Harbor BioSciences, Inc.
Form 10-K
March 30, 2010
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

x 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

For the transition period from to

Commission File Number 001-34584

HARBOR BIOSCIENCES, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**13-3697002**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
4435 Eastgate Mall, Suite 400 San Diego, CA	**92121**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number, including area code: (858) 587-9333

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.01 per share	**The Nasdaq Stock Market**

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

None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ¨ NO x

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. YES ¨ NO x

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 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 requirement for the past 90 days. YES x 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 is not contained herein, and will not be contained, to the best of the Registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. YES ¨ NO x

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 definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2. (Check One).

Large accelerated filer ¨ Accelerated filer ¨ Non-accelerated filer ¨ Smaller Reporting Company x

Indicate by check mark whether the Registrant is a shell company (as defined in Exchange Act Rule 12b-2). YES ¨ NO x

The aggregate market value of the voting stock held by nonaffiliates of the Registrant as of June 30, 2009, the end of the Company s most recently completed second fiscal quarter, was approximately $14,497,860 based on the closing stock price of $0.50 for the Registrant s Common Stock as reported by the Nasdaq Global Market*.

As of March 27, 2010, there were outstanding 29,433,939 shares of the Registrant s Common Stock, $.01 par value per share.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of Registrant's definitive proxy statement to be filed with the Securities and Exchange Commission within 120 days after Registrant s fiscal year end December 31, 2009, are incorporated by reference into Part III of this Annual Report on Form 10-K.

* Excludes the common stock held by executive officers, directors and stockholders whose ownership exceeded 10% of the Registrant s common stock outstanding at June 30, 2009. This calculation does not reflect a determination that such persons are affiliates for any other purposes.

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Harbor BioSciences, Inc.

Form 10-K

For the Fiscal Year Ended December 31, 2009

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, and the information incorporated herein, contains forward-looking statements that involve and are subject to risks and uncertainties. In particular, statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are contained or incorporated by reference in this Annual Report on Form 10-K. We have based these forward-looking statements on our current expectations about future events. While we believe these expectations reflected in this Annual Report on Form 10-K are reasonable, the inclusion of any forward-looking statements should not be regarded as a representation that any of our plans will be achieved and such forward-looking statements are inherently subject to risks and uncertainties, many of which are beyond our control. Such forward-looking statements include, but are not limited to, statements preceded by, followed by or that otherwise include the words, believe, may, might, can, could, will, would , should, estimate, continue, anticipate, intend, seek, plan, project, expect, or similar expressions. The actual future results for Harbor BioSciences, Inc. may differ materially from those discussed here for various reasons, including those discussed in this Annual Report in Part 1, Item 1A under the heading Risk Factors, Part II, Item 7 entitled Management s Discussion and Analysis of Financial Condition and Results of Operations and elsewhere throughout this Annual Report on Form 10-K. Given these risks and uncertainties, you are cautioned not to place undue reliance on such forward-looking statements. The forward-looking statements included in this Annual Report are made only as of the date hereof. We do not undertake any obligation to update any such statements or to publicly announce the results of any revisions to any of such statements as a result of new information, to reflect future events or developments. When used in this Annual Report, unless otherwise indicated, we, our and us refers to Harbor BioSciences, Inc.

PART I

Item 1. Business

GENERAL OVERVIEW

Harbor BioSciences, Inc. (Harbor BioSciences), a clinical-stage pharmaceutical company, is engaged in the discovery and development of products for the treatment of diseases related to aging. Our current development efforts are primarily focused on a series of steroid hormone analogs that are derived from the human adrenal metabolome.

We are currently focused on the development of two clinical drug development candidates APOPTONE® (HE3235), a compound in a Phase I/IIa clinical trial for late-stage prostate cancer and TRIOLEX® (HE3286), a compound currently in early Phase II clinical trials for the treatment of type 2 diabetes and staged for Phase II clinical trials in ulcerative colitis (UC) and rheumatoid arthritis (RA).

Drawn from our unique and proprietary platform, our research program has identified additional lead candidates active in preclinical models of cancer, metabolic conditions, autoimmune conditions, lung inflammation, bone degeneration and organ regeneration.

Our principal executive offices are located at 4435 Eastgate Mall, Suite 400, San Diego, California 92121, and our telephone number is (858) 587-9333. We incorporated in Delaware in 1992.

On March 26, 1997, Hollis-Eden, Inc., a Delaware corporation, was merged with and into us, then known as Initial Acquisition Corp. (IAC), a Delaware corporation. Upon consummation of the merger of Hollis-Eden, Inc. with IAC, Hollis-Eden, Inc. ceased to exist, and IAC changed its name to Hollis-Eden Pharmaceuticals, Inc.

Effective February 9, 2010, we changed our name from Hollis-Eden Pharmaceuticals, Inc. to Harbor BioSciences, Inc. The name change was effected pursuant to Section 253 of the General Corporation Law of the

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State of Delaware by the merger of our wholly owned subsidiary into us. We were the surviving corporation and, in connection with the merger, we amended our Amended and Restated Certificate of Incorporation to change our name to Harbor BioSciences, Inc.

Effective February 18, 2010, our common stock began trading under a new Nasdaq symbol, HRBR and CUSIP number 41150V 103 .

