such registration or listing. The Company agrees to notify Investor promptly upon the Company becoming an "ineligible issuer." The Company has complied in all material respects with the applicable requirements of the Nasdaq Capital Market for maintenance of inclusion of the Common Stock thereon. No person or entity has any right to cause the Company to effect the registration under the Securities Act of any securities of the Company or any Subsidiary.

3.5. SEC Reports. The Company has timely filed with the Commission all of the reports and other documents required to be filed by it under the Exchange Act and the Securities Act and any required amendments to any of the foregoing (the "SEC Reports"). The SEC Reports, when they were filed with the Commission, did not contain an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading. None of the Company's Subsidiaries is subject to the periodic reporting requirements of the Exchange Act. As of the date hereof, there are no outstanding or unresolved comments in comment letters from the Commission staff with respect to any of the SEC Reports and the Company has not been notified in writing that any of the SEC Reports is the subject of ongoing Commission review or outstanding investigation.

3.6. Financial Statements. As of its respective date, the financial statements, together with the related notes and schedules, of the Company included in the SEC Reports complied as to form in all material respects with all applicable accounting requirements and the published rules and regulations of the Commission and all other applicable rules and regulations with respect thereto. Such financial statements, together with the related notes and schedules, have been prepared in accordance with generally accepted accounting principles in the United States ("GAAP") applied on a consistent basis during the periods involved (except (i) as may be otherwise indicated in such financial statements or the notes thereto or (ii) in the case of unaudited interim statements, to the extent they may not include footnotes or may be condensed or summary statements), and fairly present in all material respects the financial condition of the Company and its consolidated subsidiaries as of the dates thereof and the results of operations and cash flows for the periods then ended (subject, in the case of unaudited statements, to normal year-end audit adjustments). Except (i) as set forth in the SEC Reports or (ii) for liabilities incurred in the ordinary course of business subsequent to the date of the most recent balance sheet contained in the SEC Reports, the Company has no liabilities, whether absolute or accrued, contingent or otherwise, required by GAAP to be set forth on a consolidated balance sheet of the Company or in the notes thereto.

3.7. Certain Registration Matters. Assuming the accuracy of the Investor's representations and warranties set forth in Section 4, no registration under the Securities Act is required for the offer and issuance of the Securities by the Company to the Investor under this Agreement and the License Agreement.

3.8. Private Placement. Subject to the accuracy of the representations made by Investor in Section 4, the offer and issuance of the Shares to Investor as contemplated hereby is exempt from the registration requirements of the Securities Act, and will have been registered or qualified (or are exempt from registration and qualification) under the registration, permit or qualification requirements of all applicable state securities Laws. Except as otherwise disclosed by Company to Investor in writing, Company has not engaged any brokers, finders or agents, nor incurred, nor will incur, directly or indirectly, any liability for brokerage or finder's fees or agents' commissions or any similar charges in connection with this Agreement and the transactions contemplated hereby.

3.9. Litigation. Other than as set forth in the SEC Reports filed prior to the Effective Date, there is no action, suit, prosecution, investigation, litigation, arbitration, hearing, order, claim, complaint or other proceeding ("Action") pending (of which the Company has received notice or otherwise has knowledge) or, to the Company's knowledge, threatened, against the Company, any of its Subsidiaries or any of their respective properties or which the Company or any of its Subsidiaries intends to initiate, except where such Action would not (a) adversely affect or challenge the legality, validity or enforceability of this Agreement or the issuance of the Shares or (ii) reasonably be expected to have a Material Adverse Effect on the Company.

3.10. Permits; Compliance with Laws. The Company has all franchises, permits, licenses and other rights and privileges ("Permits") necessary to permit it to own its properties and to conduct its business as presently conducted and is in compliance thereunder, except where the failure to be in compliance would not reasonably be expected to have a Material Adverse Effect on the Company. The Company is and has been in compliance with all laws, statutes, rules, regulations, orders, judgments, injunctions and ordinances of any Governmental Authority ("Laws") applicable to its business, properties and assets, and to the products and services sold by it, except where the failure to be in compliance has not had and would not reasonably be expected to have a Material Adverse Effect on the Company. The Company has made all material filings and obtained all such material approvals as may be required by the United States Food and Drug Administration (the "FDA") or any committee thereof or from any other U.S. or drug or medical device regulatory agency, or health care facility Institutional Review Board (collectively, the "Regulatory Agencies") to conduct the clinical trials and manufacturing activities related to such clinical trials currently being conducted by the Company, and the Company has operated and currently is in compliance in all material respects with all applicable rules, regulations and policies of the Regulatory Agencies, except where the failure to make such filings, obtain such approval or comply with such rules, regulations and policies could not reasonably be expected to have a Material Adverse Effect on the Company. The Company has not received any written notification of any pending or threatened Action from any Governmental Authority, including any Regulatory Agency, that could reasonably be expected to have a Material Adverse Effect on the Company.

3.11. Absence of Certain Changes. Since the date of the latest audited financial statements included within the SEC Reports, (a) the Company and each of its Subsidiaries has conducted its business operations in the ordinary course of business consistent with past practice, (b) there has not occurred any event, change, development, circumstance or condition that, individually or in the aggregate, has had or would reasonably be expected to have a Material Adverse Effect on the Company, (c) the Company has not (i) declared or paid any dividends, or authorized or made any distribution upon or with respect to any class or series of its capital stock, or (ii) sold, exchanged or otherwise disposed of any of its material assets or rights, and (d) the Company has not admitted in writing its inability to pay its debts generally as they become due, filed or consented to the filing against it of a petition in bankruptcy or a petition to take advantage of any insolvency act, made an assignment for the benefit of creditors, consented to the appointment of a receiver for itself or for the whole or any substantial part of its property, or had a petition in bankruptcy filed against it, been adjudicated bankrupt or filed a petition or answer seeking reorganization or arrangement under the federal bankruptcy laws or any other laws of the United States or any other jurisdiction.

3.12. Anti-Corruption and Anti-Bribery Laws. Neither the Company and its Subsidiaries, nor, to the Company's knowledge, any of their respective directors, officer, agents, employees or other authorized persons acting on behalf of the Company or its Subsidiaries is aware of or has taken any action, directly or indirectly, that could result in a violation or a sanction for violation by such persons of the Foreign Corrupt Practices Act of 1977 or the U.K. Bribery Act 2010, each as may be amended, or similar law of any other relevant jurisdiction, or the rules or regulations thereunder; and the Company has instituted and maintains policies and procedures to ensure compliance therewith.

3.13. Economic Sanctions. Neither the Company and its Subsidiaries, nor, to Company's knowledge, any of their respective directors, officers, agents, employees or other authorized person acting on behalf of the Company: (a) is, or is controlled or 50% or more owned in the aggregate by or is acting on behalf of, one or more individuals or entities that are currently the subject of any sanctions administered or enforced by the United States (collectively, "Sanctions" and such persons, "Sanctioned Persons" and each such person, a "Sanctioned Person") or (b) has, within the last five (5) years, done the Company's business in a country or territory that was, or whose government was, at such time the subject of Sanctions that broadly prohibit dealings with that country or territory. Within the past five (5) years, to the knowledge of the Company, it has neither been the subject of any governmental investigation or inquiry regarding compliance with Sanctions nor has it been assessed any fine or penalty in regard to compliance with Sanctions.

3.14. Money Laundering. The operations of the Company and its Subsidiaries are and have been conducted at all times in compliance with applicable financial record-keeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, applicable money laundering statutes and applicable rules and regulations thereunder (collectively, the "Money Laundering Laws"), and no Action by or before any court or governmental agency, authority or body or any arbitrator involving the Company or any Subsidiary with respect to the Money Laundering Laws is pending or, to the knowledge of the Company or any Subsidiary, threatened.

3.15. Accountants. The Company's registered public accounting firm is Boulay PLLP. To the Company's knowledge, Boulay PLLP are independent public accountants with respect to the Company within the meaning of the Securities Act and Exchange Act and the applicable published rules and regulations thereunder.

3.16. Incorporation of Other Representations and Warranties. The representations and warranties of the Company contained in the License Agreement are incorporated herein by reference and made a part of this Agreement as if fully set forth herein.

4. Representations and Warranties of the Investor. The Investor hereby represents and warrants to the Company that:

4.1. Authorization. This Agreement has been duly authorized, executed and delivered by the Company, and constitutes a valid, legal and binding obligation of the Company, enforceable in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization or similar laws affecting the rights of creditors generally and subject to general principles of equity.

4.2. Purchase Entirely for Own Account. The Investor is acquiring the Shares for investment for the Investor's own account, not as a nominee or agent, and not with a view to the resale or distribution of any part thereof, and the Investor has no present intention of selling, granting any participation in, or otherwise distributing the same. The Investor does not presently have any contract, undertaking, agreement or arrangement with any person to sell, transfer or grant participations to such person or to any third person, with respect to any of the Shares.

4.3. Disclosure of Information. The Investor has had an opportunity to discuss the Company's business, management, financial affairs and the terms and conditions of the offering of the Shares with the Company's management and has had an opportunity to review the Company's facilities.The foregoing, however, does not limit or modify the representations and warranties of the Company in Section 3 of this Agreement or the right of the Investor to rely thereon.

4.4. Accredited Investor. The Investor is an accredited investor as defined in Rule 501(a) of Regulation D promulgated under the Securities Act.

4.5. Restricted Securities. The Investor understands that the Shares have not been, and will not be, registered under the Securities Act, by reason of a specific exemption from the registration provisions of the Securities Act which depends upon, among other things, the bona fide nature of the investment intent and the accuracy of the Investor's representations as expressed herein. The Investor understands that the Shares are "restricted securities" under applicable U.S. federal and state securities laws and that, pursuant to these laws, the Investor must hold the Shares indefinitely unless they are registered under the Securities Act and qualified by state authorities, or an exemption from such registration and qualification requirements is available. The Investor acknowledges that the Company has no obligation to register or qualify the Shares for resale. The Investor further acknowledges that if an exemption from registration or qualification is available, it may be conditioned on various requirements including, but not limited to, the time and manner of sale, the holding period for the Shares, and on requirements relating to the Company which are outside of the Investor's control, and which the Company is under no obligation and may not be able to satisfy.

4.6. Legends. The Investor understands that the Shares may bear one or all of the following legends:

(a) "THE SHARES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AND HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE OR DISTRIBUTION THEREOF. NO SUCH TRANSFER MAY BE EFFECTED WITHOUT AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL IN A FORM SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OF 1933."

(b) Any legend required by the securities laws of any state to the extent such laws are applicable to the Shares represented by the certificate, instrument, or book entry so legended.

5. Resale of Shares.

5.1. Reports Under Exchange Act. With a view to making available to the Investor the benefits of Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended from time to time ("Rule 144"), and any other rule or regulation of the Commission that may at any time permit the Investor to sell securities of the Company to the public without registration, the Company shall:

(a) make and keep available adequate current public information, as such term is understood and defined in Rule 144, at all times after the Effective Date;

(b) use commercially reasonable efforts to file with the Commission in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act; and

(c) furnish to the Investor, so long as the Investor owns any Shares, upon request (i) to the extent accurate, a written statement by the Company that it has complied with the reporting requirements of Rule 144, the Securities Act, and the Exchange Act; (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents filed by the Company with the Commission; and (iii) such other information as may be reasonably requested in availing the Investor of any rule or regulation of the Commission that permits the selling of any such securities without registration.

