

Cyclacel Pharmaceuticals, Inc.
Form 10-K/A
May 17, 2010

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K/A
Amendment No. 1**

(Mark One)

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES
EXCHANGE ACT OF 1934
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2009
OR**

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES
EXCHANGE ACT OF 1934
Commission file number 00-50626
CYCLACEL PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)**

Delaware

91-1707622

(State or Other Jurisdiction
of Incorporation or
Organization)

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

200 Connell Drive
Suite 1500, Berkeley Heights,
New Jersey

07922

(Address of principal executive offices)

(Zip Code)

Registrant's telephone number, including area code: (908) 517-7330
Securities registered under Section 12(b) of the Exchange Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, \$0.001 par value	The NASDAQ Stock Market LLC
Preferred Stock, \$0.001 par value	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: None.

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§

232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendments to this Form 10-K.

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

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting
company

[Do not check if a smaller
reporting company]

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes No

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate), as of June 30, 2009 (based upon the closing sale price of \$1.13 of such shares on The NASDAQ Global Market on June 30, 2009) was \$19,164,232.

As of March 26, 2010, there were 35,411,325 shares of the registrant's common stock outstanding.

Explanatory Note

This Amendment No. 1 on Form 10-K/A (this **Amendment**) to the Annual Report on Form 10-K (the **Original Filing**) of Cyclacel Pharmaceuticals, Inc. (**we, us, our** or the **Company**) for the fiscal year ended December 31, 2009, filed with the Securities and Exchange Commission (the **SEC**) on March 29, 2010, is being filed for the purpose of correcting the Company's net loss per share calculation and disclosures in the consolidated statements of cash flows related to the payment of preferred dividends, as discussed in Note 20 to the Company's consolidated financial statements, **Restatement Net Loss Per Share Disclosures and Consolidated Statement of Cash Flows**.

Net loss per share

Throughout 2007, 2008 and 2009, the Company had outstanding 2,046,813 shares of 6% Convertible Exchangeable Preferred Stock (the **Preferred Stock**). The holders of the Preferred Stock are entitled to receive, when, as and if declared, a cash dividend at the annual rate of 6% of the liquidation preference of the Preferred Stock, which dividend is payable quarterly on the first day of February, May, August and November. Until April 6, 2009, the Company declared and paid these dividends. However, as part of the Company's operating plan to reduce expenditure, on April 6, 2009, June 22, 2009, October 19, 2009, January 7, 2010 and March 29, 2010, the Company's board of directors resolved not to declare payment of the cash dividend, which unpaid dividends are accrued.

Although the Company accrued for the unpaid dividends in its consolidated financial statements, it did not include the accrued amount when calculating basic and diluted loss per share of common stock for year ended December 31, 2009. As a result, the net loss per common share has been revised from \$(0.88) per share, as reported in the Original Filing, to \$(0.94), as reported in this Amendment. Similar errors occurred in 2007 and 2008 in the net loss per share disclosure.

The following tables set forth the effects of the restatement relating to net loss per share on affected line items within the Company's previously reported Consolidated Statements of Operations for the years 2007, 2008, and 2009. The restatement has no effect on net cash flows, the reported net loss or the consolidated balance sheet.

Effect on Consolidated Statements of Operations:

	Year ended December 31		
	2007	2008	2009
	(\$000s except for per share amounts)		
Net loss as reported	(24,053)	(40,386)	(19,570)
<i>Restatement changes:</i>			
Less: preferred dividends	(307)	(1,227)	(1,228)
Net loss attributable to common shareholders	(24,360)	(41,613)	(20,798)
Weighted-average shares outstanding during the period	19,873,911	20,433,129	22,196,840
Loss per share (basic and diluted) as reported	(\$1.21)	(\$1.98)	(\$0.88)
Restatement changes	(\$0.02)	(\$0.06)	(\$0.06)
Basic and diluted, as restated	(\$1.23)	(\$2.04)	(\$0.94)

Cash flows disclosures

There were errors related to the presentation and disclosure of the Company's Preferred Stock dividends in the statement of cash flows in 2007 through and including 2009. In 2009, the Preferred Stock dividend of \$307,000 paid on February 1, 2009 was disclosed incorrectly in the statement of cash flows within Net cash used in operating activities and should have been disclosed within Financing activities. Other disclosure errors were related to the terms of the make-whole dividend payment feature of the Company's Preferred Stock. This make-whole dividend payment feature was considered to be an embedded derivative and was recorded on the balance sheet at fair value as a current liability. As a consequence of this feature, which expired in November 2007, amounts paid with respect to the period

of the make-whole provision should be disclosed in Net cash used in operating activities rather than financing activities. Additionally, in the Supplemental cash flow information; Schedule of non-cash items, we have now disclosed accrued dividends on Preferred Stock for 2007 through and including 2009. All of the errors described above have been corrected in the consolidated statements of cash flows. These errors had no effect on the net cash flows or any impact on the consolidated balance sheet or consolidated statement of operations.

In the Company's Annual Report on Form 10-K for the year ended December 31, 2009, filed on March 29, 2010, management concluded that our internal control over financial reporting was effective as of December 31, 2009. Subsequently, our management identified a deficiency in respect of our internal control over financial reporting, specifically in our controls over the computation of net loss per share and the financial statement presentation of our preferred stock dividends in the statement of cash flows that constitutes a material weakness as described in the SEC's guidance regarding Management's Report on Internal Control Over Financial Reporting as of December 31, 2009. As a result of this deficiency, the financial statements included in the Form 10-K for the year ended December 31, 2009, included errors related to the presentation and disclosure of our preferred stock dividends in the net loss per share disclosure and in the statement of cash flows. As a result of this material weakness, management concluded that we did not maintain effective internal control over financial reporting as of December 31, 2009, based on the criteria established in *Internal Control - Integrated Framework*, issued by the COSO. See Item 9T - Controls and Procedures, in this Amendment.

The Company has corrected these items in this Amendment. See items 1A. (Risk Factors), 6 (Selected Financial Data), 7 (Management's Discussion and Analysis of Results of Operations and Financial Condition), 8 (Financial Statements and Supplementary Data) in this Amendment and 9T (Controls and Procedures). Pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934, as amended, the Company is including with this Amendment certain certifications dated as of the date hereof.

Except as described above, the Original Filing has not been amended, updated or otherwise modified. The Original Filing, as amended by this Amendment, continues to speak as of the date of the Original Filing and does not reflect events occurring after the filing of the Original Filing or update or otherwise modify any related or other disclosures, including forward-looking statements. Accordingly, this Amendment should be read in conjunction with our other filings made with the SEC subsequent to the filing of the Original Filing.