Harbor BioSciences, TRIOLEX, APOPTONE, and the Harbor BioSciences stylized logo are trademarks of Harbor BioSciences, Inc. This filing also includes trademarks owned by other parties. All other trademarks mentioned are the property of their respective owners. Use or display by us of other parties trademarks or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or product owners.

Our periodic and current reports that we file with the Securities and Exchange Commission, or SEC, are available free of charge, on our website, as soon as reasonably practicable after we have electronically filed them with, or furnished them to, the SEC. Our Internet address is www.harborbiosciences.com. The reference to our website does not constitute incorporation by reference of the information contained on our website.

Harbor BioSciences Approach

Over the last several decades, scientists have developed novel tools to study biological function at the molecular level. These tools enabled an intellectual approach to drug development largely centered on the selection of agents that interacted with validated molecular targets for specific diseases. While this approach has resulted in a number of successful drugs, frequently their use is limited by serious side effects.

At Harbor BioSciences, we embrace a systems biology approach to drug development, one that accounts for and leverages the complexity of tissue specific reactions integral to a variety of molecular pathways. Rather than simply blocking or stimulating an isolated target, we are attempting to integrate a number of different scientific disciplines, including molecular biology, high speed computing and engineering, to understand interactions and identify signals that restore homeostasis. There is evidence that dysregulation at the metabolome level can lead to a diverse set of diseases and conditions. Chronic inflammatory processes may be a common link to tissue destruction in diverse diseases such as arthritis, diabetes, HIV, Alzheimer s disease and cancer. All of these conditions may benefit by a blunting of the inflammatory response and the restoration of homeostasis.

Our development strategy is based on the hypothesis that adrenal products are critical to the regulation of the body s complex defense system. We believe that in young, healthy adults, adrenal products such as cortisol, dehydroepiandrosterone (DHEA) and its metabolome, provide important signals that determine whether appropriate cytokines are produced at appropriate times to properly regulate immune responses. Under conditions of stress, chronic infections or systemic inflammation, changes to adrenal products themselves, their metabolism, and perturbations of signaling pathways in peripheral tissues, may drive the growth of certain tumors and be causative to diseases of advancing age, including metabolic syndrome, autoimmune diseases, immune mediated inflammatory disease and an impaired ability to fight infections.

Most drug developers are taking a *ground up* approach, first striving to understand and identify critical components in these intricate cascades, and then trying to design drugs that can successfully block or stimulate specific pathways. In contrast, ours is a *top down* approach, beginning with the discovery of new members of the adrenal steroid metabolome. Then, by applying pharmaceutical development methodology, our goal is to design compounds that modify critical adrenocorticoid endocrine pathways. We believe this approach has the potential to identify product

candidate compounds to treat a myriad of diseases associated with advancing age, including certain cancers, metabolic and autoimmune diseases as well as immune-mediated inflammatory diseases. We believe that successfully applying these principles may have the potential to develop pharmaceuticals to address a number of large and important markets, including many unmet medical needs.

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TECHNOLOGY

Platform

Our primary technology development efforts are focused on a series of adrenal steroid hormones and synthetic analogs that may be useful in treating a wide variety of medical conditions, if successfully developed. These adrenal hormones are depleted during advancing age, a process accelerated by infectious diseases and chronic immune system disorders. High plasma concentrations of these hormones are positively correlated with attenuated disease, in certain indications, and their maintenance is often associated with healthy aging.

The chemistry and biochemistry of steroids have been extensively studied and utilized in the development of various drugs, especially for hormonal imbalance, for the treatment of infections and cancer as well as inflammation. Harbor BioSciences inventory of greater than 700 steroid compounds is a targeted library synthesized under industry standards of medicinal chemistry. The compound library takes existing drug leads and generates neighbors (analogues) of the leads in the chemical space. Many of the compounds are previously undiscovered metabolic products of (DHEA) as well as structurally novel analogues stabilized against additional metabolism. This library is the largest sample of the DHEA metabolome reported and contains many unique chemical structures with diverse biological properties.

The unifying theme of the targeted library is to make drug-like molecules that have unique target recognition characteristics used to derive a structure-activity relationship (SAR) that imparts affinity and selectivity for the selected target. In addition, design features include bioavailability, usually so that the compound can be given orally, metabolic and chemical stability, and with the necessary novelty for patent purposes. Synthesis of active compounds is optimized to be facile and cost-effective with attention to the need for commercialization.

OUR DRUG CANDIDATES IN DEVELOPMENT

We are currently focused on the development of two proprietary synthetic steroid derivatives derived from the human adrenal steroid metabolome. Our lead clinical drug development candidates are APOPTONE (HE3235), currently in clinical trials for late-stage prostate cancer and TRIOLEX (HE3286), with clinical trials conducted for the treatment of obese type 2 diabetes, metabolic and autoimmune disorders. Each of these compounds is described in more detail below. In addition, our research program, focused on the identification and characterization of new adrenal hormones, has identified additional potential, new human hormones that may become future pharmaceutical candidates or nutraceutical products.