5.2. Removal of Legends. In connection with any sale or disposition of the Shares by Investor pursuant to Rule 144 or pursuant to any other exemption under the Securities Act such that the purchaser acquires freely tradable shares and upon compliance by Investor with the requirements of this Agreement, the Company shall cause the Transfer Agent to issue replacement certificates representing the Shares sold or disposed of without restrictive legends or record the Shares sold or disposed of in book-entry form without such restrictions. Upon the Shares becoming freely tradable by Investor as a non-affiliate pursuant to Rule 144, the Company shall deliver to the Transfer Agent irrevocable instructions to remove restrictive legends or stop-transfer orders with respect to the Shares.

6. Miscellaneous.

6.1. Entire Agreement; Amendments; Waivers. This Agreement, together with the License Agreement, constitutes the entire agreement between the parties hereto pertaining to the subject matter hereof, and any and all other prior or contemporaneous written or oral agreements relating to the subject matter hereof existing between the parties hereto are expressly canceled. This Agreement may not be amended, modified or waived except by an instrument in writing signed by each of the parties hereto.

6.2. Successors and Assigns. Neither this Agreement nor any of the rights or obligations hereunder may be assigned by either party without the prior written consent of the non-assigning party;provided, however, that Investor may assign this Agreement without the Company's consent to an affiliate of the Investor. The terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective successors and assigns of the parties hereto. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and assigns any rights, remedies, obligations, or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

6.3. Further Assurances; Survival. The parties shall execute and deliver all such further instruments and documents and take all such other actions as may reasonably be required to carry out the transactions contemplated hereby and to evidence the fulfillment of the agreements herein contained. The provisions of this Agreement will survive termination.

6.4. Notices. Except as otherwise provided herein, all communications hereunder shall be in writing and, if to the Investor, shall be mailed via overnight delivery service or hand delivered to Pfizer Inc., 235 East 42nd Street, New York, NY 10017, Attention: Senior Vice President, Worldwide Business Development (with a copy to Pfizer Inc., 235 East 42nd Street, New York, NY 10017, Attention: Andrew J. Muratore);if to the Company, shall be mailed via overnight delivery service or hand delivered to Celcuity Inc., 16305 36th Avenue North, Suite 100, Minneapolis, MN 55446, Attention: Brian F. Sullivan, with a copy (which shall not constitute notice) to Fredrikson & Byron, P.A., 200 South Sixth Street, Suite 4000, Minneapolis, MN 55402, Attention: Eric O. Madson;or in each case to such other address as the person to be notified may have requested in writing. Any party to this Agreement may change such address for notices by sending to the parties to this Agreement written notice of a new address for such purpose.

6.5. Governing Law. All questions concerning the construction, validity, enforcement and interpretation of this Agreement shall be governed by and construed and enforced in accordance with the internal laws of the State of Delaware, without regard to the principles of conflicts of law thereof.

6.6. Titles and Subtitles. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

6.7. Counterparts. This Agreement may be executed and delivered by facsimile, by electronic mail attaching a portable document file (.pdf) or any electronic signature complying with the U.S. federal ESIGN Act of 2000 (*e.g.*, www.docusign.com). This Agreement may be executed in one or more counterparts and, if executed in more than one counterpart, the executed counterparts shall each be deemed to be an original and all such counterparts shall together constitute one and the same instrument.

6.8. Severability. If any provision of this Agreement should be held invalid, illegal or unenforceable in any jurisdiction, the parties will negotiate in good faith a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the parties and all other provisions hereof will remain in full force and effect in such jurisdiction and will be liberally construed in order to carry out the intentions of the parties hereto as nearly as may be possible. Such invalidity, illegality or unenforceability will not affect the validity, legality or enforceability of such provision in any other jurisdiction.

6.9. No Strict Construction. The language used in this Agreement is deemed to be the language chosen by the parties to express their mutual intent, and no rules of strict construction will be applied against a party.

6.10. Expenses. The Company and Investor are each liable for, and will pay, their own expenses incurred in connection with the negotiation, preparation, execution and delivery of this Agreement, including, without limitation, attorneys' and consultants' fees and expenses. The Company shall pay any and all transfer, stamp, issuance and similar taxes, costs and expenses (including, without limitation, fees and expenses of the transfer agent) that may be payable with respect to the delivery of the Shares to Investor.

[Signature page follows]

IN WITNESS WHEREOF, the parties have executed this Equity Grant Agreement as of the Effective Date.

THE COMPANY:

CELCUITY INC.

By: /s/ Brian F. Sullivan

Name: Brian F. Sullivan
Title: Chief Executive Officer

INVESTOR:

PFIZER INC.

By: /s/ Jeff Settleman

Name: Jeff Settleman
Title: Senior Vice President & Chief Scientific Officr, Pfizer Oncology R&d

Exhibit 4.2

THIS WARRANT AND THE SHARES ISSUABLE HEREUNDER HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN SECTIONS 5.3 AND 5.4 BELOW, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED (I) UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR (II) WITHOUT AN OPINION OF COUNSEL, IN FORM AND SUBSTANCE REASONABLY SATISFACTORY TO THE COMPANY, THAT SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

WARRANT TO PURCHASE STOCK[1]

Company	CELCUITY, INC.
Number of Shares	26,042
Type/Series of Stock	Common Stock, par value $0.01 per share of the Company ("Common Stock")
Warrant Price	$14.40 per share[2]
Issue Date	April 8, 2021
Expiration Date	April 8, 2031 (See also Section 5.1(b))
Credit Facility	This Warrant to Purchase Stock ("Warrant") is issued in connection with that certain Loan and Security Agreement, dated April 8, 2021, among Innovatus Life Sciences Lending Fund I, LP, as Lender and Collateral Agent, the Lenders from time to time party thereto, and the Company (as modified, amended and/or restated from time to time, the "Loan Agreement").

THIS WARRANT CERTIFIES THAT, for good and valuable consideration, INNOVATUS LIFE SCIENCES LENDING FUND I, LP ("Innovatus"), a Delaware limited partnership with an office located at 777 Third Avenue, 25th Floor, New York, NY 10017 (together with any successor or permitted assignee or transferee of this Warrant or of any shares issued upon exercise hereof, "Holder") is entitled to purchase the number of fully paid and non-assessable shares (the "Shares") of the above-stated Type/Series of Stock (the "Class") of the above-named company (the "Company") at the above-stated Warrant Price, all as set forth above and as adjusted pursuant to Section 2 of this Warrant, subject to the provisions and upon the terms and conditions set forth in this Warrant.

_____

[1] The Company acknowledges and agrees that this Warrant is issued in connection with the Term A Loan under, and as defined in, the Loan Agreement, and that, in the event the Company draws the Term B Loan and/or the Term C Loan, each as defined therein, the Company shall issue the Holder additional Warrants to purchase shares of the Company's Common Stock, equal to 2.5% of the funded amount of such Term B and Term C Loans, at the price per share described above, subject to any adjustments to the shares and/or price, on substantially the terms and conditions set forth in this Warrant.

[2] The exercise price for the warrant issued at the execution of the Loan and Security Agreement or subsequently, will be equal to the lower of (i) the volume weighted average price per share of Celcuity's stock for the 5- trading day period ending on the last trading day immediately preceding the date of the Loan and Security Agreement or (ii) the closing price per share for the last trading immediately preceding the date of the Loan and Security Agreement. The exercise price for Warrants issued on the funding dates of Term B Loan and Term C Loans will be the lower of (i) the exercise price for Warrant issued on the closing date of the Loan Agreement or (ii) the volume weighted average price per share of the Company's stock for the 5- trading day period ending on the last trading day immediately preceding the funding date of Term B Loan or Term C Loan, as applicable.

SECTION 1. EXERCISE.

1.1. Method of Exercise. Holder may at any time and from time to time after June 1, 2021 exercise this Warrant, in whole or in part, by delivering to the Company the original of this Warrant together with a duly executed Notice of Exercise in substantially the form attached hereto as Appendix 1 and, unless Holder is exercising this Warrant pursuant to a cashless exercise set forth in Section 1.2, a check, wire transfer of same-day funds (to an account designated by the Company), or other form of payment acceptable to the Company for the aggregate Warrant Price for the Shares being purchased; provided that if an Acquisition occurs the Holder may exercise this Warrant according to the terms hereof at any time.

1.2. Cashless Exercise. On any exercise of this Warrant, in lieu of payment of the aggregate Warrant Price in the manner as specified in Section 1.1 above, but otherwise in accordance with the requirements of Section 1.1, Holder may elect to receive Shares equal to the value of this Warrant, or portion hereof as to which this Warrant is being exercised. Thereupon, the Company shall issue to the Holder such number of fully paid and non-assessable Shares as are computed using the following formula:

$$X = Y(A-B)/A$$

where:

X = the number of Shares to be issued to the Holder;

Y = the number of Shares with respect to which this Warrant is being exercised (inclusive of the Shares surrendered to the Company in payment of the aggregate Warrant Price);

A = the Fair Market Value (as determined pursuant to Section 1.3 below) of one Share; and

B = the Warrant Price.

1.3. Fair Market Value. If the Common Stock is then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "Trading Market"), the fair market value of a Share shall be the closing price of a share of Common Stock reported for the Business Day immediately before the date on which Holder delivers this Warrant together with its Notice of Exercise to the Company. If the Common Stock is not traded in a Trading Market, the Board of Directors of the Company shall determine the fair market value of a Share in its reasonable good faith judgment.

1.4. Delivery of Certificate and New Warrant. Promptly after Holder exercises this Warrant in the manner set forth in Section 1.1 or 1.2 above, the Company shall deliver to Holder a certificate (via an electronic shares program, if applicable) representing the Shares issued to Holder upon such exercise and, if this Warrant has not been fully exercised and has not expired, a new warrant of like tenor representing the Shares not so acquired.

1.5. Replacement of Warrant. On receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant and, in the case of loss, theft or destruction, on delivery of an indemnity agreement reasonably satisfactory in form, substance and amount to the Company or, in the case of mutilation, on surrender of this Warrant to the Company for cancellation, the Company shall, within a reasonable time, execute and deliver to Holder, in lieu of this Warrant, a new warrant of like tenor and amount.

1.6. Treatment of Warrant Upon Acquisition of Company.

(a) Acquisition. For the purpose of this Warrant, "Acquisition" means any transaction or series of related transactions involving: (i) the sale, lease, exclusive license or other disposition of all or substantially all of the assets of the Company; (ii) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization; or (iii) any sale or other transfer by the stockholders of the Company of shares representing a majority of the Company's then-total outstanding combined voting power.

(b) Treatment of Warrant at Acquisition. In the event of an Acquisition in which the consideration to be received by the Company's stockholders consists solely of cash, solely of Marketable Securities or a combination of cash and Marketable Securities (a "Cash/Public Acquisition"), either (i) Holder shall exercise this Warrant pursuant to Section 1.1 and/or 1.2 and such exercise will be deemed effective immediately prior to and contingent upon the consummation of such Acquisition or (ii) if Holder elects not to exercise the Warrant, this Warrant will expire immediately prior to the consummation of such Acquisition. For the avoidance of doubt, "Acquisition" shall exclude any sale and issuance by the Company of shares of its capital stock, or securities or instruments exercisable for or convertible into or otherwise representing the right to acquire shares of capital stock, to one or more investors in a transaction or series of related transactions the primary purpose of which is a bona fide equity financing of the Company.

(c) The Company shall provide Holder with written notice of its request relating to the Cash/Public Acquisition (together with such reasonable information as Holder may reasonably require regarding the treatment of this Warrant in connection with such contemplated Cash/Public Acquisition giving rise to such notice), which is to be delivered to Holder not less than seven (7) Business Days prior to the closing of the proposed Cash/Public Acquisition. Notwithstanding the foregoing, if, immediately prior to the Cash/Public Acquisition, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above would be greater than the Warrant Price in effect on such date, then this Warrant shallautomatically be deemed on and as of such date to be exercised pursuant to Section 1.2 above as to all Shares (or such other securities) for which it shall not previously have been exercised, and the Company shall promptly notify the Holder of the number of Shares (or such other securities) issued upon such exercise to the Holder.