Item 1A. Risk Factors

In analyzing our company, you should consider carefully the following risk factors, together with all of the other information included in this annual report on Form 10-K. Factors that could cause or contribute to differences in our actual results include those discussed in the following subsection, as well as those discussed in Management's Discussion and Analysis of Financial Condition and Results of Operations and elsewhere throughout this annual report on Form 10-K. Each of the following risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our company.

We believe regulatory agencies will not accept registration pathways based on Phase 2 data and, therefore, we will need to conduct randomized Phase 3 studies, which are time-consuming and expensive.

Regulatory agencies, including, but not limited to, the FDA, have in certain instances accepted Phase 2 data from uncontrolled studies as sufficient for approval in indications where an unmet medical need exists or in exceptional circumstances. Recently, however, the Oncologic Drugs Advisory Committee (ODAC), which is the cancer drug advisory panel of the FDA, voted in favor of completion of a randomized trial prior to regulatory approval with respect to drugs submitted for approval as treatments for patients with AML and likely in respect of drugs submitted for approval as treatments for patients with other forms of cancer. Therefore, we believe that to gain regulatory approval from the FDA, we will need to conduct a randomized Phase 3 trial. Randomized Phase 3 studies are time-consuming and expensive, and because we have limited resources any such requirements may adversely impact our operating results and financial condition and delay or block our ability to commercialize our lead drug candidates. Even if we believe that the data collected from clinical trials of our drug candidates are promising with respect to safety and efficacy, such data may not be deemed sufficient by regulatory authorities to warrant product approval. Clinical data can be interpreted in different ways. Regulatory officials could interpret such data in different ways than we do which could delay, limit or prevent regulatory approval. The FDA, other regulatory authorities or we may suspend or terminate clinical trials at any time. Any failure or significant delay in completing clinical trials for our lead drug candidates, or in receiving regulatory approval for the commercialization of our lead drug candidates, may adversely affect our business.

The current economic conditions and financial market turmoil could adversely affect our business and results of operations.

Economic conditions remain difficult with the continuing uncertainty in the global credit markets, the financial services industry and the United States capital markets and with the United States economy as a whole experiencing a period of substantial turmoil and uncertainty characterized by unprecedented intervention by the United States federal government and the failure, bankruptcy, or sale of various financial and other institutions. We believe the current economic conditions and financial market turmoil could adversely affect our operations, business and prospects, as well as our ability to obtain funds and manage our liquidity. If these circumstances persist or continue to worsen, our future operating results could be adversely affected, particularly relative to our current expectations.

We are at an early stage of development as a company and we do not have, and may never have, any products that generate significant revenues.

We are at an early stage of development as a company and have a limited operating history on which to evaluate our business and prospects. While we have earned modest product revenues from the ALIGN business acquired in October 2007, since beginning operations in 1996, we have not generated any product revenues from our product candidates currently in development. We cannot guarantee that any of our product candidates currently in development will ever become marketable products and we do not anticipate material revenues from the ALIGN products in the foreseeable future. We must demonstrate that our drug candidates satisfy rigorous standards of safety and efficacy for their intended uses before the FDA, and other regulatory authorities in the United States, the European Union and elsewhere. Significant additional research, preclinical testing and clinical testing is required before we can file applications with the FDA or other regulatory authorities for premarket

approval of our drug candidates. In addition, to compete effectively, our drugs must be easy to administer, cost-effective and economical to manufacture on a commercial scale. We may not achieve any of these objectives. Sapacitabine and seliciclib, our most advanced drug candidates for the treatment of cancer, are currently our only drug candidates in Phase 2 clinical trials. A combination trial of sapacitabine and seliciclib and CYC116 are currently in a Phase 1 clinical trial. We cannot be certain that the clinical development of these or any other drug candidates in preclinical testing or clinical development will be successful, that we will receive the regulatory approvals required to commercialize them or that any of our other research and drug discovery programs will yield a drug candidate suitable for investigation through clinical trials. Our commercial revenues from our product candidates currently in development, if any, will be derived from sales of drugs that will not become marketable for several years, if at all. ***We have a history of operating losses and we may never become profitable. Our stock is a highly speculative investment.***

We have incurred operating losses in each year since beginning operations in 1996 due to costs incurred in connection with our research and development activities and selling, general and administrative costs associated with our operations, and we may never achieve profitability. As of December 31, 2009, our accumulated deficit was \$222.3 million. Our net loss for the years ended December 31, 2008 and 2009 was \$40.4 million and \$19.6 million, respectively. Our net loss attributable to common shareholders from inception through December 31, 2009 was \$263.2 million. Our drug candidates are in the mid-stages of clinical testing and we must conduct significant additional clinical trials before we can seek the regulatory approvals necessary to begin commercial sales of our drugs. We expect to incur continued losses for several years, as we continue our research and development of our drug candidates, seek regulatory approvals, commercialize any approved drugs and market and promote the ALIGN products: Xclair[®] Cream, Numoisyn[®] Liquid and Numoisyn[®] Lozenges. If our drug candidates are unsuccessful in clinical trials or we are unable to obtain regulatory approvals, or if our drugs are unsuccessful in the market, we will not be profitable. If we fail to become and remain profitable, or if we are unable to fund our continuing losses, particularly in light of the current economic conditions, you could lose all or part of your investment.

Capital markets are currently experiencing a period of disruption and instability, which has had and could continue to have a negative impact on the availability and cost of capital.

The general disruption in the United States capital markets has impacted the broader worldwide financial and credit markets and reduced the availability of debt and equity capital for the market as a whole. These global conditions could persist for a prolonged period of time or worsen in the future. Our ability to access the capital markets may be restricted at a time when we would like, or need, to access those markets, which could have an impact on our flexibility to react to changing economic and business conditions. The resulting lack of available credit, lack of confidence in the financial sector, increased volatility in the financial markets could materially and adversely affect the cost of debt financing and the proceeds of equity financing may be materially adversely impacted by these market conditions.

If we fail to comply with the continued listing requirements of the NASDAQ Global Market our common stock price may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

Our common stock is currently listed for trading on the NASDAQ Global Market. We must satisfy NASDAQ's continued listing requirements, including among other things, a minimum stockholders' equity of \$10.0 million and a minimum bid price for our common stock of \$1.00 per share, or risk delisting, which would have a material adverse affect on our business. A delisting of our common stock from the NASDAQ Global Market could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, suppliers, customers and employees and fewer business development opportunities. During 2009, Cyclacel received notification from the NASDAQ Stock Market that the Company was not in compliance with the minimum \$10 million stockholders' equity requirement for continued listing set forth in NASDAQ Marketplace Rule 5450(b)(1)(A). On January 27, 2010, NASDAQ notified the Company that it regained compliance with the minimum \$50 million market value of listed securities requirement and that it currently complies with all other applicable standards for continued listing on The NASDAQ Global Market.