APOPTONE (HE3235)

Prostate Cancer

APOPTONE is a second-generation compound we have selected for clinical development in the area of hormone driven cancers, such as prostate cancer. APOPTONE was discovered by screening our proprietary steroid chemical library against a prostate cancer LNCaP cell line. It was selected based on a combination of its potency against cancer and desirable pharmaceutical properties. It has been tested in a number of

preclinical cancer models and has shown indications of activity in controlling the incidence, growth and development of new tumors in these models. We believe that APOPTONE is a disease-modifying agent that may directly induce apoptosis, or cell death, in tumor cells, a result that differs from traditional hormone blockade therapies that interrupt the tumor cell growth signal through direct androgen or estrogen receptor mediated mechanisms. While hormone blockade therapy can effectively control prostate cancer for a period of time, it often fails and the cancer grows again and spreads to other organs, usually the bone.

In 2008, we initiated a Phase I/IIa clinical trial with APOPTONE in late-stage castrate resistant prostate cancer (CRPC) patients who have failed hormone therapy and at least one round of chemotherapy. In December

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2009, the trial was amended to include a group of CRPC patients with progressive disease that have not been previously treated with chemotherapy. The open-label dose ranging clinical trial is being conducted in various clinical sites including some sites within the Prostate Cancer Clinical Trial Consortium (PCCTC). It is evaluating the safety, tolerance, pharmacokinetics and potential activity of APOPTONE when administered twice daily in late-stage prostate cancer patients. Potential activity of the compound is measured by the effect on time to disease progression, as determined by prostate-specific antigen (PSA) blood tests, computerized tomography (CT), magnetic resonance imaging (MRI), or bone scintigraphy, and its effect on circulating tumor cells (CTC). Approximately 234,000 patients are diagnosed each year with prostate cancer, and global sales for leading prostate cancer drugs range approximately from $500 million to $1 billion annually.

Breast Cancer

We are also exploring the potential of APOPTONE in breast cancer. In pre-clinical models of MNU-induced breast cancer, APOPTONE successfully treated established tumors and prevented the formation of new tumors. It appeared to be synergistic when given in combination with concurrent taxane chemotherapy.

APOPTONE Development Status

APOPTONE is manufactured using several organic synthesis steps from the starting material androsterone. The active pharmaceutical ingredient is formulated to an oral dosage form using commonly used excipients in approved (oral dosage) products. Non-clinical toxicology studies have been done that enable the use of APOPTONE in clinical studies in late-stage prostate cancer and breast cancer patients using 28-day cycles of therapy. Encouraging data were reported from an ongoing Phase I/IIa clinical trial for castration resistant prostate cancer (CRPC) also referred to as hormone resistant prostate cancer at the ASCO Genitourinary Cancers Symposium in San Francisco, March 6, 2010. Preliminary results from the study, conducted which included participating member sites of the Prostate Cancer Clinical Trial Consortium (PCCTC), were first reported on November 16, 2009. The phase I/IIa trial is an open-label study with the primary objectives of assessing safety, tolerability, pharmacokinetics and activity of APOPTONE in men with CRPC and an ECOG performance status score of less than or equal to 2 (ambulatory and capable of at least self-care). Patient cohorts are defined by oral daily doses of 10 mg, 20 mg, 30 mg, 50 mg, 100 mg, 200 mg and 350 mg. Subjects are treated on 28-day cycles until toxicity or disease progression; CT and bone scans are obtained every two cycles to assess progression. Based on encouraging signs of activity, the PCCTC recommended an extension of the current trial into patients that have not been treated with chemotherapy. Accordingly, the subject eligibility criteria were amended to include earlier-stage, chemotherapy-naïve patients in a 100 mg expansion cohort and 10 patients have been enrolled to date. As of February 17, 2010, 42 taxane-resistant prostate cancer patients have been entered into the clinical trial at 7 dose levels. Of these 28 (67%) reached their first reassessment (two 28-day cycles), 15 (54%) of these had stable disease on scans or imaging and have received 1-8 additional treatment cycles before disease progression. Six patients continue to receive treatment. The Kaplan-Meier estimate for the median time to progression is 15.3 weeks (range 4-40) for this ongoing trial. The data are essentially complete for the low dose groups. Due to early signs of activity, the 20 mg dose group was expanded to include 14 patients. Eleven of these were evaluable with an actual median time to progression of 20 weeks (range 8-28). Changes in PSA levels were consistent with the properties of this class of agent. The drug has been well tolerated and dose escalation has proceeded to 350 mg per day with no overt dose-limiting toxicities reported. The 350 mg dose group was expanded to include 10 additional pre-chemotherapy patients in order to gain additional information on the tolerability of APOPTONE at this dose level. Several patent applications have been filed for the pharmaceutical formulation of APOPTONE and its use for the treatment of prostate cancer, breast cancer and benign prostate hypertrophy.