(d) Upon the closing of any Acquisition other than a Cash/Public Acquisition defined above, the acquiring, surviving or successor entity shall assume the obligations of this Warrant, and this Warrant shall thereafter be exercisable for the same securities and/or other property as would have been paid for the Shares issuable upon exercise of the unexercised portion of this Warrant as if such Shares were outstanding on and as of the closing of such Acquisition, subject to further adjustment from time to time in accordance with the provisions of this Warrant.

(e) As used in this Warrant, "Marketable Securities" means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and is then current in its filing of all required reports and other information under the Act and the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by Holder in connection with the Acquisition were Holder to exercise this Warrant on or prior to the closing thereof is then traded in Trading Market; and (iii) Holder would be able to publicly re-sell, within six (6) months following the closing of such Acquisition, all of the issuer's shares and/or other securities that would be received by Holder in such Acquisition were Holder to exercise this Warrant in full on or prior to the closing of such Acquisition.

SECTION 2. ADJUSTMENTS TO THE SHARES AND WARRANT PRICE.

2.1. Stock Dividends, Splits, Etc. If the Company declares or pays a dividend or distribution on the outstanding shares of the Class payable in common stock or other securities or property (other than cash), then upon exercise of this Warrant, for each Share acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the Shares of record as of the date the dividend or distribution occurred. If the Company subdivides the outstanding shares of the Class by reclassification or otherwise into a greater number of shares, the number of Shares purchasable hereunder shall be proportionately increased and the Warrant Price shall be proportionately decreased. If the outstanding shares of the Class are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Warrant Price shall be proportionately increased and the number of Shares shall be proportionately decreased.

2.2. Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the outstanding shares of the Class are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the Shares been outstanding on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 2.2 shall similarly apply to successive reclassifications, exchanges, combinations substitutions, replacements or other similar events.

2.3. Intentionally Omitted.

2.4. Intentionally Omitted.

2.5. No Fractional Share. No fractional Share shall be issuable upon exercise of this Warrant and the number of Shares to be issued shall be rounded down to the nearest whole Share. If a fractional Share interest arises upon any exercise of the Warrant, the Company shall eliminate such fractional Share interest by paying Holder in cash the amount computed by multiplying the fractional interest by (a) the fair market value (as determined in accordance with Section 1.3 above) of a full Share, less (b) the then-effective Warrant Price.

2.6. Notice/Certificate as to Adjustments. Upon each adjustment of the Warrant Price, Class and/or number of Shares, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Warrant Price, Class and/or number of Shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Warrant Price, Class and number of Shares in effect upon the date of such adjustment.

SECTION 3. REPRESENTATIONS AND COVENANTS OF THE COMPANY.

3.1. Representations and Warranties. The Company represents and warrants to, and agrees with, the Holder as follows:

(a) The initial Warrant Price referenced on the first page of this Warrant is not greater than the price per share at which shares of the Class were last sold and issued prior to the Issue Date hereof in an arms-length transaction in which at least $500,000 of such shares were sold.

(b) All Shares which may be issued upon the exercise of this Warrant, and all securities, if any, issuable upon conversion of the Shares, shall, upon issuance, be duly authorized, validly issued, fully paid and non-assessable, and free of any liens and encumbrances except for restrictions on transfer provided for herein or under applicable federal and state securities laws. The Company covenants that it shall at all times cause to be reserved and kept available out of its authorized and unissued capital stock such number of shares of the Class as will be sufficient to permit the exercise in full of this Warrant.

3.2. Notice of Certain Events. If the Company proposes at any time to:

(a) declare any dividend or distribution upon the outstanding shares of the Class, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

(b) offer for subscription or sale pro rata to the holders of the outstanding shares of the Class any additional shares of any class or series of the Company's stock (other than pursuant to contractual pre-emptive rights);

(c) effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the outstanding shares of the Class;or

(d) effect an Acquisition or to liquidate, dissolve or wind up;

then, in connection with each such event, the Company shall give Holder:

(1) at least seven (7) Business Days prior written notice of the date on which a record will be taken for such dividend, distribution, or subscription rights (and specifying the date on which the holders of outstanding shares of the Class will be entitled thereto) or for determining rights to vote, if any, in respect of the matters referred to in (a) and (b) above;and

(2) in the case of the matters referred to in (c) and (d) above at least seven (7) Business Days prior written notice of the date when the same will take place (and specifying the date on which the holders of outstanding shares of the Class will be entitled to exchange their shares for the securities or other property deliverable upon the occurrence of such event).

Reference is made to Section 1.6(c) whereby this Warrant will be deemed to be exercised pursuant to Section 1.2 hereof if the Company does not give written notice to Holder of a Cash/Public Acquisition as required by the terms hereof. Company will also provide information requested by Holder that is reasonably necessary to enable Holder to comply with Holder's accounting or reporting requirements.

SECTION 4. REPRESENTATIONS, WARRANTIES OF THE HOLDER.

The Holder represents and warrants to the Company as follows:

4.1. Purchase for Own Account. This Warrant and the securities to be acquired upon exercise of this Warrant by Holder are being acquired for investment for Holder's account, not as a nominee or agent, and not with a view to the public resale or distribution within the meaning of the Act. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the Shares.

4.2. Disclosure of Information. Holder is aware of the Company's business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities. Holder further has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

4.3. Investment Experience. Holder understands that the purchase of this Warrant and its underlying securities involves substantial risk. Holder has experience as an investor in securities of companies in the development stage and acknowledges that Holder can bear the economic risk of such Holder's investment in this Warrant and its underlying securities and has such knowledge and experience in financial or business matters that Holder is capable of evaluating the merits and risks of its investment in this Warrant and its underlying securities and/or has a preexisting personal or business relationship with the Company and certain of its officers, directors or controlling persons of a nature and duration that enables Holder to be aware of the character, business acumen and financial circumstances of such persons.

4.4. Accredited Investor Status. Holder is an "accredited investor" within the meaning of Regulation D promulgated under the Act.

4.5. The Act. Holder understands that this Warrant and the Shares issuable upon exercise hereof have not been registered under the Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of the Holder's investment intent as expressed herein. Holder understands that this Warrant and the Shares issued upon any exercise hereof must be held indefinitely unless subsequently registered under the Act and qualified under applicable state securities laws, or unless exemption from such registration and qualification are otherwise available. Holder is aware of the provisions of Rule 144 promulgated under the Act.

4.6. No Voting Rights. Holder, as a Holder of this Warrant, will not have any voting rights until the exercise of this Warrant.

SECTION 5. MISCELLANEOUS.

5.1. Term and Automatic Conversion Upon Expiration.

(a) Term. Subject to the provisions of Section 1.6 above, this Warrant is exercisable in whole or in part at any time and from time to time on or before 6:00 P.M., Eastern time, on the Expiration Date and shall be void thereafter.

(b) Automatic Cashless Exercise upon Expiration. In the event that, upon the Expiration Date, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above is greater than the Warrant Price in effect on such date, then this Warrant shall automatically be deemed on and as of such date to be exercised pursuant to Section 1.2 above as to all Shares (or such other securities) for which it shall not previously have been exercised, and the Company shall, within a reasonable time, deliver a certificate (via an electronic shares program, if applicable) representing the Shares (or such other securities) issued upon such exercise to Holder.

5.2. Legends. The Shares (and the securities issuable, directly or indirectly, upon conversion of the Shares, if any) shall be imprinted with a legend in substantially the following form:

> THE SHARES EVIDENCED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN THAT CERTAIN WARRANT TO PURCHASE STOCK ISSUED BY THE ISSUER TO INNOVATUS LIFE SCIENCES LENDING FUND I, LP DATED APRIL 8, 2021, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED (I) UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR (II) WITHOUT AN OPINION OF COUNSEL, IN FORM AND SUBSTANCE REASONABLY SATISFACTORY TO THE ISSUER, THAT SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

5.3. Compliance with Securities Laws on Transfer. This Warrant and the Shares issuable upon exercise of this Warrant (and the securities issuable, directly or indirectly, upon conversion of the Shares, if any) may not be transferred or assigned in whole or in part except in compliance with applicable federal and state securities laws by the transferor and the transferee (including, without limitation, the delivery of investment representation letters and legal opinions reasonably satisfactory to the Company, as reasonably requested by the Company). The Company shall not require Holder to provide an opinion of counsel if the transfer is to an affiliate of Holder. Additionally, the Company shall also not require an opinion of counsel if there is no material question as to the availability of Rule 144 promulgated under the Act.

5.4. Transfer Procedure. Subject to the provisions of Section 5.3 and upon providing the Company with written notice, Holder may transfer all or part of this Warrant or the Shares issuable upon exercise of this Warrant (or the securities issuable directly or indirectly, upon conversion of the Shares, if any) to any transferee, provided, however, in connection with any such transfer, Holder will give the Company notice of the portion of the Warrant being transferred with the name, address and taxpayer identification number of the transferee and Holder will surrender this Warrant to the Company for reissuance to the transferee(s) (and Holder if applicable); and provided further, that any subsequent transferee shall agree in writing with the Company to be bound by all of the terms and conditions of this Warrant.

5.5. Notices. All notices and other communications hereunder from the Company to the Holder, or vice versa, shall be deemed delivered and effective (i) when given personally, (ii) on the third (3rd) Business Day after being mailed by first-class registered or certified mail, postage prepaid, (iii) upon actual receipt if given by facsimile or electronic mail and such receipt is confirmed in writing by the recipient, or (iv) on the first Business Day following delivery to a reliable overnight courier service, courier fee prepaid, in any case at such address as may have been furnished to the Company or Holder, as the case may be, in writing by the Company or such Holder from time to time in accordance with the provisions of this Section 5.5. All notices to Holder shall be addressed as follows until the Company receives notice of a change of address in connection with a transfer or otherwise:

INNOVATUS LIFE SCIENCES LENDING FUND I, LP
777 Third Avenue, 25th Floor
New York, NY 10017
Attention: Claes Ekstrom
Email: cekstrom@innovatuscp.com

Notice to the Company shall be addressed as follows until Holder receives notice of a change in address:

CELCUITY, INC.
16305 – 36th Avenue North
Suite 100
Minneapolis, MN 55446
Attn: Chief Financial Officer
Facsimile No.:_____
Email: vhahne@celcuity.com

With a copy (which shall not constitute notice) to:

Fredrikson & Byron, P.A.200 South Sixth Street, Suite 4000
Minneapolis, MN 55402
Attn: Brad WallaceFax: (612) 492-7077
Email: bwallace@fredlaw.com

5.6. Waiver. This Warrant and any term hereof may be changed, waived, discharged or terminated (either generally or in a particular instance and either retroactively or prospectively) only by an instrument in writing signed by the party against which enforcement of such change, waiver, discharge or termination is sought.

5.7. Attorneys' Fees. In the event of any dispute between the parties concerning the terms and provisions of this Warrant, the party prevailing in such dispute shall be entitled to collect from the other party all costs incurred in such dispute, including reasonable attorneys' fees.

5.8. Counterparts; Facsimile/Electronic Signatures. This Warrant may be executed in counterparts, all of which together shall constitute one and the same agreement. Any signature page delivered electronically or by facsimile shall be binding to the same extent as an original signature page with regards to any agreement subject to the terms hereof or any amendment thereto.

5.9. Governing Law. This Warrant shall be governed by and construed in accordance with the laws of the State of New York, without giving effect to its principles regarding conflicts of law.