Accordingly, the Company's shares of common and preferred stock will continue to trade on The NASDAQ Global Market.

Raising additional capital in the future may not be available to us on reasonable terms, if at all, when or as we require additional funding. If we issue additional shares of our common stock or other securities that may be convertible into, or exercisable or exchangeable for, our common stock, our existing stockholders would experience further dilution. If we fail to obtain additional funding, we may be unable to complete the development and commercialization of our lead drug candidate, sapacitabine, or continue to fund our research and development programs.

We have funded all of our operations and capital expenditures with proceeds from the issuance of public equity securities, private placements of our securities, interest on investments, licensing revenue, government grants, research and development tax credits and product revenue. In order to conduct the lengthy and expensive research, preclinical testing and clinical trials necessary to complete the development and marketing of our drug candidates, we will require substantial additional funds. Based on our current operating plans of focusing on the advancement of sapacitabine, we expect our existing resources to be sufficient to fund our planned operations for at least the next twelve months. To meet our long-term financing requirements, we may raise funds through public or private equity offerings, debt financings or strategic alliances. Raising additional funds by issuing equity or convertible debt securities may cause our stockholders to experience substantial dilution in their ownership interests and new investors may have rights superior to the rights of our other stockholders. Raising additional funds through debt financing, if available, may involve covenants that restrict our business activities and options. To the extent that we raise additional funds through collaborations and licensing arrangements, we may have to relinquish valuable rights to our drug discovery and other technologies, research programs or drug candidates, or grant licenses on terms that may not be favorable to us. Additional funding may not be available to us on favorable terms, or at all, particularly in light of the current economic conditions. If we are unable to obtain additional funds, we may be forced to delay or terminate our current clinical trials and the development and marketing of our drug candidates including sapacitabine.

Our committed equity financing facility with Kingsbridge may not be available to us if we elect to make a draw down or may require us to make additional blackout or other payments to Kingsbridge, which may result in dilution to our stockholders.

On December 10, 2007 and as amended on November 24, 2009, we entered into the committed equity financing facility, or CEFF, with Kingsbridge Capital Limited, or Kingsbridge. The CEFF entitles us to sell and obligates Kingsbridge to purchase from us the lesser of 4,084,590 shares of our common stock or \$60 million of our common stock, during the next three years, subject to certain conditions and restrictions. Kingsbridge will not be obligated to purchase shares under the CEFF unless certain conditions are met, which include, among other things, a minimum price for our common stock of \$0.40 per share, effectiveness of the registration statement covering the shares subject to the CEFF and the continued listing of our stock on The NASDAQ Global Market.

Kingsbridge is permitted to terminate the CEFF if it determines that a material and adverse event has occurred affecting our business, operations, properties or financial condition and if such condition continues for a period of 10 days from the date Kingsbridge provides us notice of such material and adverse event. In such a case, we would be unable to access any capital through the CEFF.

We are entitled, in certain circumstances, to deliver a blackout notice to Kingsbridge to suspend the use of the registration statement which became effective in December 2007, and prohibit Kingsbridge from selling shares. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the registration statement is not effective in circumstances not permitted by the CEFF, then we must make a payment to Kingsbridge, or issue Kingsbridge additional shares in lieu of this payment, calculated on the basis of the number of shares held by Kingsbridge exclusive of shares that Kingsbridge may hold pursuant to exercise of the Kingsbridge warrant and the change in the market price of our common stock during the period in which the use of the registration statement is suspended. If the trading price of our common stock declines during a suspension of the registration statement, the blackout or other payment to be made by us could be significant.

Should we sell shares to Kingsbridge under the CEFF, or issue shares in lieu of a blackout payment, it will have a dilutive effect on the holdings of our current stockholders, and may result in downward pressure on the price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to 20% from the volume weighted average price of our common stock. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price. During December 2009 and January 2010, we sold an aggregate of 1,583,626 shares of our common stock to Kingsbridge under the terms of the CEFF in consideration of an aggregate of \$1.3 million in funds drawn down from the CEFF by us. During March 2010, we sold another 1,234,606 shares of our common stock to Kingsbridge in consideration of an aggregate of \$2.8 million in funds drawn down from the CEFF by us. However, because we have not declared dividends on our preferred stock for several quarters during the fiscal year 2009, we will not be able to use our Registration Statement on Form S-3, which covers the shares subject to the CEFF and therefore, we may not be able to access the CEFF until such time as an effective registration statement covering such shares be in place. This may limit our ability to access capital markets on short notice or make the cost of capital more expensive.

To the extent we elect to fund the development of a drug candidate or the commercialization of a drug at our expense, we will need substantial additional funding.

We plan to market drugs on our own, with or without a partner, that can be effectively commercialized and sold in concentrated markets that do not require a large sales force to be competitive. To achieve this goal, we will need to establish our own specialized sales force, marketing organization and supporting distribution capabilities. The development and commercialization of our drug candidates is very expensive, including our anticipated Phase 3 clinical trials for sapacitabine. To the extent we elect to fund the full development of a drug candidate or the commercialization of a drug at our expense, we will need to raise substantial additional funding to:

- fund research and development and clinical trials connected with our research;
- fund clinical trials and seek regulatory approvals;
- build or access manufacturing and commercialization capabilities;
- implement additional internal control systems and infrastructure;
- commercialize and secure coverage, payment and reimbursement of our drug candidates, if any such candidates receive regulatory approval;
- maintain, defend and expand the scope of our intellectual property; and
- hire additional management, sales and scientific personnel.

Our future funding requirements will depend on many factors, including:

- the scope, rate of progress and cost of our clinical trials and other research and development activities;
- the costs and timing of seeking and obtaining regulatory approvals;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the costs associated with establishing sales and marketing capabilities;

the costs of acquiring or investing in businesses, products and technologies;
the effect of competing technological and market developments; and
the payment, other terms and timing of any strategic alliance, licensing or other arrangements that we may establish.

If we are not able to secure additional funding when needed, especially in light of the current economic conditions and financial market turmoil, we may have to delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or future commercialization efforts.

If we do not realize the expected benefits from the restructuring plans we announced in September 2008 and June 2009, our operating results and financial conditions could be negatively impacted.