Competition

Taxotere chemotherapy is presently the only approved therapy to treat castrate resistant prostate cancer. Despite current treatments, there is an ongoing need for novel oral agents that can control the growth of prostate

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cancer that is progressing on conventional therapies or hormone treatments. Accordingly, there are a number of companies with drug candidates in development targeting late-stage castration resistant prostate cancer, including compounds already in Phase III clinical trials. Abiraterone produced by Cougar Biotechnology, Inc. is an agent that impedes the synthesis of androgens by inhibition of an enzyme that transforms precursor molecules into the hormone testosterone. Many forms of prostate cancer are dependent on the presence of androgens in order to grow. MDV-3100, produced by Medivation, Inc., is an agent that blocks the action of androgens on prostate cancer cells through interference at the androgen receptor and stopping their growth. Provenge, produced by Dendreon, Inc., is an autologous immune cell therapy that primes the patients cells against prostate cancer cells. All three of these therapies are in late stage clinical and regulatory development. Apoptone is believed to be a disease modification agent with a mechanism of action that distinguishes it from these competitive drug candidates.

TRIOLEX (HE3286)

Inflammatory Processes in Chronic Diseases

One of our primary focus areas is diseases of chronic inflammation. Properly regulated, inflammation is a protective, life saving response to invading pathogens. However, when inflammation goes awry and becomes chronic, it can cause devastating tissue damage and loss of organ function. Chronic inflammation is associated with an over-stimulation of the immune system, often resulting in the release of destructive products such as reactive oxygen species, destructive enzymes and other pro-inflammatory mediators. The over-production of these dangerous products is often due to persistent low-grade infections, aging and the body s inability to differentiate between itself and foreign invaders. Chronic inflammation has been implicated in the pathogenesis of many diseases ranging from autoimmune conditions, such as arthritis and psoriasis, to infectious diseases, including human immunodeficiency virus (HIV), malaria and tuberculosis, and to metabolic diseases, including diabetes and cardiovascular diseases as well as a number of different cancer types.

Current Treatments for Chronic Inflammation

Some of the most widely used drugs for reducing inflammation belong to the corticosteroid class of compounds, which are also derived from the adrenal metabolom. Market research indicates that U.S. physicians issue tens of millions of new prescriptions for corticosteroids each year for a wide range of conditions. While these drugs are highly effective, chronic use leads to immune suppression and other serious side effects including bone loss.

Over the last decade, a number of new drugs have been introduced that are focused on inhibiting a specific component of the pro-inflammatory cascade, including agents that block specific inflammatory cytokines, such as TNF-alpha and IL-1 beta, as well as drugs that inhibit specific enzymes, such as COX-2, that produce pro-inflammatory mediators. While these drugs have demonstrated significant activity in a number of clinical trials involving chronic inflammatory diseases, such as arthritis, inflammatory bowel disease and psoriasis, most have also demonstrated significant limitations. Many cause dangerous immune suppression and other serious side effects that limit usage. Most focus on one specific mediator of inflammation, which means they may not remain effective and are vulnerable to redundancies in biological pathways. Our goal is to develop compounds that provide appropriate regulatory signals at multiple levels to regain control of the inflammatory process and restore homeostasis.

Diabetes, Insulin Resistance, and Chronic Inflammation

Diabetes is a disease of insulin signaling that is comprised of a constellation of syndromes. Insulin is a hormone needed to move glucose from the blood into cells, where it can be stored, or converted to the energy needed to perform properly. When insulin is not present in sufficient quantity or when signaling pathways do not function correctly, the result is high levels of glucose in the blood. Over time, chronically-elevated blood glucose can lead to a host of severe medical conditions including nerve disease, blindness, limb amputation, heart attack,

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stroke and death. There are two forms of diabetes: type 1, a chronic condition in which little or no insulin is produced, and type 2, a condition in which the body becomes resistant to the effects of insulin or the body produces some, but not enough, insulin to maintain a normal blood sugar level.

Epidemiological studies have clearly defined risk factors for the development or progression of type 2 diabetes, including genetics, and prenatal and postnatal environmental factors, including low birth weight, obesity, nutrient excess, inactivity, gestational diabetes and advancing age. Each of these risk factors can, *via* largely undefined mechanisms, lead to insulin resistance, beta-cell dysfunction and overt diabetes. In turn, diabetes-related hyperglycemia and associated metabolic abnormalities can further alter signal transduction and gene-expression thus contributing to a vicious cycle. It is likely that each of these risk factors alter gene expression, possibly in a unique but partly overlapping way. Therefore, superimposition of multiple risk-related and tissue-specific changes in gene expression are required to produce the phenotype of type 2 diabetes.

The need for new classes of agents to treat type 2 diabetes is significant. There are over 22 million Americans with type 2 diabetes and over 170 million type 2 diabetics worldwide. Obese diabetes is a syndrome that is increasing rapidly as a result of advancing age and the rising incidence of obesity. Clinical data indicates only 36% of type 2 diabetics are currently able to maintain the American Diabetes Association maximum recommended HbA1c, (a form of hemoglobin that is primarily used to identify the average plasma glucose concentration over a prolonged period of time), glucose level of less than 7.0 %. Large clinical studies have shown that failure to achieve these glucose targets, especially in obese patients, can progressively lead to severe health consequences including neuropathy, blindness, amputation, heart attack, stroke and death. Patients in large clinical trials consistently have a median BMI of 32 indicating that over half the population of T2DM is obese.