5.10. Headings. The headings in this Warrant are for purposes of reference only and shall not limit or otherwise affect the meaning of any provision of this Warrant.

5.11. Business Days. "Business Day" is any day that is not a Saturday, Sunday or a day on which banks in New York, New York are closed.

[Signature page follows]

IN WITNESS WHEREOF, the parties have caused this Warrant to Purchase Stock to be executed by their duly authorized representatives effective as of the Issue Date written above.

"COMPANY"

CELCUITY, INC.

By: /s/ Brian F. Sullivan

Name: Brian F. Sullivan
(Print)
Title: Chairman and Chief Executive Officer

"HOLDER"

INNOVATUS LIFE SCIENCES LENDING FUND I, LP

By: /s/ Andrew Hobson

Name: Andrew Hobson
(Print)
Title: Authorized Signatory

APPENDIX 1
NOTICE OF EXERCISE

1. The undersigned Holder hereby exercises its right purchase _____ shares of the Common Stock of CELCUITY, INC. (the "Company") in accordance with the attached Warrant To Purchase Stock, and tenders payment of the aggregate Warrant Price for such shares as follows:

[ ] check in the amount of $_____ payable to order of the Company enclosed herewith

[ ] Wire transfer of immediately available funds to the Company's account

[ ] Cashless Exercise pursuant to Section 1.2 of the Warrant

[ ] Other [Describe] _____

2. Please issue a certificate or certificates representing the Shares in the name specified below:

_____
Holder's Name

_____

_____
(Address)

3. By its execution below and for the benefit of the Company, Holder hereby restates each of the representations and warranties in Section 4 of the Warrant to Purchase Stock as of the date hereof.

HOLDER:

_____

By:_____

Name:_____

Title:_____

Date: _____

Schedule 1

Exhibit 99.1

Celcuity Announces Worldwide Licensing Agreement with Pfizer to Develop and Commercialize Gedatolisib, a First-in-Class PI3K/mTOR Inhibitor for Breast Cancer

-Preliminary data from 103 patients in the expansion portion of a Phase 1b clinical trial demonstrated the drug was well tolerated and anti-tumor activity was noted

- Unique opportunity to leverage our CELsignia platform to advance development of a first-in-class targeted therapy

- Management to host conference call/webcast today, April 8, 2021, at 5:00 p.m. ET

MINNEAPOLIS - April 8, 2021 - Celcuity Inc. (Nasdaq:CELC), a clinical-stage biotechnology company pursuing an integrated companion diagnostic and therapeutic strategy for treating patients with cancer, today announced it has entered into a global licensing agreement with Pfizer Inc. (NYSE:PFE) granting Celcuity exclusive rights to Pfizer's gedatolisib, a Phase 1b pan-PI3K/mTOR inhibitor. Gedatolisib is in clinical development for the treatment of patients with ER+/HER2-negative advanced or metastatic breast cancer.

Under the terms of the licensing agreement, Pfizer provided Celcuity with a world-wide license to develop and commercialize gedatolisib. Celcuity paid an upfront license fee of $5 million of cash and $5 million of Celcuity's common stock as upfront payment. Pfizer is eligible to receive up to $330 million of development and sales-based milestone payments and tiered royalties on potential sales. Additional financial terms of the agreement were not disclosed.

"We are excited about the opportunity to utilize our CELsignia platform to support the development of a potential first-in-class targeted therapy like gedatolisib," said Brian Sullivan, CEO and co-founder of Celcuity. "In light of the important role the PI3K/mTOR pathway plays in driving tumor growth when patients become resistant to endocrine therapies, we believe gedatolisib is a highly promising drug candidate to improve outcomes for patients with breast cancer. Supporting development of a potential first-in-class therapy for breast cancer, such as gedatolisib, with our CELsignia platform is a natural extension of our strategy to develop CELsignia CDx for other breast cancer therapies. We believe developing targeted therapies that benefit from the CELsignia platform while also offering companion diagnostics that enable new drug indications, creates a synergistic advantage for each program."

Approximately 70%-80% of breast cancers in the United States express the estrogen receptor and are thus likely dependent on estrogen signaling to promote tumor growth. Patients with estrogen receptor-positive (ER+)/HER2- metastatic tumors typically receive endocrine therapies, such as tamoxifen, letrozole, or fulvestrant. Most women with ER+/HER2- metastatic breast cancer ultimately develop resistance to these endocrine therapies. One new strategy to treat metastatic ER+/HER2- breast cancer involves blocking pathways enabling partial and complete endocrine resistance by combining gedatolisib and a cyclin-dependent kinases 4 and 6 (CDK 4/6) inhibitor with existing endocrine therapy.

To evaluate the efficacy and safety of this new treatment strategy, gedatolisib is currently being evaluated in combination with palbociclib, an oral CDK 4/6 inhibitor, and either letrozole or fulvestrant in the expansion portion of a Phase 1b clinical trial in patients with ER+/HER2-negative advanced or metastatic breast cancer. A total of 103 patients were enrolled in one of four different arms according to their prior treatment history for metastatic breast cancer. A preliminary analysis of the objective response rates as of a January 11, 2021 data cut-off demonstrated that gedatolisib combined with palbociclib and an endocrine therapy achieved superior objective response rates relative to historical control data. Gedatolisib was also generally well tolerated, with the majority of treatment related adverse events (TRAE) being Grade 1 or 2. The most common Grade 3 or 4 TRAE's were neutrophil count decrease and stomatitis.

Added Art DeCillis, M.D., Celcuity's Chief Medical Officer, "In light of the data reported as of the January 11, 2021 data cut-off, we intend to initiate, subject to feedback from the FDA, a Phase 2/3 clinical trial evaluating gedatolisib in combination with palbociclib and an endocrine therapy in patients with ER+/HER2- advanced or metastatic breast cancer in the first half of 2022."

Webcast Presentation and Conference Call Information
The Celcuity management team will host a webcast/conference call today, April 8, 2021, at 5:00 p.m. ET to discuss the gedatolisib license agreement. To participate in the call, dial 1-877-407-8035. A live webcast presentation can also be accessed using this weblink at: https://www.webcaster4.com/Webcast/Page/2678/40570 or via Celcuity's website at https://celcuity.com/home/investors/events-webcasts/. A replay of the webcast will be available on the Celcuity website for a limited time following the event.

About Celcuity
Celcuity is a clinical-stage biotechnology company seeking to extend the lives of cancer patients by pursuing an integrated companion diagnostic and therapeutic strategy. Our CELsignia companion diagnostic platform 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. Our therapeutic efforts are focused on in-licensing and developing molecularly targeted therapies that address the same cancer driver our companion diagnostics can identify. By pursuing an integrated companion diagnostic and therapeutic strategy, we believe we are uniquely positioned to achieve our goal of helping cancer patients receive the therapeutic best suited to treat their cancer driver. Celcuity is headquartered in Minneapolis. Further information about Celcuity can be found at www.celcuity.com.

Forward-Looking Statements
This press release contains statements that constitute "forward-looking statements." In some cases, you can identify forward-looking statements by terminology such as "may," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "intends" or "continue," and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. Forward looking statements in this press release include, without limitation, expectations with respect to the results from the B2151009 Phase 1b clinical trial, the timing of launching a Phase 2/3 clinical trial, the future payments that may be owed to Pfizer under the license agreement, the expected benefits of gedatolisib, and other statements regarding the future of Celcuity's business and results of operations. . Forward-looking statements are subject to numerous conditions, many of which are beyond the control of Celcuity, which include, but are not limited to, the unknown impact of the COVID-19 pandemic on Celcuity's business and those other risks set forth in the Risk Factors section in Celcuity's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the Securities and Exchange Commission on February 16, 2021. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Celcuity undertakes no obligation to update these statements for revisions or changes after the date of this press release, except as required by law.

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Exhibit 99.2

Celcuity Reports Preliminary Data from Phase 1b Trial of Gedatolisib plus Ibrance® and Endocrine Therapy for Patients with ER+/HER2- Metastatic Breast Cancer and Provides Corporate Update

Preliminary Phase 1b Data

- 53 of the 88 evaluable patients (60%) had an objective response -

- Gedatolisib showed a potentially differentiated safety and tolerability profile -

Corporate Update

- Entered $25 million debt financing agreement with Innovatus Capital Partners -

- Proceeds from first $15 million tranche increase cash-on-hand to $44 million -

- Drug development capabilities and team broadened and expanded -

- Conference call and webcast scheduled for today, April 8 at 5 p.m. Eastern Time -

MINNEAPOLIS, April 8, 2021 - Celcuity Inc. (Nasdaq:CELC), a clinical-stage biotechnology company pursuing an integrated companion diagnostic and therapeutic strategy for treating patients with cancer, today reported preliminary data for the 103 patients enrolled in the expansion portion of an ongoing Phase 1b clinical trial evaluating gedatolisib, a first-in-class PI3K/mTOR inhibitor, plus Ibrance and endocrine therapy, in ER+/HER2- advanced or metastatic breast cancer patients. As of the January 11, 2021 data cut-off date, 53 of the 88 evaluable patients (60%) had an objective response. Gedatolisib was also generally well tolerated, with the majority of treatment-related adverse events (TRAE) being Grade 1 or 2. The most common Grade 3 or 4 TRAEs related to gedatolisib were stomatitis and rash.

“We are very encouraged by this preliminary data for gedatolisib from our ongoing Phase 1b trial in patients with breast cancer,” said Brian Sullivan, CEO and Co-Founder of Celcuity. “The robust response rate and the observed tolerability profile are particularly compelling given the need for a therapeutic regimen that can address endocrine therapy resistance. We look forward to sharing additional data from the study at a future medical conference in 2021. Developing a therapeutic such as gedatolisib allows us to more fully leverage our CELsignia cellular analysis platform.“

Preliminary Phase 1b Data for Gedatolisib:

The preliminary Phase 1b data set for the 103 patients enrolled utilized a January 11, 2021 data cut-off. Patients were enrolled in one of four expansion arms (A, B, C, D), according to their prior treatment history for metastatic breast cancer. 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 gedatolisib on a four-week cycle of three weeks-on, one week-off. The primary endpoint was objective response as determined using Response Evaluation Criteria in Solid Tumors v1.0, or RECIST v1.0.

The preliminary efficacy and safety analysis showed:

- 53 of the 88 evaluable patients (60%) had an objective response.
- 66 of the 88 evaluable patients (75%) had a clinical benefit, defined as either a confirmed objective response or stable disease for at least 24 weeks.
- Gedatolisib was also generally well tolerated, with the majority of treatment related adverse events (TRAE) being Grade 1 or 2. The most common Grade 3 or 4 TRAEs associated with gedatolisib were stomatitis and rash. Gedatolisib was discontinued in 10% of patients.
- 22 patients were continuing to receive gedatolisib in combination with the other study drugs, 17 of whom have been on study treatment for more than two years.

In light of these encouraging results, Celcuity is planning to initiate, subject to feedback from the FDA, a Phase 2/3 clinical trial evaluating gedatolisib in combination with palbociclib and an endocrine therapy in patients with ER+/HER2- advanced or metastatic breast cancer in the first half of 2022.

Corporate Update

Management team expanded in key areas

With the in-licensing of gedatolisib, Celcuity has broadened and deepened its management team with experienced pharmaceutical development and regulatory affairs experts.

Arthur DeCillis, M.D., Chief Medical Officer
Dr. DeCillis was the Chief Medical Officer for Eleven Biotherapeutics (now known as Sesen Bio Inc.) and VP Clinical Research for Exelixis. Prior to that, he served in senior drug development roles at Novartis and Bristol-Myers Squibb. Arthur has been involved in the development of several commercialized oncology drugs, including SPRYCEL® (dasatinib), AFINITOR® (everolimus), FARYDAK® (panobinostat), and CABOMETYX® (cabozantinib).