In September 2008 and June 2009, we announced a strategic restructuring designed to focus our resources on our lead drug, sapacitabine, while maintaining the Company's core competency in drug discovery and cell cycle biology. We cannot guarantee that we will not have to undertake additional restructuring activities, that any of our restructuring efforts will be successful, or that we will be able to realize the cost savings and other anticipated benefits from our restructuring. If we are unable to realize the expected operational efficiencies from our restructuring activities, our operating results and financial condition could be adversely affected.

Any future workforce and expense reductions may have an adverse impact on our internal programs, strategic plans, and our ability to hire and retain key personnel, and may also be distracting to our management.

Further workforce and expense reductions in addition to those carried out in September 2008 and June 2009 could result in significant delays in implementing our strategic plans. In addition, employees, whether or not directly affected by such reduction, may seek future employment with our business partners or competitors. Although our employees are required to sign a confidentiality agreement at the time of hire, the confidential nature of certain proprietary information may not be maintained in the course of any such future employment. In addition, any additional workforce reductions or restructurings would be expected to involve significant expense as a result of contractual terms in certain of our existing agreements, including potential severance obligations as well as any payments that may, under certain circumstances, be required under our agreement with the Scottish Enterprise. Further, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled personnel. We may have difficulty retaining and attracting such personnel as a result of a perceived risk of future workforce and expense reductions. Finally, the implementation of expense reduction programs may result in the diversion of the time and attention of our executive management team and other key employees, which could adversely affect our business.

Budget constraints resulting from our restructuring plan may negatively impact our research and development, forcing us to delay our efforts to develop certain product candidates in favor of developing others, which may prevent us from commercializing our product candidates as quickly as possible.

Research and development is an expensive process. As part of our restructuring plan, we have decided to focus our clinical development priorities on sapacitabine, while still possibly continuing to progress additional programs pending the availability of clinical data and the availability of funds, at which time we will determine the feasibility of pursuing, if at all, further advanced development of seliciclib, CYC116 or additional programs. Because we have had to prioritize our development candidates as a result of budget constraints, we may not be able to fully realize the value of our product candidates in a timely manner, if at all.

If we fail to enter into and maintain successful strategic alliances for our drug candidates, we may have to reduce or delay our drug candidate development or increase our expenditures.

An important element of our strategy for developing, manufacturing and commercializing our drug candidates is entering into strategic alliances with pharmaceutical companies or other industry participants to advance our programs and enable us to maintain our financial and operational capacity.

We face significant competition in seeking appropriate alliances. We may not be able to negotiate alliances on acceptable terms, if at all. In addition, these alliances may be unsuccessful. If we fail to create and maintain suitable alliances, we may have to limit the size or scope of, or delay, one or more of our drug development or research programs. If we elect to fund drug development or research programs on our own, we will have to increase our expenditures and will need to obtain additional funding, which may be unavailable or available only on unfavorable terms.

We are exposed to risks related to foreign currency exchange rates.

Some of our costs and expenses are denominated in foreign currencies. Most of our foreign expenses are associated with our research and development operations of our United Kingdom-based wholly-owned subsidiary. When the United States dollar weakens against the British pound, the United States dollar value of the foreign currency denominated expense increases, and when the United States dollar strengthens against the British pound, the United States dollar value of the foreign currency denominated expense decreases. Consequently, changes in exchange rates, and in particular a weakening of the United States dollar, may adversely affect our results of operations.

We are exposed to risk related to the marketable securities we may purchase.

We may invest cash not required to meet short term obligations in short term marketable securities. We may purchase securities in United States government, government-sponsored agencies and highly rated corporate and asset-backed securities subject to an approved investment policy. Historically, investment in these securities has been highly liquid and has experienced only very limited defaults. However, recent volatility in the financial markets has created additional uncertainty regarding the liquidity and safety of these investments. Although we believe our marketable securities investments are safe and highly liquid, we cannot guarantee that our investment portfolio will not be negatively impacted by recent or future market volatility or credit restrictions.

Clinical trials are expensive, time consuming, subject to delay and may be required to continue beyond our available funding.

Clinical trials are expensive, complex can take many years to conduct and may have uncertain outcomes. We estimate that clinical trials of our most advanced drug candidates may be required to continue beyond our available funding and may take several years more to complete. The designs used in some of our trials have not been used widely by other pharmaceutical companies. Failure can occur at any stage of the testing and we may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent commercialization of our current or future drug candidates, including but not limited to:

- delays in securing clinical investigators or trial sites for our clinical trials;
- delays in obtaining institutional review board, or IRB, and other regulatory approvals to commence a clinical trial;
- slower than anticipated rates of patient recruitment and enrollment, or reaching the targeted number of patients because of competition for patients from other trials or other reasons;
- negative or inconclusive results from clinical trials;
- unforeseen safety issues;

uncertain dosing issues may or may not be related to suboptimal pharmacokinetic and pharmacodynamic behaviors;
approval and introduction of new therapies or changes in standards of practice or regulatory guidance that render our clinical trial endpoints or the targeting of our proposed indications obsolete;
inability to monitor patients adequately during or after treatment or problems with investigator or patient compliance with the trial protocols;
inability to replicate in large controlled studies safety and efficacy data obtained from a limited number of patients in uncontrolled trials;
inability or unwillingness of medical investigators to follow our clinical protocols; and
unavailability of clinical trial supplies.

If we suffer any significant delays, setbacks or negative results in, or termination of, our clinical trials, we may be unable to continue development of our drug candidates or generate revenue and our development costs could increase significantly.

Adverse events have been observed in our clinical trials and may force us to stop development of our product candidates or prevent regulatory approval of our product candidates.

Adverse or inconclusive results from our clinical trials may substantially delay, or halt entirely, any further development of our drug candidates. Many companies have failed to demonstrate the safety or effectiveness of drug candidates in later stage clinical trials notwithstanding favorable results in early stage clinical trials. Previously unforeseen and unacceptable side effects could interrupt, delay or halt clinical trials of our drug candidates and could result in the FDA or other regulatory authorities denying approval of our drug candidates. We will need to demonstrate safety and efficacy for specific indications of use, and monitor safety and compliance with clinical trial protocols throughout the development process. To date, long-term safety and efficacy has not been demonstrated in clinical trials for any of our drug candidates. Toxicity and serious adverse events as defined in trial protocols have been noted in preclinical and clinical trials involving certain of our drug candidates. For example, neutropenia and gastro-intestinal toxicity were observed in patients receiving sapacitabine and elevations of liver enzymes and decrease in potassium levels have been observed in patients receiving seliciclib.