Academic researchers have increasingly linked obesity-induced chronic inflammation with type 2 diabetes and elucidated its potential role in leading to insulin resistance in type 2 diabetes. In the setting of type 2 diabetes, evidence suggests that the pathology may arise through perturbations in NF-kappaB signaling, particularly *via* the TLR4 receptor. TLR4 is a receptor expressed on the surface of macrophages and other cells and is stimulated by certain pathogens such as bacteria and viruses or certain substances such as dietary fatty acids. Stimulation of the TLR4 receptor induces a cascade of pro-inflammatory signals, which in turn, results in activation events that set a complex network of signaling pathways in motion, which culminates with the activation of NF-kappaB and a number of genes under its control that are involved in the inflammatory and cellular stress response. Persistent stimulation can lead to the chronic inflammatory state and associated pathologies.

The development of widely effective agents to treat type 2 diabetes has been difficult because of heterogeneity in the underlying causes of the disease. Advances in genomic, proteomic and metabolomic sciences over the last decade, however, have led to the development of targeted diagnostics and therapeutics. These leverage knowledge of an individual s genetic makeup to create a more personalized approach to healthcare. Genomic testing enables identification of an individual s susceptibility to disease, predict how a given patient will respond to a particular drug, and match patients with the right therapeutics. This new science of personalized medicine has the potential to improve the design of clinical trials, eliminate unnecessary treatments, reduce the incidence of adverse reactions to drugs, increase the efficacy of treatments and through identifying the right drug for the right patient, ultimately improves health outcomes.

Current Treatments for Type 2 Diabetes

There are several pharmaceutical approaches to treating type 2 diabetes. These include drugs designed to increase insulin production by the pancreas, reduce glucose production by the liver, and drugs, referred to as insulin sensitizers, designed to increase the body s sensitivity to insulin, thereby improving glucose disposal from the bloodstream. Metformin is usually the first intervention prescribed by physicians when an individual is diagnosed with type 2 diabetes. Frequently clinicians will combine drugs that have different mechanistic approaches to controlling the diabetes in an effort to achieve appropriate glucose control.

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TRIOLEX to Treat Chronic Inflammation in Type 2 Diabetes

TRIOLEX is a next-generation compound that we are developing for the treatment of individuals diagnosed with certain chronic inflammatory processes.

In the setting of type 2 diabetes, evidence suggests that the mechanism of action for TRIOLEX may be through the regulation of the NF-kappaB pathway, particularly when it s stimulated through the TLR4 receptor. TRIOLEX may be the first in a new class of insulin sensitizers to target obesity-mediated dysregulated metabolism. This is a major component of the type 2 diabetes syndrome that is characterized by the presence of a chronic inflammatory state. Through regulation of the NF-kappaB pathway, our scientists believe potential mechanisms of action for TRIOLEX involve control of genes whose products are involved in the inflammatory signaling pathway including TNF-alpha and IL-6. These cytokines are also thought to be critically involved in the pathogenesis of certain autoimmune diseases such as ulcerative colitis and rheumatoid arthritis, and are also implicated in the pathogenesis of metabolic diseases such as non-alcoholic steatohepatitis, cardiovascular disorders, cancer and in general, diseases associated with advancing age.

Based on biochemical experiments, we believe TRIOLEX action on the NF-kappaB pathway is independent of the PPAR-gamma pathway targeted by other insulin sensitizers. Instead, the action of TRIOLEX is associated with a downregulation of pro-inflammatory JNK, IKK and p38 kinase pathways. Chronic activation of these kinase pathways lead to impairment of the insulin receptor substrate-1 protein (IRS-1) function, an important cellular mediator of insulin signaling.

A single-dose Phase I clinical trial conducted during 2007 demonstrated that TRIOLEX is orally bioavailable in humans, with significant drug concentrations detected in the blood at the lowest dose tested. The findings also showed that all doses of TRIOLEX tested appear to be safe and well tolerated in healthy volunteers with no reported drug related serious adverse side effects to date.

A Phase I/II double-blind, placebo-controlled, multi-dose ranging clinical trial with TRIOLEX in obese insulin-resistant subjects was initiated in 2007 and evaluated the safety, tolerance and pharmacokinetics of TRIOLEX when administered for 28 days to obese adult subjects. The potential activity of TRIOLEX to decrease insulin resistance was assessed. In addition, an open-label cohort of six patients with type 2 diabetes mellitus was studied. TRIOLEX was found to be safe and increased insulin sensitivity in insulin resistant subjects.

During 2008, a Phase IIa clinical trial was initiated with TRIOLEX in type 2 diabetes patients that proceeded in two stages. Stage 1 of this double-blinded placebo controlled 12-week dosing trial was exploratory in nature and enrolled 96 patients who were on a stable dose of metformin with hemoglobin A1c (HbA1c) level in excess of 7.5 percent. The primary objectives of this trial were to evaluate the change in HbA1c from baseline to week 12 and to evaluate the safety and tolerance of TRIOLEX given 10 mg per day (5 mg BID) as compared to placebo. A final analysis of activity (HbA1c) in the clinical study of unaudited data was performed on all subjects that completed dosing on day 84 of the study (72 patients). There was no statistical difference between treatment and placebo for HbA1c in the overall patient population.