John R. MacDonald, Ph.D., DABT, Senior Vice President of R&D
Dr. MacDonald led the preclinical and clinical R&D efforts at MGI Pharma, an oncology-focused pharmaceutical company until its sales to Eisai Co. He has over 30 years of experience in all aspects of pharmaceutical drug development and licensing. Prior to MGI, he worked for Warner-Lambert (now Pfizer).

Sheri Smith, Head of Clinical Operations (Acting)
Ms. Smith was the former Senior Director of Clinical Operations at MGI Pharma, where she was responsible for all clinical operations. For the past 17 years, she has served as President of Courante Oncology, a specialty clinical research services company serving pharmaceutical and medical device companies.

Bernhard Lampert, Ph.D., Head of CMC
Dr. Lampert has extensive drug development experience in the pharmaceutical and biotech industries, including ten years in large, fully integrated pharmaceutical companies, including Gilead and GSK. He received his Ph.D. in Medicinal Chemistry from the University of Georgia in 1989.

Marie DeGayner Kuker, Head of Regulatory

Ms. Kuker has more than 35 years of experience in the pharmaceutical industry, most recently as head of global regulatory affairs for 3M Pharmaceuticals and Drug Delivery Systems before founding her consultancy in 2007. Marie is an appointed Fellow of the Regulatory Affairs Professionals Society.

Celcuity announces $25 million debt financing agreement with Innovatus Capital Partners, LLC

Celcuity has entered into a debt financing agreement with Innovatus Capital Partners, LLC (Innovatus) to provide Celcuity with up to $25 million in term loans with the first $15 million tranche funded at closing. Celcuity will be able to draw on two additional tranches of $5 million each upon the achievement of certain clinical trial and financing milestones. Celcuity is entitled to make interest only payments for 36 months or up to 48 months if certain conditions are met. The loans will mature on the fifth anniversary of the initial funding date. Innovatus has the right to convert up to 20% of the outstanding principal amount into shares of Celcuity common stock until the third anniversary of the loan agreement. The loan agreement includes customary warrant coverage and is secured by all of Celcuity's assets. Armentum Partners LLC acted as sole advisor to Celcuity on this transaction.

Webcast Presentation and Conference Call Information

The Celcuity management team will host a webcast/conference call today, April 8, 2021, at 5:00 p.m. ET to discuss the gedatolisib license agreement and provide a corporate update. To participate in the call, dial 1-877-407-8035. A live webcast presentation can be accessed using this weblink: https://www.webcaster4.com/Webcast/Page/2678/40570 or via Celcuity's website at https://celcuity.com/home/investors/events-webcasts/. A replay of the webcast will be available on the Celcuity website for a limited time following the event.

About the Phase 1b Gedatolisib Clinical Trial

The B2151009 trial is a multicenter, open-label, on-going Phase 1b study in patients with ER+/HER2- metastatic breast cancer. Four dose expansion arms enrolled 103 patients 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). More information about the trial is available at NCT02684032.

About 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. Celcuity licensed exclusive global rights to gedatolisib from Pfizer in April 2021. An on-going Phase 1b trial evaluating patients with ER+/HER2- metastatic breast cancer was initiated in 2016 and subsequently enrolled 138 patients. Patient enrollment for the four expansion arms of the trial is complete. Based on the favorable preliminary results reported to date from the Phase 1b trial, we intend to initiate, subject to feedback from the FDA, a Phase 2/3 clinical trial evaluating gedatolisib in combination with palbociclib and an endocrine therapy in patients with ER+/HER2- advanced or metastatic breast cancer in the first half of 2022.

About Celcuity
Celcuity is a clinical-stage biotechnology company seeking to extend the lives of cancer patients by pursuing an integrated companion diagnostic and therapeutic strategy. Our CELsignia companion diagnostic platform 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. Our therapeutic efforts are focused on in-licensing and developing molecularly targeted therapies that address the same cancer driver our companion diagnostics can identify. By pursuing an integrated companion diagnostic and therapeutic strategy, we believe we are uniquely positioned to achieve our goal of helping cancer patients receive the therapeutic best suited to treat their cancer driver. Celcuity is headquartered in Minneapolis. Further information about Celcuity can be found at www.celcuity.com.

Innovatus Capital Partners, LLC
Innovatus Capital Partners, LLC, is an independent adviser and portfolio management firm with approximately $1.54B in assets under management. Innovatus adheres to an investment strategy that identifies disruptive and growth opportunities across multiple asset categories with a unifying theme of capital preservation, income generation, and upside optionality. The firm has a dedicated team of life sciences investment professionals with deep experience in healthcare, including life sciences. Innovatus and its principals have significant experience providing debt financing to medical device, diagnostics, and biotechnology companies that address unmet medical needs, improve patient outcomes, and reduce overall healthcare expenditures. Further information can be found atwww.innovatuscp.com.

Forward-Looking Statements
This press release contains statements that constitute "forward-looking statements." In some cases, you can identify forward-looking statements by terminology such as "may," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "intends" or "continue," and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. Forward looking statements in this press release include, without limitation, expectations with respect the results from the B2151009 Phase 1b clinical trial, the timing of launching a Phase 2/3 clinical trial, the expected benefits of gedatolisib, the growth of Celcuity's management team, and other statements regarding the future of Celcuity's business and results of operations. . Forward-looking statements are subject to numerous conditions, many of which are beyond the control of Celcuity, which include, but are not limited to, the unknown impact of the COVID-19 pandemic on Celcuity's business and those other risks set forth in the Risk Factors section in Celcuity's Annual Report on Form 10-K for the year ended December 31, 2020 filed with the Securities and Exchange Commission on February 16, 2021. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Celcuity undertakes no obligation to update these statements for revisions or changes after the date of this press release, except as required by law.

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Unless otherwise provided in this Business Update, 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 Business Update, 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.

Overview

We are a clinical-stage biotechnology company seeking to extend the lives of cancer patients by pursing an integrated companion diagnostic (CDx) and therapeutic (Rx) strategy that leverages our CELsignia CDx platform. 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. Our therapeutic strategy aims to utilize CELsignia's unique insights into tumor cell biology to identify, in-license, and develop potential first-in-class or best-in-class targeted therapies that treat the same cancer driver a CELsignia CDx can identify. We believe this integrated CDx and Rx strategy will maximize the impact our CELsignia platform has on the treatment landscape for cancer patients.

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.

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 six 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.

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 1 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 interest in gedatolisib was prompted after we conducted a study of various PI3K targeted therapeutics while developing our CELsignia PI3K Activity test. Our CELsignia platform allows us to obtain proprietary insights about the relative effectiveness of PI3K targeted therapies. This study found that gedatolisib inhibited higher levels of PI3K-involved signaling activity than the other PI3K targeted therapeutics we evaluated and demonstrated superior drug synergy when combined with other targeted therapies. Gedatolisib's initial clinical development program will focus on the treatment of patients with estrogen receptor positive (ER+), 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 endometrial, ovarian, or prostate 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. 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

CELsignia CDx Programs

We are collaborating with Genentech, Pfizer, Novartis, and Puma to conduct five Phase 2 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. Our CELsignia Multi-Pathway Activity Test, or CELsignia MP Test, analyzes HER2, c-MET, and PI3K signaling activity using a patient's live tumor cells. These tests have the potential to diagnose oncogenic signaling activity undetectable by molecular tests in up to one in three HER2-negative breast cancer patients and one in five ovarian cancer patients. We intend to use this test to identify HER2-negative breast cancer patients whose tumors have either abnormal HER2 signaling, abnormal c-Met and HER2 signaling, or abnormal PI3K signaling. Our overall commercialization strategy for our CELsignia CDx is to collaborate with pharmaceutical companies to advance the clinical development of their targeted therapies with the eventual goal of obtaining FDA approval of a new drug indication.

Our current programs include:

- Herceptin® and Perjeta® for HER2-negative early-stage breast cancer patients. Each drug targets the HER2 receptor and is owned by Genentech, Inc. These drugs are only currently approved to treat cancer patients who are HER2+.
- Vizimpro® and Xalkori® for HER2-negative late-stage breast cancer patients. Vizimpro, a pan-HER inhibitor, and Xalkori, a c-Met inhibitor, are owned by Pfizer, Inc. These drugs are currently only approved to treat patients with non-small cell lung cancer who have specific molecular mutations.
- Tabrecta® and Nerlynx® for HER2-negative late-stage breast cancer patients. Tabrecta, a c-Met inhibitor, is owned by Novartis AG and Nerlynx is owned by Puma Biotechnology, Inc. Tabrecta is currently only approved to treat patients with non-small cell lung cancer who have specific molecular mutations. Nerlynx is currently only approved to treat HER2+ breast cancer patients.
- Nerlynx and Faslodex for ER+/HER2-negative late-stage breast cancer patients. Faslodex, a selective estrogen receptor degrader, is owned by AstraZeneca.
- Nerlynx for ER-/HER2- early-stage breast cancer patients.

Gedatolisib

We are initially developing gedatolisib for the treatment of patients with ER+/HER2-negative advanced or metastatic breast cancer. The PI3K/mTOR pathway is one of the most important signal transduction pathways driving breast cancer growth in the setting of resistance to endocrine and CDK4/6 therapies. Inhibition of this pathway by gedatolisib may thus provide an important new therapeutic strategy to delay tumor progression by reversing therapeutic resistance. Our strategy is to treat metastatic ER+/HER2- breast cancer with a combination of gedatolisib, palbociclib, an oral CDK 4/6 inhibitor, marketed as Ibrance® by Pfizer, and an existing endocrine therapy, to enable a more complete blockade of endocrine and CDK4/6 resistance. We believe gedatolisib in combination with palbociclib and an endocrine therapy has the potential to become a standard of care treatment for patients with ER+/HER2- metastatic breast cancer, if approved.

Gedatolisib is currently being evaluated in combination with palbociclib and an endocrine therapy, either letrozole, or fulvestrant in an on-going Phase 1b clinical trial that has enrolled 138 patients with ER+/HER2-negative advanced or metastatic breast cancer. Based on preliminary results from the on-going dose expansion portion of this Phase 1b trial as of the database cutoff date of January 11, 2021, 53 of the 88 evaluable patients had either a confirmed or unconfirmed partial response, an objective response rate of 60%. In addition, 66 of the 88 evaluable patients had either a confirmed PR or had stable disease for 24 weeks, a 75% clinical benefit rate (CBR). In light of the results reported to date from the Phase 1b trial, we intend to initiate, subject to feedback from the FDA, a Phase 2/3 clinical trial evaluating gedatolisib in combination with palbociclib and an endocrine therapy in patients with ER+/HER2- advanced or metastatic breast cancer in the first half of 2022.

The remainder of this Business Update will focus on the specific impacts of Gedatolisib on our business. For more information on our ongoing CELsignia CDx programs, please see Part I, Item 1 of our Annual Report for the year ended December 31, 2020.

Our Pipeline

Our integrated CDx and Rx approach has allowed us to develop a broad pipeline of potential new targeted therapy options for breast cancer patients. Our current focus is supporting the development of new drug indications for already approved targeted therapies or developing our own drug candidates for breast cancer. The following table summarizes our current pipeline of targeted therapy development efforts.