In addition, we may pursue clinical trials for sapacitabine and seliciclib in more than one indication. There is a risk that severe toxicity observed in a trial for one indication could result in the delay or suspension of all trials involving the same drug candidate. Even if we believe the data collected from clinical trials of our drug candidates are promising with respect to safety and efficacy, such data may not be deemed sufficient by regulatory authorities to warrant product approval. Clinical data can be interpreted in different ways. Regulatory officials could interpret such data in different ways than we do which could delay, limit or prevent regulatory approval. The FDA, other regulatory authorities or we may suspend or terminate clinical trials at any time. Any failure or significant delay in completing clinical trials for our drug candidates, or in receiving regulatory approval for the commercialization of our drug candidates, may severely harm our business and reputation.

If our understanding of the role played by CDKs or AKs in regulating the cell cycle is incorrect, this may hinder pursuit of our clinical and regulatory strategy.

Our development of small molecule inhibitors of CDK and AK is based on our understanding of the mechanisms of action of CDK and AK inhibitors and their interaction with other cellular mechanisms. One of our drug candidates, seliciclib, is a CDK inhibitor, and CYC116 is an AK and VEGFR2 inhibitor. Although a number of pharmaceutical and biotechnology companies are attempting to develop CDK or AK inhibitor drugs for the treatment of cancer, no CDK or AK inhibitor has yet reached the market. If our understanding of the role played by CDK or AK inhibitors in regulating the cell cycle is incorrect, seliciclib and/or CYC116 may fail to produce therapeutically relevant results hindering our ability to pursue our clinical and regulatory strategy.

We are making use of biomarkers, which are not scientifically validated, and our reliance on biomarker data may thus lead us to direct our resources inefficiently.

We are making use of biomarkers in an effort to facilitate our drug development and to optimize our clinical trials. Biomarkers are proteins or other substances whose presence in the blood can serve as an indicator of specific cell processes. We believe that these biological markers serve a useful purpose in helping us to evaluate whether our drug candidates are having their intended effects through their assumed mechanisms, and thus enable us to identify more promising drug candidates at an early stage and to direct our resources efficiently. We also believe that biomarkers may eventually allow us to improve patient selection in connection with clinical trials and monitor patient compliance with trial protocols.

For most purposes, however, biomarkers have not been scientifically validated. If our understanding and use of biomarkers is inaccurate or flawed, or if our reliance on them is otherwise misplaced, then we will not only fail to realize any benefits from using biomarkers, but may also be led to invest time and financial resources inefficiently in attempting to develop inappropriate drug candidates. Moreover, although the FDA has issued for comment a draft guidance document on the potential use of biomarker data in clinical development, such data are not currently accepted by the FDA or other regulatory agencies in the United States, the European Union or elsewhere in applications for regulatory approval of drug candidates and there is no guarantee that such data will ever be accepted by the relevant authorities in this connection. Our biomarker data should not be interpreted as evidence of efficacy.

Due to our reliance on contract research organizations or other third parties to conduct clinical trials, we may be unable to directly control the timing, conduct and expense of our clinical trials.

We do not have the ability to independently conduct clinical trials required to obtain regulatory approvals for our drug candidates. We must rely on third parties, such as contract research organizations, data management companies, contract clinical research associates, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. In addition, we rely on third parties to assist with our preclinical development of drug candidates. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our drug candidates.

To the extent we are able to enter into collaborative arrangements or strategic alliances, we will be exposed to risks related to those collaborations and alliances.

Although we are not currently party to any collaboration arrangement or strategic alliance that is material to our business, in the future we expect to be dependent upon collaborative arrangements or strategic alliances to complete the development and commercialization of some of our drug candidates particularly after the Phase 2 stage of clinical testing. These arrangements may place the development of our drug candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

We may be unable to locate and enter into favorable agreements with third parties, which could delay or impair our ability to develop and commercialize our drug candidates and could increase our costs of development and commercialization. Dependence on collaborative arrangements or strategic alliances will subject us to a number of risks, including the risk that:

- we may not be able to control the amount and timing of resources that our collaborators may devote to the drug candidates;
- our collaborators may experience financial difficulties;

we may be required to relinquish important rights such as marketing and distribution rights; business combinations or significant changes in a collaborator's business strategy may also adversely affect a collaborator's willingness or ability to complete our obligations under any arrangement; a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors; and collaborative arrangements are often terminated or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

We have no manufacturing capacity and will rely on third party manufacturers for the late stage development and commercialization of any drugs or devices we may develop or sell.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates under development or our currently marketed ALIGN products. We currently lack the resources or the capacity to manufacture any of our products on a clinical or commercial scale. We depend upon a third party, Sinclair, to manufacture the commercial products sold by our ALIGN subsidiary and we can not rely upon Sinclair to continue to supply the products. We anticipate future reliance on a limited number of third party manufacturers until we are able, or decide to, expand our operations to include manufacturing capacities. Any performance failure on the part of manufacturers could delay late stage clinical development or regulatory approval of our drug, the commercialization of our drugs or our ability to sell our commercial products, producing additional losses and depriving us of potential product revenues.

If the FDA or other regulatory agencies approve any of our drug candidates for commercial sale, or if we significantly expand our clinical trials, we will need to manufacture them in larger quantities and will be required to secure alternative third-party suppliers to our current suppliers. To date, our drug candidates have been manufactured in small quantities for preclinical testing and clinical trials and we may not be able to successfully increase the manufacturing capacity, whether in collaboration with our current or future third-party manufacturers or on our own, for any of our drug candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA and other regulatory bodies must review and approve. If we are unable to successfully increase the manufacturing capacity for a drug candidate whether for late stage clinical trials or for commercial sale or are unable to secure alternative third-party suppliers to our current suppliers, the drug development, regulatory approval or commercial launch of any related drugs may be delayed or blocked or there may be a shortage in supply. Even if any third party manufacturer makes improvements in the manufacturing process for our drug candidates, we may not own, or may have to share, the intellectual property rights to such innovation.

As we evolve from a company primarily involved in discovery and development to one also involved in the commercialization of drugs and devices, we may encounter difficulties in managing our growth and expanding our operations successfully.

In order to execute our business strategy, we will need to expand our development, control and regulatory capabilities and develop financial, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. If our operations expand, we expect that we will need to manage additional relationships with various collaborative partners, suppliers and other third parties. Our ability to manage our operations and any growth will require us to make appropriate changes and upgrades, as necessary, to our operational, financial and management controls, reporting systems and procedures wherever we may operate. Any inability to manage growth could delay the execution of our business plan or disrupt our operations.

The failure to attract and retain skilled personnel and key relationships could impair our drug development and commercialization efforts.