A retrospective analysis of unaudited data was performed on the subpopulation of patients that represent the inflamed, obese, insulin-resistant, diabetic population. This group is reflective of the impaired glucose tolerance subjects that responded to treatment in the company s Phase I study. This analysis included patients who met the following criteria at baseline: BMI greater than or equal to 28; fasting plasma insulin levels greater than or equal to 4 μU/mL; fasting plasma C-peptide levels greater than or equal to 2 ng/mL; and serum monocyte chemotactic protein-1 (MCP-1) levels greater than or equal to 400 pg/mL. This phenotype represented 35% of all subjects (89 patients) with values for these parameters at baseline. Twenty-two individuals with this phenotype completed the 84 days of dosing. Those treated with TRIOLEX (10 patients) were found to show improvements in clinical parameters compared to placebo patients (12 patients). These included statistical trends for a

decrease in HbA1c (-0.53%, $p = 0.06$) and a decrease in fasting plasma glucose (-28.75 mg/dL, $p = 0.09$), as well as non-significant

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decreases in fasting plasma C-peptide (-0.43 ng/mL), fasting plasma insulin (0.48 µU/mL), fructosamine (25.75 µmol/L), HOMA2 insulin resistance (0.65 IR), and increases in HOMA2 insulin sensitivity (11.3 %S) and HOMA2 beta cell function (17.95 %B). The observed changes in these secondary indicators of activity are all consistent with the observed decreases in HbA1c and glucose in this diabetic subpopulation.

Sensitivity analysis using last observation carried forward indicated that individuals in this subpopulation who completed at least 29 days of dosing showed improvement. A biostatistician who is an expert in analyzing data from type 2 diabetes clinical trials independently confirmed these results.

Stage 2 of the Phase IIa clinical trial was designed to be confirmatory of the HbA1c activity and is presently in progress. Overall Triolex has a good safety profile with no consistent pattern of adverse events associated with its use. The side effects associated with the use of currently approved thiazolidenedione insulin sensitizers, have not been observed with TRIOLEX.

Competition in Diabetes

Given the large market opportunities for products that treat the indications for which we are currently developing our compounds, most major pharmaceutical companies and many biotechnology companies have programs directed toward finding drugs to treat the indications that we are exploring and the competition in these markets is intense. In metabolism and type 2 diabetes, there are a number of drugs, such as Actos® from Takeda Pharmaceuticals and Avandia® from GlaxoSmithKline (already approved for improving insulin sensitivity), glucagon-like peptide-1 (such as Victoza by Novo Nordisk), dipeptidyl peptidase-4 inhibitors (such as Januvia by Merck and Onglyza by Bristol Myers Squibb) and numerous other drugs in various stages of development. While Actos® and Avandia® currently account for a significant share of the market for insulin sensitizers to treat type 2 diabetes, they are known to cause the unwanted side effects of weight gain and edema. In addition, both have been given black box warnings by the FDA because of increased risk of treatment-related heart failure.

Autoimmune Disease and Chronic Inflammation

Current Treatments for Autoimmune Diseases

Immune modulators that correct immune dysregulation and chronic inflammatory conditions by inhibition or enhancement of single cytokine targets such as TNF alpha and IL-1 beta or their receptors have been developed by a number of companies. For example, Amgen s Enbrel® targets TNF-alpha, as does Johnson & Johnson s Remicade®. Other immune-modulating drugs such as Celebrex from Pfizer target COX-2. While these targeted approaches have shown clinical benefit and have generated significant sales volumes, redundancy in the immune system can limit their effectiveness. In addition, side effects, health care costs and reimbursement issues may limit their long-term global utility. In contrast, we believe our compounds may affect cytokine cascades through direct interactions in the endocrine system. This may make them more attractive drug candidates than those currently available, assuming they are successfully developed and commercialized.

Rheumatoid Arthritis

Rheumatoid arthritis is a type of chronic arthritis that occurs in joints on both sides of the body (such as hands, wrists or knees). In rheumatoid arthritis, the immune system attacks the joints and sometimes other organs. According to the Centers for Disease Control and Prevention, or (CDCP), an estimated 46 million people were treated for some form of arthritis and other rheumatic conditions in 2003, the latest year for which data is available, and an estimated 8 million more people will suffer from arthritis between 2005 and 2015.

Based upon the published studies in rodent models of collagen-induced and collagen antibody-induced arthritis where TRIOLEX demonstrated activity, a Phase I clinical trial was initiated with TRIOLEX in 2008 in rheumatoid arthritis patients. A 28-day oral dose ranging study assessed the safety, pharmacokinetics and

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potential for drug-drug interactions in stable rheumatoid arthritis patients also receiving methotrexate. TRIOLEX was found to be safe and well tolerated. No drug-drug interaction was found. TRIOLEX is now positioned to enter clinical studies in patients with active rheumatoid arthritis.

Ulcerative Colitis

Inflammatory bowel disease is comprised of ulcerative colitis, a chronic inflammation of the large intestine, or colon, and Crohn s disease, a condition of inflammation of the small intestines. Ulcerative colitis and Crohn s disease together affect approximately 500,000 to 2 million people in the United States.