	Indication	Treatment Approach (Pathways)	Population	Phase 1/1b	Phase 2	Phase 3	Drug Sponsor
Gedatolisib: pan-PI3K/mTOR							
Metastatic Breast Cancer	1L/2L	Gedatolisib + Ibrance + Endocrine *(PI3K/mTOR + CDK4/6 + ER)*	ER+/HER2-				Celcuity
	2L	Gedatolisib + Ibrance + Faslodex *(PI3K/mTOR + CDK4/6 + ER)*	ER+/HER2-	*Planned 1H 2022*			Celcuity
CELsignia Supported Targeted Therapy Programs							
Early Breast Cancer	1L	Herceptin + Perjeta + chemo *(HER2)*	HER2-/HER2s+ *(HER2 Signaling +)*				Genentech
	1L	Nerlynx + chemo *(pan-HER)*	ER-/PR-/HER2-/HER2s+ *(HER2 Signaling +)*				Puma
Metastatic Breast Cancer	2L/3L	Xalkori + Vizimpro *(c-Met + pan-HER)*	HER2- *(HER2/c-Met Signaling +)*				Pfizer
	2L/3L	Nerlynx + Fulvestrant *(pan-HER + ER)*	ER+/HER2-/HER2s+ *(HER2 Signaling +)*				Puma
	2L/3L	Tabrecta + Nerlynx *(c-Met + pan-HER)*	HER2- *(HER2/c-Met Signaling +)*				Novartis

Strategy

Our strategy is to pursue the development of complementary companion diagnostics and therapeutics that leverage our CELsignia platform. CELsignia companion diagnostics are uniquely able to analyze live patient tumor cells to identify new groups of cancer patients likely to benefit from targeted therapies. We aim to utilize CELsignia's unique insights into tumor cell biology to identify, in-license, and develop potential first-in-class or best-in-class targeted therapies that treat the same cancer driver a CELsignia CDx can identify. We believe this integrated CDx and Rx strategy will maximize the impact our CELsignia platform has on the treatment landscape for cancer patients.

Key elements of our strategy include:

- **Leverage the proprietary insights CELsignia provides into live patient tumor cell function.**

  Determining the dysfunction driving most patient's cancer using molecular tests remains elusive. Less than 20% of Americans who died of cancer in 2018 had actionable genetic or proteomic mutations that made them eligible for treatment with a targeted therapy. This reflects the limitations of using static measurements of proteins or genetic mutations in cell fragments to characterize the dynamic and complex cell signaling activity that may be driving a patient's cancer.

  Our CELsignia platform represents a significant departure from molecular-based analyses. CELsignia companion diagnostics directly measure dynamic cell signaling activity in patient tumors lacking actionable genomic or proteomic mutations. Unlike molecular tests that use cell fragments and can only measure the static composition of a cell, our CELsignia platform measures real-time signaling activity in a patient's live tumor cells. This enables us to (1) identify the cellular signaling dysfunction driving a patient's cancer; and (2) identify the targeted therapy that matches the dysfunction in the patient's cells.

- **Use a CELsignia CDx to enable new indications for the paired targeted therapy.**

  Our CELsignia platform enables us to discover new groups of patients that, we believe, are likely to respond positively to a matching targeted therapy. Since these new patient groups cannot otherwise be identified, each CELsignia CDx creates an opportunity to expand the number of patients approved for treatment with the targeted therapy. Our current commercial strategy is to collaborate with pharmaceutical companies on clinical trials to confirm the efficacy of their already approved therapeutics in patients selected with a CELsignia CDx. If these collaborations are successful, we believe our CELsignia tests would expand the market for the targeted therapy because they enable approval of new drug indications that a pharmaceutical company would not otherwise be able to obtain.

- **In-license additional drug candidates that CELsignia is uniquely able to evaluate.**

  Supporting the development of potential first-in-class targeted therapies for breast cancer, such as gedatolisib, with our CELsignia platform is a natural extension of our strategy to develop CELsignia CDx for other breast cancer therapies. We intend to focus on drug candidates with mechanisms of action CELsignia is uniquely able to evaluate. We believe this gives a proprietary advantage to identify potential first-in-class or best-in-class drug candidates for patient populations that are most likely to respond to the compound.

- **Maximize the impact of our CELsignia platform.**

  We believe developing targeted therapies for breast cancer that benefit from the CELsignia platform while also offering companion diagnostics that enable new drug indications for breast cancer patients, creates a synergistic advantage for each program. Our goal is to play a direct role in improving the outcomes of breast cancer patients at all stages of their disease.

- **Use CELsignia to maximize the likelihood of obtaining regulatory approval.**

  CELsignia tests enable enrollment of patients in clinical trials who we believe are most likely to benefit because their tumors have the same cellular dysfunction the targeted therapy being evaluated is designed to inhibit. We believe this will improve patient response rates, increasing the likelihood the trial meets its endpoint target and thus the likelihood the drug receives FDA approval. Improved patient response rates would also help reduce the size, cost, and length of clinical trials. Thus, 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 pursuing an indication for a large, but unselected patient population, as we plan to do for the initial gedatolisib indication. Thus, our CELsignia platform gives us the unique ability to pursue indications for unselected patient populations with a back-up indication for a CELsignia selected patient sub-group.

- **Employ efficient and flexible approaches to accelerate clinical development.**

  The members of our development leadership team have successfully identified, developed and obtained regulatory approval of oncology products. These experiences provide our team with the knowledge to test multiple clinical hypotheses in a single trial that can be accelerated once a signal of clinical benefit is observed. This approach may increase the likelihood of seeing results early in clinical trials with fewer patients, reducing our clinical development risk and development costs, and allowing us to potentially accelerate the development of our product pipeline.

Gedatolisib

Overview

Gedatolisib (PF-05212384) 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. An on-going Phase 1b trial evaluating patients with ER+/HER2- metastatic breast cancer was initiated in 2016 and subsequently enrolled 138 patients. Patient enrollment for the four expansion arms of the trial is complete. Based on the favorable preliminary results reported to date from the Phase 1b trial, we intend to initiate, subject to feedback from the FDA, a Phase 2/3 clinical trial evaluating gedatolisib in combination with palbociclib and an endocrine therapy in patients with ER+/HER2- advanced or metastatic breast cancer in the first half of 2022.

Background on Breast Cancer and Current Treatments

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 270,000 new cases of breast cancer would be diagnosed in the United States in 2019, and approximately 42,000 breast cancer patients would die of the disease. Approximately 190,000, or 70%, of these new cases are for ER+/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 ER+/HER2-, which is indicative of hormone dependency. Despite progress in treatment strategies, metastatic ER+/HER2- breast cancer (mBC) remains an incurable disease, with a median overall survival (OS) of three years and a five-year survival rate of 25%.

Four different classes of targeted therapies are currently used to treat ER+/HER2- tumors. These drugs generated revenues of nearly $10 billion globally in 2019.

Endocrine-based therapies. Selective ER modulators (tamoxifen), selective ER degrader (fulvestrant), and aromatase inhibitors (AIs) are established standards of care in women with HR+/HER2- mBC. The choice between these regimens when treating mBC depends on the type and duration of prior endocrine therapy treatment as well as the time elapsed from the end of prior endocrine therapy. Besides the well-known efficacy of these treatments as first-line therapies in women without visceral crisis, most patients develop endocrine resistance leading to therapeutic failure. Primary endocrine resistance is defined as relapse during the first two years of prior endocrine therapy or progressive disease within the first six months of first-line endocrine therapy for mBC. Secondary resistance is present (1) when a relapse occurs after the first two years of adjuvant endocrine therapy; (2) when a relapse occurs within 12 months of completing adjuvant endocrine therapy; or (3) when a progressive disease occurs after more than six months from the beginning of endocrine therapy for mBC.

Several mechanisms are responsible for endocrine resistance, including the dysregulation of multiple components of the ER pathway (aberration in ER expression, over-expression of ER co-activators, and down-regulation of co-repressors), altered regulation of signaling molecules involved in cell cycle or cell survival, and the activation of escape pathways that can provide cell replication.

CDK4/6 inhibitors. One common mechanism of resistance to endocrine therapies is the activation of the cyclin-dependent kinases 4 and 6 (CDK4/6) pathway. These kinases drive cell cycle progression and division. Inhibiting activation of the CDK4/6 prevents estrogen from activating the cyclin D1-CDK4/6-Rb complex, thus blockading an important mechanism of resistance to endocrine therapies. The resulting cell cycle arrest induces a significant delay in tumor progression.

CDK 4/6 inhibitors were first introduced in 2015. Endocrine therapies administered in combination with oral CDK4/6 inhibitors lead to improved clinical efficacy when compared with endocrine therapies as monotherapy. In two randomized, double-blind clinical trials, treatment of HR+/HER2- advanced breast cancer patients with a combination of palbociclib and either letrozole or fulvestrant demonstrated a significant increase in the median progression free survival (PFS) period for patients who received palbociclib in combination with either letrozole or fulvestrant compared to patients who received letrozole or fulvestrant as single agents. These patients had previously progressed on or after prior endocrine therapy. Worldwide sales of currently marketed CDK4/6 inhibitors, which are indicated for the treatment of breast cancer, were $6.0 billion in 2019, and are expected to grow to $14.4 billion in 2026. Worldwide sales of Pfizer's leading CDK4/6 inhibitor, palbocicib, or Ibrance®, were $5.4 billion in 2020.

PI3K inhibitors. Another common mechanism of resistance to endocrine inhibitors is the activation of the PI3K pathway, an important intracellular pathway that regulates cell growth and metabolism. Approximately one third of HR+ breast cancer tumors resistant to endocrine therapy harbor activating mutations of the catalytic subunit of PI3K, referred to as PIK3CA. Fulvestrant used in combination with alpelisib, an oral PI3K-α inhibitor marketed as Piqray® by Novartis approved by the FDA in May 2019, has demonstrated improved clinical efficacy in patients whose tumors had a PIK3CA mutation and had not yet received treatment with a CDK4/6 inhibitor. These patients had previously progressed on or after prior endocrine therapy. Worldwide sales of Piqray®, currently the only FDA-approved for the treatment of breast cancer, limited to patients with PIK3CA mutations, were approximately $320.0 million in 2020.

mTOR inhibitors. Similar to CDK4/6 and PI3K, the mTOR pathway has also been identified as a mechanism of resistance to endocrine therapy. Everolimus is an mTOR inhibitor that is currently approved by the FDA for the treatment of HR+/HER2- advanced breast cancer in combination with exemestane, an AI. Everolimus has also shown clinical benefit in combination with fulvestrant. These patients had previously progressed on or after prior AI therapy. Worldwide sales in breast cancer of everolimus, marketed as Afinitor® by Novartis and a leading mTOR inhibitor, were approximately $831.0 million in 2019.

The Importance of Targeting PI3K and mTOR in Cancer

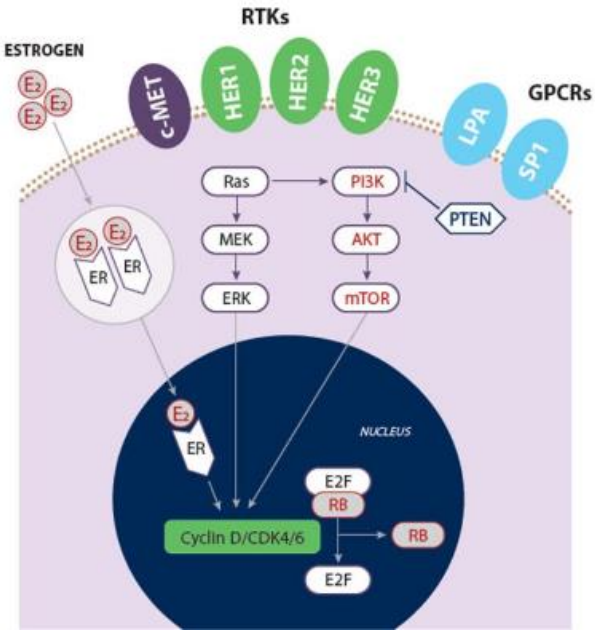
Activation of the PI3K/mTOR pathway has been implicated in a wide variety of human cancers, involving either activating mutations, or other unknown drivers of pathway amplification. These include cancers of the breast, prostate, endometrial, colon, rectum, and lung, among others.