We are highly dependent on our senior management and key scientific, technical and sales and marketing personnel. Competition for these types of personnel is intense. The loss of the services of any member of our senior management, scientific, technical or sales or marketing staff may significantly delay or prevent the achievement of drug development and other business objectives and could have a material adverse effect on our business, operating results and financial condition. We also rely on consultants and advisors to assist us in formulating our strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us. The success of the commercialization of the ALIGN products depends, in large part, on our continued ability to develop and maintain important relationships with distributors and research and medical institutions. Failure to do that could have a material adverse effect on our ability to commercialize the ALIGN products.

We intend to expand and develop new drug candidates. We will need to hire additional employees in order to continue our clinical trials and market our drug candidates and medical devices. This strategy will require us to recruit additional executive management and scientific and technical personnel. There is currently intense competition for skilled executives and employees with relevant scientific and technical expertise, and this competition is likely to continue. The inability to attract and retain sufficient scientific, technical and managerial personnel could limit or delay our product development efforts, which would adversely affect the development of our drug candidates and commercialization of our potential drugs and growth of our business.

Our drug candidates are subject to extensive regulation, which can be costly and time-consuming, and we may not obtain approvals for the commercialization of any of our drug candidates.

The clinical development, manufacturing, selling and marketing of our drug candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States, the European Union and elsewhere. These regulations also vary in important, meaningful ways from country to country. We are not permitted to market a potential drug in the United States until we receive approval of an NDA from the FDA. We have not received an NDA approval from the FDA for any of our drug candidates.

Obtaining an NDA approval is expensive and is a complex, lengthy and uncertain process. The FDA approval process for a new drug involves completion of preclinical studies and the submission of the results of these studies to the FDA, together with proposed clinical protocols, manufacturing information, analytical data and other information in an Investigational New Drug, or IND, which must become effective before human clinical trials may begin. Clinical development typically involves three phases of study: Phase 1, 2 and 3. The most significant costs associated with clinical development are the pivotal or suitable for registration late Phase 2 or Phase 3 clinical trials as they tend to be the longest and largest studies conducted during the drug development process. After completion of clinical trials, an NDA may be submitted to the FDA. In responding to an NDA, the FDA may refuse to file the application, or if accepted for filing, the FDA may grant marketing approval, request additional information or deny the application if it determines that the application does not provide an adequate basis for approval. In addition, failure to comply with the FDA and other applicable foreign and U.S. regulatory requirements may subject us to administrative or judicially imposed sanctions. These include warning letters, civil and criminal penalties, injunctions, product seizure or detention, product recalls, total or partial suspension of production and refusal to approve either pending NDAs, or supplements to approved NDAs.

Despite the substantial time and expense invested in preparation and submission of an NDA or equivalents in other jurisdictions, regulatory approval is never guaranteed. The FDA and other regulatory authorities in the United States, the European Union and elsewhere exercise substantial discretion in the drug approval process. The number, size and design of preclinical studies and clinical trials that will be required for FDA or other regulatory approval will vary depending on the drug candidate, the disease or condition for which the drug candidate is intended to be used and the regulations and guidance documents applicable to any particular drug candidate. The FDA or other regulators can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to:

those discussed in the risk factor which immediately follows;

the fact that the FDA or other regulatory officials may not approve our or our third party manufacturer's processes or facilities; or

the fact that new regulations may be enacted by the FDA or other regulators may change their approval policies or adoption of new regulations requiring new or different evidence of safety and efficacy for the intended use of a drug candidate.

With regard to the ALIGN products, and following regulatory approval of any of our drug candidates, we are subject to ongoing regulatory obligations and restrictions, which may result in significant expense and limit our ability to commercialize our potential products.

With regard to our ALIGN products and our drug candidates, if any, approved by the FDA or by another regulatory authority, we are held to extensive regulatory requirements over product manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping. Regulatory approvals may also be subject to significant limitations on the indicated uses or marketing of the drug candidates. Potentially costly follow-up or post-marketing clinical studies may be required as a condition of approval to further substantiate safety or efficacy, or to investigate specific issues of interest to the regulatory authority. Previously unknown problems with the product or drug candidate, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the drug or device, and could include withdrawal of the drug or device from the market.

In addition, the law or regulatory policies governing pharmaceuticals may change. New statutory requirements may be enacted or additional regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or elsewhere. If we are not able to maintain regulatory compliance, we might not be permitted to market our drugs and our business could suffer.

Our applications for regulatory approval could be delayed or denied due to problems with studies conducted before we in-licensed the rights to some of our product candidates.

We currently license some of the compounds and drug candidates used in our research programs from third parties. These include sapacitabine which was licensed from Daiichi-Sankyo. Our present research involving these compounds relies upon previous research conducted by third parties over whom we had no control and before we in-licensed the drug candidates. In order to receive regulatory approval of a drug candidate, we must present all relevant data and information obtained during our research and development, including research conducted prior to our licensure of the drug candidate. Although we are not currently aware of any such problems, any problems that emerge with preclinical research and testing conducted prior to our in-licensing may affect future results or our ability to document prior research and to conduct clinical trials, which could delay, limit or prevent regulatory approval for our drug candidates.

We face intense competition and our competitors may develop drugs that are less expensive, safer, or more effective than our drug candidates.

A large number of drug candidates are in development for the treatment of leukemia, lung cancer, lymphomas and nasopharyngeal cancer. Several pharmaceutical and biotechnology companies have nucleoside analogs or other products on the market or in clinical trials which may be competitive to sapacitabine in both hematological and oncology indications. These include Celgene, Cephalon, Eisai, Johnson & Johnson, Eli Lilly, Genzyme, GlaxoSmithKline, Hospira, Pfizer, Seattle Genetics, Sunesis and Vion. We believe that we are currently the only company that has an orally available CDK-specific agent in Phase 2 clinical trials but that there are a number of companies, including AstraZeneca, Eisai, Pfizer, Piramal Life Sciences, Roche, Merck and Bayer-Schering that are

developing CDK inhibitors in early stage clinical trials in cancer patients. Although Aventis,

a predecessor of Sanofi-Aventis, had previously announced that it has ceased Phase 2 development of alvocidib or flavopiridol, a CDK inhibitor, we believe that the National Cancer Institute's Cancer Therapy Evaluation Program, or CTEP, is continuing to enroll patients in a CTEP sponsored trial in patients with chronic leukemia. A number of companies are pursuing discovery and research activities in each of the other areas that are the subject of our research and drug development programs. We believe that AstraZeneca, Entremed, Merck, jointly with Vertex, Nerviano Medical Sciences, Pfizer, Rigol, Sunesis and Takeda-Millennium have commenced Phase 1 or Phase 2 clinical trials of Aurora kinase inhibitors in patients with advanced cancers. Several companies have reported selection of Aurora kinase inhibitor candidates for development and may have started or are expected to start clinical trials within the next twelve months. We believe that Boehringer Ingelheim, GlaxoSmithKline, Onconova and Nerviano Medical Sciences have commenced Phase 1 or Phase 2 clinical trials with Plk inhibitor candidates for oncology indications. For our ALIGN products, we believe that Beiersdorf, Daiichi-Sankyo, Eisai, Johnson & Johnson, MPM Medical and other companies market products for radiation dermatitis and xerostomia.