Based upon published observations with TRIOLEX in preclinical models widely used by the pharmaceutical industry and academia to test agents as potential treatments for ulcerative colitis, in 2008, we commenced a Phase I/II clinical trial with TRIOLEX in ulcerative colitis patients. This Phase I/II dose ranging study evaluated the safety, tolerance, pharmacokinetics and activity of TRIOLEX when administered orally for 28 days to patients with active, mild-to-moderate ulcerative colitis. TRIOLEX at the doses studied was found to be safe and well tolerated but offered no indication of a treatment advantage in this acute inflammatory setting when compared to placebo. Triolex is staged for long-term clinical trials directed towards the control of the chronic inflammatory processes associated with this disease, a clinical setting believed to be consistent with the pharmacological properties of the compound.

Pulmonary Diseases and other Autoimmune Diseases

The Company is also interested in exploring the potential for TRIOLEX and other new compounds from our technology platform in a variety of pulmonary diseases including, cystic fibrosis, chronic pulmonary disease and asthma. In addition TRIOLEX has shown utility in pre-clinical models of multiple sclerosis and lupus erythematosus.

Triolex Development Status

TRIOLEX is manufactured economically using a multi-step organic synthesis from the widely abundant and inexpensive starting material, DHEA. It is formulated for oral administration with commonly used excipients in approved (oral dosage) products. Long term toxicology studies have been completed that qualify TRIOLEX for use in clinical studies of 6 months duration or longer. Diseases associated with chronic inflammation are thought to require drug exposures of extended duration to observe definitive treatment effects. Patent applications have been filed for the composition, pharmaceutical formulations and methods of use to treat a variety of inflammatory diseases including type 2 diabetes and autoimmune conditions such as rheumatoid arthritis and ulcerative colitis.

Government Regulation

General

The manufacturing and marketing of our proposed drug candidates and our research and development activities are, and will continue to be, subject to regulation by federal, state and local governmental authorities in the U.S. and other countries. In the U.S., pharmaceuticals are subject to rigorous regulation by the Food and Drug Administration, (FDA), which reviews and approves the marketing of drugs. The Federal Food, Drug and Cosmetic Act, the regulations promulgated thereunder, and other federal and state statutes and regulations govern, among other things, the testing, manufacturing, labeling, storage, record keeping, advertising and promotion of our potential products.

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Approval Process

The process of obtaining FDA approval for a new drug may take many years and generally involves the expenditure of substantial resources. The steps required before a new drug can be produced and marketed for human use include clinical trials and the approval of a New Drug Application.

Preclinical Testing. In the preclinical phase of development, the promising compound is subjected to extensive laboratory and animal testing to determine if the compound is biologically active and safe.

Investigational New Drug, or IND. Before human tests can start, the drug sponsor must file an IND application with the FDA, showing how the drug is made and the results of animal testing. An IND becomes effective 30 days following receipt by the FDA.

Human Clinical Testing. The human clinical testing program usually involves three phases which generally are conducted sequentially, but which, particularly in the case of anti-cancer and other life-saving drugs, may overlap or be combined. Clinical trials are conducted in accordance with protocols that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Each protocol is submitted to the FDA as part of the IND filing. Each clinical study is conducted under the auspices of an independent Institutional Review Board, or IRB, for each institution at which the study will be conducted. The IRB will consider, among other things, the design of the clinical trial, ethical factors, the risk to human subjects and the potential benefits of therapy relative to risk.

In Phase I clinical trials, studies usually are conducted on healthy volunteers or, in the case of certain terminal illnesses such as AIDS or cancer, patients with disease that has failed to respond to other treatment, to determine the maximum tolerated dose, side effects and pharmacokinetics of a product. Phase II studies are conducted on a small number of patients having a specific disease to determine initial efficacy in humans for that specific disease, the most effective doses and schedules of administration, and possible adverse effects and safety risks. Phase II/III differs from Phase II in that the trials involved may include more patients and, at the sole discretion of the FDA, be considered the pivotal trials, or trials that will form the basis for FDA approval. Phase III normally involves the pivotal trials of a drug, consisting of wide-scale studies on patients with the same disease, in order to evaluate the overall benefits and risks of the drug for the treated disease compared with other available therapies. The FDA continually reviews the clinical trial plans and results and may suggest design changes or may discontinue the trials at any time if significant safety or other issues arise.

New Drug Application, or NDA. Upon successful completion of Phase III clinical trials, the drug sponsor files an NDA with the FDA for approval containing all information that has been gathered. The NDA must include the chemical composition of the drug, manufacturing and production details, nonclinical data, results of human tests, and proposed labeling.

The testing and approval process is likely to require substantial time, from several months to years, and there can be no assurance that any FDA approval will be granted on a timely basis, if at all. The approval process is affected by a number of factors, primarily the side effects of the drug (safety) and its therapeutic benefits (efficacy). Additional preclinical or clinical trials may be required during the FDA review period and may delay marketing approval. The FDA may also deny an NDA if applicable regulatory criteria are not met.

Outside the U.S., we will be subject to foreign regulatory requirements governing human clinical trials and marketing approval for our products. The requirements governing human clinical trials ex-US usually follow ICH cGCP or country-specific cGCPs which are based on the ICH

cGCPs. Regulatory approval outside the U.S. typically includes the risks and costs associated with obtaining FDA approval but may also include additional risks and costs.