PI3K constitutes a lipid kinase family involved in the regulation of diverse cellular processes, including cell proliferation, survival, cytoskeletal organization, and glucose transport. Class I PI3Ks are of particular therapeutic interest. They are heterodimers, comprising a catalytic (p110α, p110β, p110δ, or p110γ) and a regulatory (p85α, p55α, p50α, p85β, p55γ, or p101) subunit. Oncogenic PI3K signaling is activated by cell-surface receptors such as receptor tyrosine kinases, G-protein-coupled receptors, and also by well-known oncogenic proteins such as RAS.

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. Each of the 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. For example, studies have demonstrated the p110α catalytic isoform is necessary for the growth of tumors driven by PIK3CA mutations and/or oncogenic RAS and receptor tyrosine kinases; the p110β catalytic isoform mediates tumorigenesis arising from the loss of the dephosphorylase activity of PTEN; and the p110δ catalytic isoform is highly expressed in leukocytes, making it a desirable target for inhibition in the treatment of hematologic malignancies. 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 as 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: mTOR complex 1 (mTORC1) and mTOR complex 2 (mTORC2). mTORC1 belongs to a complex network of regulatory feedback loops, and once certain levels of activation are reached, is normally responsible for limiting the proliferative signals transmitted by upstream effectors such as PI3K/AKT activity. Equally complex mTORC2 regulates AKT phosphorylation, GSK3β, and control over glycolysis, and participates in organizing the cellular actin cytoskeleton. In addition, mTORC1 activation leads to the direct reduction of mTORC2 activity and mTOR can activate the functional domain of the ER, leading to ligand-independent hormone receptor activation. In cancer, dysfunctional signaling leads to various constitutive activities of mTOR complexes, making mTOR a good therapeutic target.

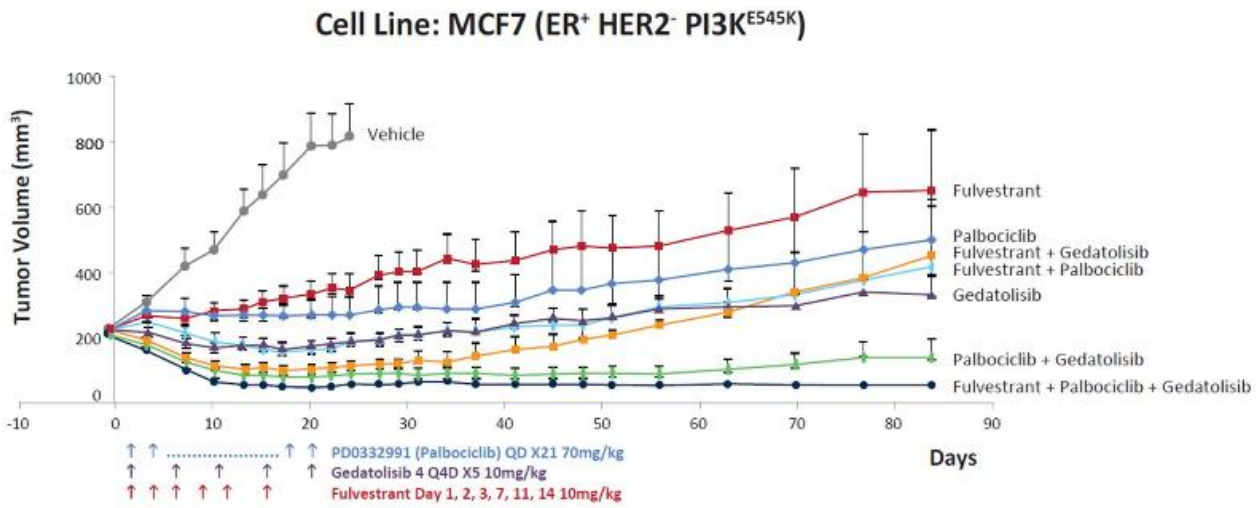
The illustration below depicts the PI3K/AKT/mTOR pathway and various pathway activation mechanisms.



PI3K/mTOR as Resistance Mechanism to Endocrine and CDK4/6 Inhibitors

The upregulation of the PI3K/AKT/mTOR pathway promotes hormone dependent and independent ER transcriptional activity, which contributes to endocrine resistance, leading to tumor cell growth, survival, motility, and metabolism. It has also been demonstrated in vivo that PI3K and mTOR inhibition can restore sensitivity to endocrine therapy, providing a strong rationale for the combination of the two therapies.

In addition, the PI3K/AKT/mTOR pathway, like other mitogenic pathways, can also promote the activities of cyclin D and CDK4/6 to drive proliferative cell cycling. Internal preclinical studies conducted by Pfizer provided evidence in cell-line xenograft models that the combination of PI3K and CDK4/6 inhibitors may overcome both intrinsic and adaptive resistance to endocrine therapy, leading to tumor regressions. In an MCF7 xenograft model (ER+/HER2-/PIK3CA mutant) the combination of gedatolisib with palbociclib and fulvestrant led to durable tumor regressions. Importantly, tumors regressed to minimal volumes within 20 days of triplet therapy, and continued to remain dormant, without further therapy, for up to 90 days.



Advantages of Gedatolisib over other PI3K and mTOR inhibitors

The important role the PI3K/AKT/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. These challenges may explain why PI3K and mTOR inhibitors have not yielded the outstanding clinical activity many researchers expected.

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

- **Overcomes drug resistance that can occur with isoform-specific PI3K inhibitors.**

  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. A pan-PI3K inhibitor can thus treat tumors harboring abnormalities that signal through different PI3K isoforms, which would potentially induce anti-tumor activity in a broader population of patients than an isoform-specific PI3K inhibitor. In addition, it has been reported that inhibition of one PI3K isoform may be offset by the increased activity of the other isoforms through different adaptive mechanisms. Inhibiting all four PI3K isoforms, as gedatolisib does, can thus prevent the confounding effect of isoform interaction that may occur with isoform-specific PI3K inhibitors.

- **Overcomes paradoxical activation of PI3K induced by mTOR inhibition.**

  As a potent inhibitor of mTOR, in addition to PI3K, gedatolisib, inhibits the PI3K/AKT/mTOR pathway both upstream and downstream of AKT. Furthermore, it has been demonstrated that the PI3K pathway is activated following selective mTOR inhibition by relief of normal feedback regulatory mechanisms, thus providing a compelling rationale for simultaneous inhibition of PI3K and mTOR.

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

  Gedatolisib is administered intravenously (IV) once weekly or 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/AKT/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 related to hyperglycemia in 39% of patients evaluated. In addition, 26% of patients discontinued treatment. 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 January 11, 2021, 457 patients with solid tumors have received gedatolisib in eight clinical trials sponsored by Pfizer. Of the 457 patients, 129 were treated with gedatolisib as a single agent in three clinical trials. The remaining 328 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.

Phase 1 First-in-Human Study

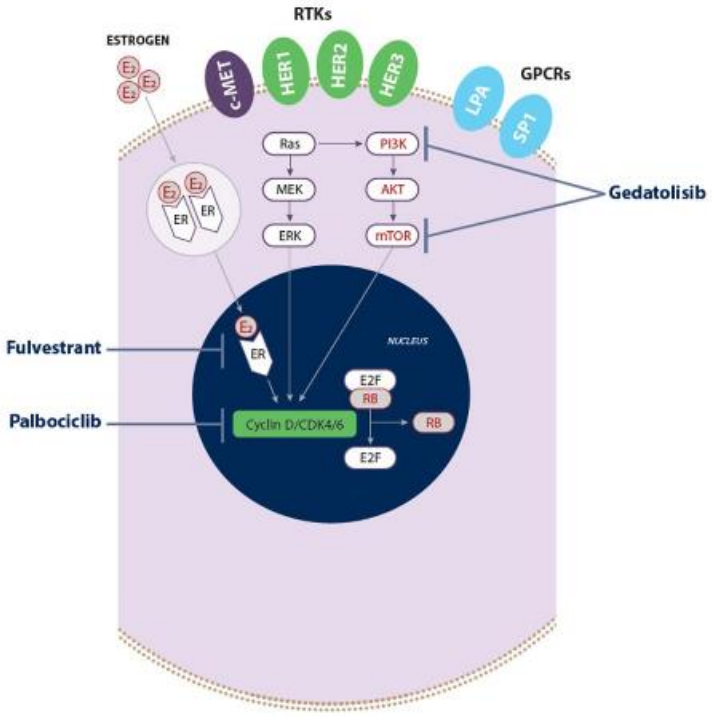
Pfizer conducted a Phase 1, open-label, dose-escalation first-in human study of single-agent gedatolisib in patients with advanced solid tumors. The primary objective of Part 1 of the study was to determine the safety, tolerability, and maximum tolerated dose (MTD) of single-agent gedatolisib administered 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 ALT (7.1%), and increased AST (4.8%). No treatment-related AEs of grade 4 or 5 severity were reported at any dose level.

Phase 1b ER+/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 ER+/HER2- metastatic breast cancer. PI3K mutation status was not used as an eligibility criterion. Patient enrollment for the trial is complete.

The illustration below depicts how the combination of gedatolisib, palbociclib, and fulvestrant is intended to simultaneously block interdependent ER, PI3K, mTOR & CDK signaling pathways in ER+ breast cancer to address ER and CDKi resistance mechanisms.



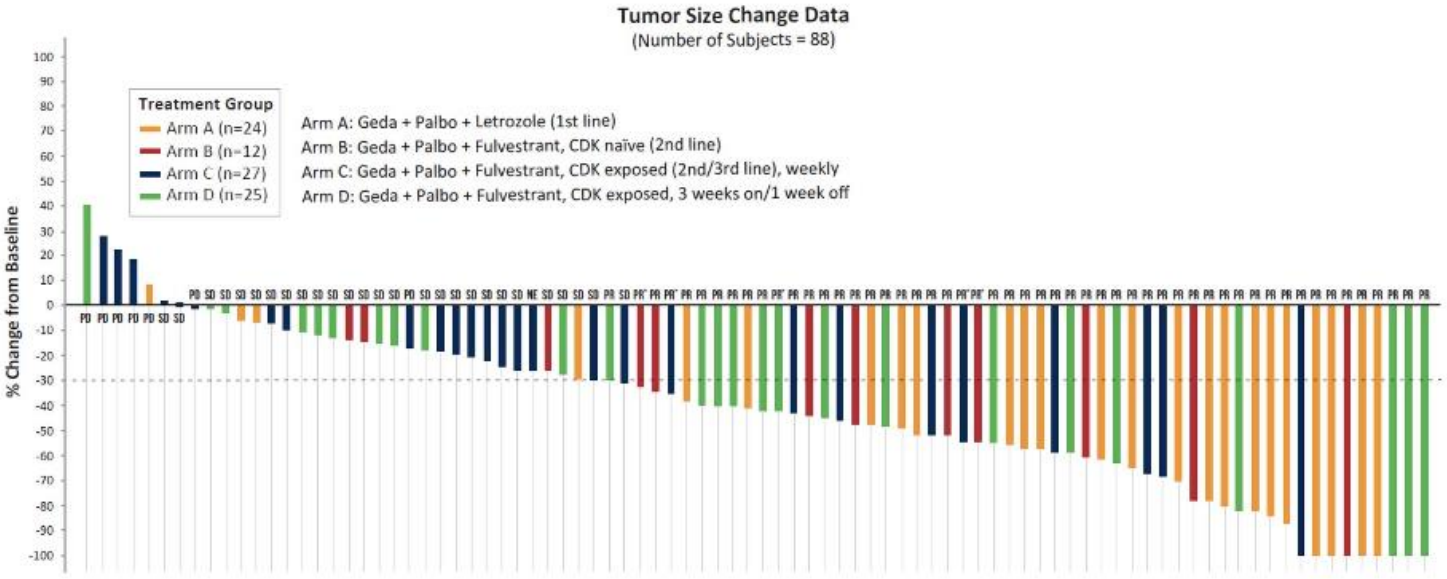
A total of 138 patients with ER+/HER2- metastatic breast cancer were dosed in the clinical trial.