Our competitors, either alone or together with collaborators, may have substantially greater financial resources and research and development staff. Our competitors may also have more experience:

- developing drug candidates;
- conducting preclinical and clinical trials;
- obtaining regulatory approvals; and
- commercializing product candidates.

Our competitors may succeed in obtaining patent protection and regulatory approval and may market drugs before we do. If our competitors market drugs that are less expensive, safer, more effective or more convenient to administer than our potential drugs, or that reach the market sooner than our potential drugs, we may not achieve commercial success. Scientific, clinical or technical developments by our competitors may render our drug candidates obsolete or noncompetitive. We anticipate that we will face increased competition in the future as new companies enter the markets and as scientific developments progress. If our drug candidates obtain regulatory approvals, but do not compete effectively in the marketplace, our business will suffer.

The commercial success of the ALIGN products and our drug candidates depends upon their market acceptance among physicians, patients, healthcare providers and payors and the medical community.

It is necessary that our and our distribution partners' products, including Xclafit[®] Cream, Numoisyn[®] Liquid and Numoisyn[®] Lozenges achieve and maintain market acceptance. If our drug candidates are approved by the FDA or by another regulatory authority, the resulting drugs, if any, may not gain market acceptance among physicians, healthcare providers and payors, patients and the medical community. The degree of market acceptance of any of our approved drugs or devices will depend on a variety of factors, including:

- timing of market introduction, number and clinical profile of competitive drugs;
- our ability to provide acceptable evidence of safety and efficacy;
- relative convenience and ease of administration;
- cost-effectiveness;
- availability of coverage, reimbursement and adequate payment from health maintenance organizations and other third party payors;
- prevalence and severity of adverse side effects; and
- other potential advantages over alternative treatment methods.

If our drugs fail to achieve market acceptance, we may not be able to generate significant revenue and our business would suffer.

If we are unable to compete successfully in our market place, it will harm our business.

There are existing products in the marketplace that compete with our products. Companies may develop new products that compete with our products. Certain of these competitors and potential competitors have longer operating histories, substantially greater product development capabilities and financial, scientific, marketing and sales resources. Competitors and potential competitors may also develop products that are safer, more effective or have other potential advantages compared to our products. In addition, research, development and commercialization efforts by others could render our products obsolete or non-competitive. Certain of our competitors and potential competitors have broader product offerings and extensive customer bases allowing them to adopt aggressive pricing policies that would enable them to gain market share. Competitive pressures could result in price reductions, reduced margins and loss of market share. We could encounter potential customers that, due to existing relationships with our competitors, are committed to products offered by those competitors. As a result, those potential customers may not consider purchasing our products.

There is uncertainty related to coverage, reimbursement and payment by healthcare providers and payors for the ALIGN products and newly approved drugs, if any. The inability or failure to obtain or maintain coverage could affect our ability to market the ALIGN products and our future drugs and decrease our ability to generate revenue.

The availability and levels of coverage and reimbursement of newly approved drugs by healthcare providers and payors is subject to significant uncertainty. The commercial success of the ALIGN products and our drug candidates in both the United States and international markets is substantially dependent on whether third party coverage and reimbursement is available. The United States Centers for Medicare and Medicaid Services, health maintenance organizations and other third party payors in the United States, the European Union and other jurisdictions are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs and, as a result, they may not cover or provide adequate payment for our potential drugs. The ALIGN products and our drug candidates may not be considered cost-effective and reimbursement may not be available to consumers or may not be sufficient to allow the ALIGN products or our drug candidates to be marketed on a competitive basis. In some countries, pricing of prescription drugs is subject to government control. In such countries, pricing negotiations with governmental authorities can take three to 12 months or longer following application to the competent authorities. To obtain reimbursement or pricing approval in such countries may require conducting an additional clinical trial comparing the cost-effectiveness of the drug to other alternatives. In the United States, the Medicare Part D drug benefit implemented in 2006 will limit drug coverage through formularies and other cost and utilization management programs, while Medicare Part B limits drug payments to a certain percentage of average price or through restrictive payment policies of least costly alternatives and inherent reasonableness. Our business could be materially harmed if coverage, reimbursement or pricing is unavailable or set at unsatisfactory levels.

We may be exposed to product liability claims that may damage our reputation and we may not be able to obtain adequate insurance.

Because we conduct clinical trials in humans, we face the risk that the use of our drug candidates will result in adverse effects. We believe that we have obtained reasonably adequate product liability insurance coverage for our trials. We cannot predict, however, the possible harm or side effects that may result from our clinical trials. Such claims may damage our reputation and we may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limit of, our insurance coverage.

As we market commercialized products through our ALIGN subsidiary we are exposed to additional risks of product liability claims. These risks exist even with respect to drugs and devices that are approved for commercial sale by the FDA or other regulatory authorities in the United States, the European Union or elsewhere and manufactured in facilities licensed and regulated by the FDA or other such regulatory authorities. We have secured limited product liability insurance coverage, but may not be able to maintain such insurance on acceptable terms with adequate coverage, or at a reasonable cost. There is also a risk that third parties that we have agreed to indemnify could incur liability. Even if we were ultimately successful in product liability litigation, the litigation would consume substantial amounts of our financial and managerial resources and may exceed insurance coverage creating adverse publicity, all of which would impair our ability to generate sales of the litigated product as well as our other potential drugs.

We may be subject to damages resulting from claims that our employees or we have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper or prevent our ability to commercialize certain potential drugs, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Defending against claims relating to improper handling, storage or disposal of hazardous chemical, radioactive or biological materials could be time consuming and expensive.

Our research and development involves the controlled use of hazardous materials, including chemicals, radioactive and biological materials such as chemical solvents, phosphorus and bacteria. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from those materials. Various laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

We may be required to defend lawsuits or pay damages in connection with the alleged or actual violation of healthcare statutes such as fraud and abuse laws, and our corporate compliance programs can never guarantee that we are in compliance with all relevant laws and regulations.