- 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 180mg 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 January 11, 2021, showed:

- Efficacy analysis for all arms in aggregate:
    - 60% objective response rate (ORR): 53 of the 88 evaluable patients had either a confirmed or unconfirmed partial response, or PR (48 confirmed, 5 unconfirmed).
    - 75% clinical benefit rate (CBR): 66 of the 88 evaluable patients had either a confirmed PR or had stable disease for 24 weeks.
- Best responses, as measured by RECIST v1.0, are shown in the following chart. The dotted line represents the cutoff for PR (defined as a 30% reduction from baseline).



- Preliminary safety analysis:
    - For all arms in aggregate, 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%), dysegeusia (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 recommended phase two dose, Grade 3 and 4 treatment-emergent adverse events occurring in at least 20% of patients were neutropenia (67%) stomatitis and (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 7% of patients
    - 22 patients were continuing to receive gedatolisib in combination with the other study drugs, 17 of whom have been on study treatment for more than two years.
- Preliminary best overall response data for each arm is presented in the table below:

Arm (evaluable patients)	**A(N=24)**	**B(N=12)**	**C(N=27)**	**D(N=25)**
Patients	1L: CDKi-Naïve	2L+: CDKi-naïve	2L/3L: CDKi-pretreated	2L/3L: Immediately prior CDKi
Overall Response Rate (evaluable patients)	84%	75%[1]	33%[2]	60%[3]
Clinical Benefit Rate (evaluable patients)	92%	92%	48%	76%

1. Arm A: 20 of the 24 evaluable patients had a confirmed PR.
2. Arm B: 9 of the 12 evaluable patients had either a confirmed PR or unconfirmed PR (7 confirmed PR, 2 unconfirmed PR).
3. Arm C: 9 of the 27 evaluable patients had either a confirmed PR or unconfirmed PR (7 confirmed PR, 2 unconfirmed PR).
4. Arm D: 15 of the 25 evaluable patients had either a confirmed PR or unconfirmed PR (14 confirmed PR, 1 unconfirmed PR).

- Preliminary progression free survival (PFS) data for each arm is presented in the table below:

Arm (enrolled patients)	**A(N=31)**	**B(N=13)**	**C(N=32)**	**D(N=27)**
Median PFS (months) (95% CI)	>29 (Not Yet Reached)	11.9 (3.7, NR)	5.1 (3.4, 7.5)	13.2 (9.0, 16.7)

In light of the preliminary results reported to date from the Phase 1b trial, we intend to initiate, subject to feedback from the FDA, a Phase 2/3 clinical trial evaluating gedatolisib in combination with palbociclib and an endocrine therapy in patients with ER+/HER2- advanced or metastatic breast cancer in the first half of 2022.

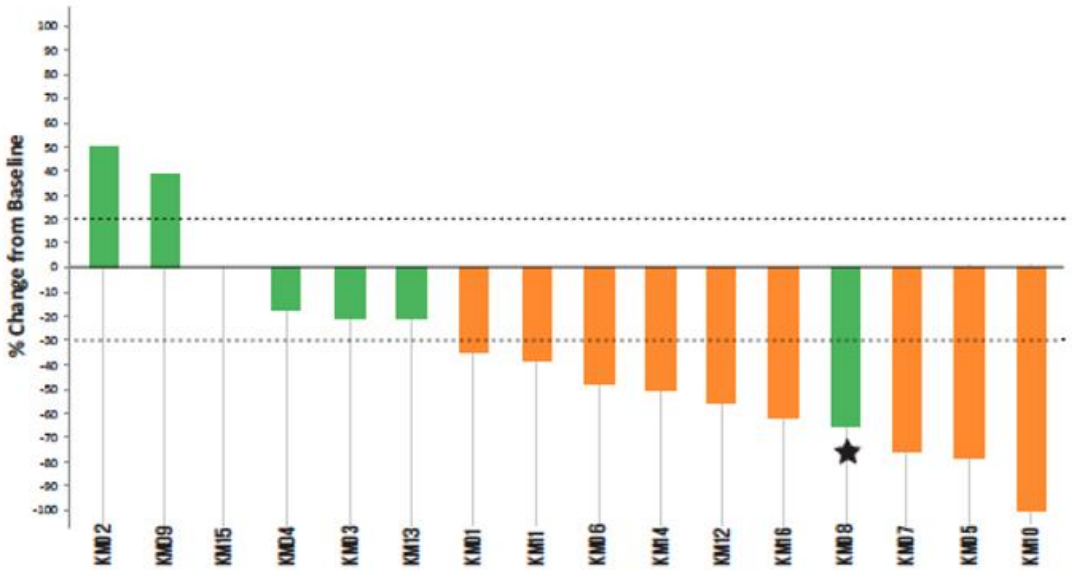
We expect to use the CELsignia PI3K activity test to help support development of gedatolisib for breast cancer indications. Our internal studies demonstrate how measurement of PI3K-involved signaling may provide a sensitive and specific method of identifying patients most likely to benefit from PI3K 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.

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 trastusumab 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).

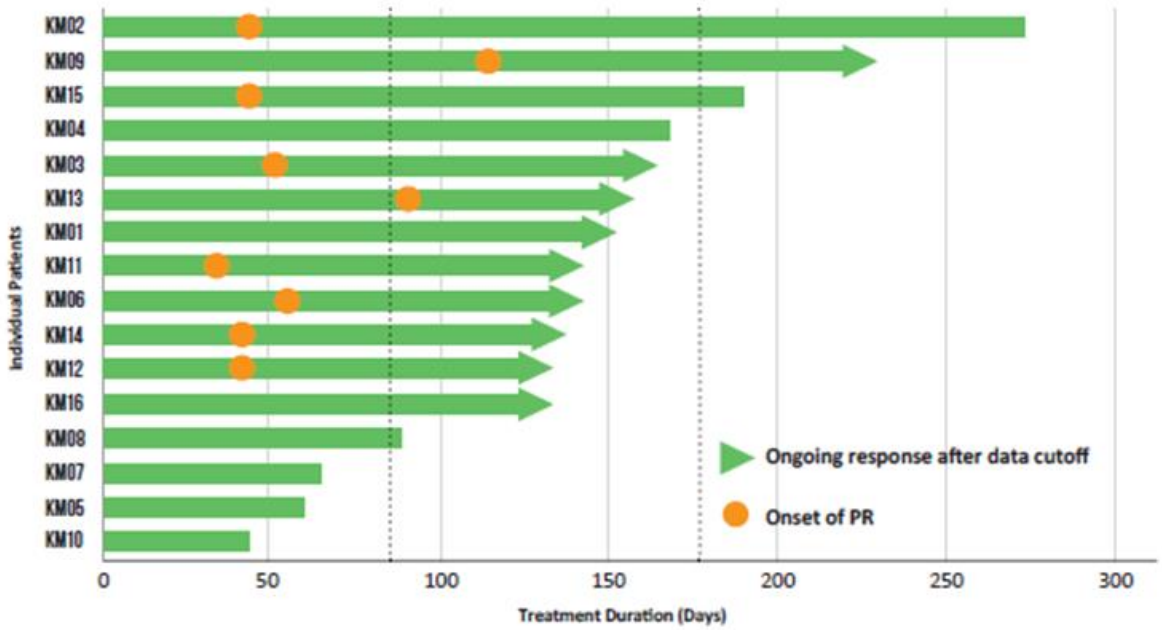
Best Response



* 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



Pfizer License Agreement

In April 2020, 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 $330.0 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.

Intellectual Property for Gedatolisib

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, manufacturing on 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 position using a variety of methods, which include pursuit of U.S. and foreign patent applications related to proprietary technology, inventions and improvements, such as compositions of matter and methods-of-use, 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 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.

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.

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.

Coverage, Pricing and Reimbursement

Successful commercialization of new drug products depends in part on the extent to which reimbursement for those drug products will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which drug products they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford a drug product. Sales of drug products depend substantially, both domestically and abroad, on the extent to which the costs of drug products are paid for by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drug products. In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the U.S. Other countries allow companies to fix their own prices for drug products, but monitor and control company profits. Accordingly, in markets outside the U.S., the reimbursement for drug products may be reduced compared with the U.S. In the U.S., the principal decisions about reimbursement for new drug products are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the Department of Health and Human Services, or HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under certain federal governmental healthcare programs, such as Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. In the U.S., the process for determining whether a third-party payor will provide coverage for a biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. With respect to biologics, third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost sharing obligation imposed on patients. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of a product. Moreover, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable a manufacturer to maintain price levels sufficient to realize an appropriate return on its investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product does not ensure that other payors will also provide coverage for the medical product, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process usually requires manufacturers to provide scientific and clinical support for the use of their products to each payor separately and is a time-consuming process.

Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical products, in addition to questioning safety and efficacy. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover that product after FDA approval or, if they do, the level of payment may not be sufficient to allow a manufacturer to sell its product at a profit.

In addition, in many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. In the European Union, or EU, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. The downward pressure on healthcare costs in general, particularly prescription products, has become very 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 a commercial pressure on pricing within a country.

Government Regulation

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.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or 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 the 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.

U.S. – FDA regulation

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 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.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an IRB for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances where the trial is a large multi-center trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

Pursuant to the 21st Century Cures Act, which was enacted on December 13, 2016, the manufacturer of an investigational drug for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access. This requirement applies on the later of 60 days after the date of enactment or the first initiation of a Phase 2 or Phase 3 trial of the investigational drug. 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.

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.

EU Regulation

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.

Other 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.

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 any drugs for which we obtain marketing approval. 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.

Although we would not submit claims directly to payors, drug manufacturers can 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, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. The government may deem manufacturers 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 distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, 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 for which we obtain marketing approval. 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 for any approved products.

The ACA, for example, contains provisions that subject biological products to potential competition by lower-cost biosimilars and may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs address a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increase the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establish annual fees and taxes on manufacturers of certain branded prescription drugs, and create a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

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 manufacturers set prices for their marketed 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 manufacturer 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. For example, the U.S. government has passed legislation requiring pharmaceutical manufacturers to provide rebates and discounts to certain entities and governmental payors to participate in federal healthcare programs. The Trump administration's budget proposal for fiscal year 2021 included a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Further, the Trump administration also previously released a "Blueprint" to lower drug prices and reduce out-of-pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. The Blueprint contains certain measures that HHS is already working to implement. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. However, it is unclear whether the Biden administration will challenge, reverse, revoke or otherwise modify these executive and administrative actions after January 20, 2021.

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 Trump 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.

Risk Factor Update

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 herein. 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. ***This risk factor update is focused on the specific impacts of gedatolisib on our business. For more information on the risks related to our operations as a whole and our specific CELsignia CDx programs, please see Part I, Item 1A of our Annual Report for the year ended December 31, 2020.***

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 companion diagnostic and therapeutic strategy.

We may require additional capital to finance capital expenditures and operating expenses over the next several years as we launch our integrated companion diagnostic and therapeutic 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.

Risks Related to Our Initial 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 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.

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.

Risks Related to Intellectual Property

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

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 may seek Breakthrough Therapy Designation or Fast Track 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.