Our commercialization efforts in the United States are subject to various federal and state laws pertaining to promotion and healthcare fraud and abuse, including federal and state anti-kickback, fraud and false claims laws. Anti-kickback laws make it illegal for a manufacturer to offer or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase of a product. The federal government has published many regulations relating to the anti-kickback statutes, including numerous safe harbors or exemptions for certain arrangements. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment to third-party payers including Medicare and Medicaid, claims for reimbursed products or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

Our activities relating to the sale and marketing of our products will be subject to scrutiny under these laws and regulations. It may be difficult to determine whether or not our activities, comply with these complex legal requirements. Violations are punishable by significant criminal and/or civil fines and other penalties, as well as the possibility of exclusion of the product from coverage under governmental healthcare programs, including Medicare and Medicaid. If the government were to investigate or make allegations against us or any of our employees, or sanction or convict us or any of our employees, for violations of any of these legal requirements, this could have a material adverse effect on our business, including our stock price. Our activities could be subject to challenge for many reasons, including the broad scope and complexity of these laws and regulations, the difficulties in interpreting and applying these legal requirements, and the high degree of prosecutorial resources

and attention being devoted to the biopharmaceutical industry and health care fraud by law enforcement authorities. During the last few years, numerous biopharmaceutical companies have paid multi-million dollar fines and entered into burdensome settlement agreements for alleged violation of these requirements, and other companies are under active investigation. Although we have developed and implemented corporate and field compliance programs as part of our commercialization efforts, we cannot assure you that we or our employees, directors or agents were, are or will be in compliance with all laws and regulations or that we will not come under investigation, allegation or sanction. In addition, we may be required to prepare and report product pricing-related information to federal and state governmental authorities, such as the Department of Veterans Affairs and under the Medicaid program. The calculations used to generate the pricing-related information are complex and require the exercise of judgment. If we fail to accurately and timely report product pricing-related information or to comply with any of these or any other laws or regulations, various negative consequences could result, including criminal and/or civil prosecution, substantial criminal and/or civil penalties, exclusion of the approved product from coverage under governmental healthcare programs including Medicare and Medicaid, costly litigation and restatement of our financial statements. In addition, our efforts to comply with this wide range of laws and regulations are, and will continue to be, time-consuming and expensive.

If we fail to enforce adequately or defend our intellectual property rights our business may be harmed.

Our commercial success depends in large part on obtaining and maintaining patent and trade secret protection for our drug candidates, the methods used to manufacture those drug candidates and the methods for treating patients using those drug candidates.

Specifically, sapacitabine is covered in granted, composition of matter patents that expire in 2014 in the US and 2012 outside the US. Sapacitabine is further protected by additional granted, composition of matter patents claiming certain, stable crystalline forms of sapacitabine and their pharmaceutical compositions and therapeutic uses that expire in 2022. In early development, amorphous sapacitabine was used. We have used one of the stable, crystalline forms of sapacitabine in nearly all our Phase 1 and in all of our Phase 2 clinical studies. We have also chosen this form for commercialization. Additional patents claim certain medical uses and formulations of sapacitabine which have emerged in our clinical trials. Seliciclib is protected by granted, composition of matter patents that expire in 2016. Additional patents claim certain medical uses which have emerged from our research programs.

Failure to obtain, maintain or extend the patents could adversely affect our business. We will only be able to protect our drug candidates and our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

Our ability to obtain patents is uncertain because legal means afford only limited protections and may not adequately protect our rights or permit it to gain or keep any competitive advantage. Some legal principles remain unresolved and the breadth or interpretation of claims allowed in patents in the United States, the European Union or elsewhere can still be difficult to ascertain or predict. In addition, the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific and factual issues. Changes in either patent laws or in interpretations of patent laws in the United States, the European Union or elsewhere may diminish the value of our intellectual property or narrow the scope of our patent protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products and technologies. In addition, we generally do not control the patent prosecution of subject matter that we license from others and have not controlled the earlier stages of the patent prosecution. Accordingly, we are unable to exercise the same degree of control over this intellectual property as we would over our own.

Even if patents are issued regarding our drug candidates or methods of using them, those patents can be challenged by our competitors who may argue such patents are invalid and/or unenforceable. Patents also will not protect our drug candidates if competitors devise ways of making or using these product candidates without legally infringing our patents. The U.S. Federal Food, Drug and Cosmetic, or FD&C, Act and FDA regulations and policies and equivalents in other jurisdictions provide incentives to manufacturers to challenge patent validity or create modified, noninfringing versions of a drug in order to facilitate the approval of abbreviated new drug applications for generic substitutes. These same types of incentives encourage manufacturers to submit new drug applications that rely on

literature and clinical data not prepared for or by the drug sponsor.

Proprietary trade secrets and unpatented know-how are also very important to our business. We rely on trade secrets to protect our technology, especially where we do not believe that patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. Our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Enforcing a claim that a third party obtained illegally and is using trade secrets is expensive and time consuming, and the outcome is unpredictable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Intellectual property rights of third parties may increase our costs or delay or prevent us from being able to commercialize our drug candidates and/or the ALIGN products.

There is a risk that we are infringing or will infringe the proprietary rights of third parties because patents and pending applications belonging to third parties exist in the United States, the European Union and elsewhere in the world in the areas of our research and/or the ALIGN products. Others might have been the first to make the inventions covered by each of our or our licensors' pending patent applications and issued patents and might have been the first to file patent applications for these inventions. We are aware of several published patent applications, and understand that others may exist, that could support claims that, if granted, could cover various aspects of our developmental programs, including in some cases particular uses of our lead drug candidate sapacitabine, seliciclib or other therapeutic candidates, or gene sequences and techniques that we use in the course of our research and development. In addition, we understand that other applications and patents exist relating to potential uses of sapacitabine and seliciclib that are not part of our current clinical programs for these compounds. Numerous third-party United States and foreign issued patents and pending applications exist in the area of kinases, including CDK, AK and Plk for which we have research programs. For example, some pending patent applications contain broad claims that could represent freedom to operate limitations for some of our kinase programs should they be issued unchanged. Although we intend to continue to monitor these applications, we cannot predict what claims will ultimately be allowed and if allowed what their scope would be. In addition, because the patent application process can take several years to complete, there may be currently pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our drug candidates. If we wish to use the technology or compound claimed in issued and unexpired patents owned by others, we will need to obtain a license from the owner, enter into litigation to challenge the validity of the patents or incur the risk of litigation in the event that the owner asserts that we infringe its patents. In one case we have opposed a European patent relating to human aurora kinase and the patent has been finally revoked (no appeal was filed). We are also aware of a corresponding U.S. patent containing method of treatment claims for specific cancers using aurora kinase modulators which, if held valid, could potentially restrict the use of our aurora kinase inhibitors once clinical trials are completed.

There has been substantial litigation and other proceedings regarding patent and other i