Post Approval. If the FDA approves an NDA, the drug sponsor is required to submit reports periodically to the FDA containing adverse reactions, production, quality control and distribution records. The FDA may also

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require post-marketing testing to support the conclusion of efficacy and safety of the product, which can involve significant expense. After FDA approval is obtained for initial indications, further clinical trials may be necessary to gain approval for the use of the product for additional indications.

Manufacturing

We do not have, and do not intend to establish, manufacturing facilities to produce our drug candidates or any future products. We plan to control our capital expenditures by using contract manufacturers to make our products. We believe that there are a sufficient number of high-quality FDA-approved contract manufacturers available, and we have had discussions, and in some cases established relationships, to fulfill our near-term production needs for both clinical and commercial use.

The manufacture of our drug candidates or any future products, whether done by outside contractors as planned or internally, will be subject to rigorous regulations, including the need to comply with the FDA s current Good Manufacturing Practice regulations. As part of obtaining FDA approval for each product, each of the manufacturing facilities must be inspected, approved by and registered with the FDA. In addition to obtaining FDA approval of the prospective manufacturer s quality control and manufacturing procedures, domestic and foreign manufacturing facilities are subject to periodic inspection by the FDA and/or foreign regulatory authorities.

Patents

We currently own or have obtained licenses to a number of U.S. and foreign patents and patent applications. We consider the protection of our technology, whether owned or licensed, to the exclusion of use by others, to be vital to our business. While we intend to focus primarily on patented or patentable technology, we may also rely on trade secrets, unpatented property, know-how, regulatory exclusivity, patent extensions and continuing technological innovation to develop our competitive position. In the U.S. and certain foreign countries, the exclusivity period provided by patents covering pharmaceutical products may be extended by a portion of the time required to obtain regulatory approval for a product.

In certain countries, some pharmaceutical-related technology such as disease treatment methods are not patentable or only recently have become patentable, and enforcement of intellectual property rights in many countries has been limited or non-existent. Future enforcement of patents and proprietary rights in many countries can be expected to be problematic or unpredictable. We cannot guarantee that any patents issued or licensed to us will provide us with competitive advantages or will not be challenged by others. Furthermore, we cannot be certain that others will not independently develop similar products or will not design around patents issued or licensed to us.

In most cases, patent applications in the U.S. are maintained in secrecy until 18 months after the earliest filing or priority date. Publication of discoveries in the scientific or patent literature, if made, tends to lag behind actual discoveries by at least several months. U.S. patent applicants can elect to prevent publication until the application issues by agreeing not to file the application outside the U.S. This option is rarely used for pharmaceutical patent applications. Consequently, we cannot be certain that a patent owner or licensor of its intellectual property was the first to invent the technology or compounds covered by pending patent applications or issued patents or that it was the first to file patent applications for such inventions. In addition, the patent positions of biotechnology and pharmaceutical companies, including our own, are generally uncertain, partly because they involve complex legal and factual questions.

In addition to the considerations discussed above, companies that obtain patents claiming products, uses or processes that are necessary for, or useful to, the development of our drug candidates or future products could bring legal actions against us claiming infringement. Patent litigation is typically costly and time consuming, and if such an action were brought against us, it could result in significant cost and diversion of our attention. We

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may be required to obtain licenses to other patents or proprietary rights, and we cannot guarantee that licenses would be made available on terms acceptable to us. If we do not obtain such licenses, we could encounter delays in product market introductions while we attempt to develop or license technology designed around such patents, or we could find that the development, manufacture or sale of products requiring such licenses is foreclosed.

Further, we cannot guarantee that patents that are issued will not be challenged, invalidated or infringed upon or designed around by others, or that the claims contained in such patents will not interfere with the patent claims of others, or provide us with significant protection against competitive products, or otherwise be commercially valuable. To the extent that we are unable to obtain patent protection for our products or technology, our business may be materially adversely affected by competitors who develop substantially equivalent technology.

For a discussion of the risks associated with patent and proprietary rights, see below under Item 1A Risk Factors .

Technology Agreements

In August 2002, we entered into a Sublicense Agreement with Pharmadigm, Inc. (currently known as Inflabloc Pharmaceuticals, Inc.). Under the agreement, we obtained exclusive worldwide rights to certain intellectual property of Pharmadigm and the University of Utah and we agreed to make aggregate payments of $0.9 million in cash or in shares of our common stock, at our option, over the next year. We elected to make such payments in equity and have issued a total of 168,921 shares of our common stock in complete satisfaction of this requirement. We will also make additional milestone and royalty payments to Pharmadigm if we meet specified development and commercialization milestones for products covered by the patents. No such milestones have been met to date. The principal patents licensed under the agreement, originally licensed to Pharmadigm from the University of Utah, relate to inventions by Dr. Raymond Daynes and Dr. Barbara A. Areneo. Dr. Daynes served as a scientific consultant for us from 1999 to mid-2003.

In October 2000, we acquired a 21% equity stake in Aeson Therapeutics Inc. (Aeson) and an exclusive worldwide sublicense to three issued patents in the area of adrenal steroids in exchange for $2.0 million in cash and 208,672 shares of our common stock valued at $2 million. As part of the transaction, Aeson and its stockholders granted us an exclusive option to acquire the remainder of Aeson at a predetermined price. In March 2002, we amended certain aspects of our agreements with Aeson. Under the amendments, we paid Aeson $1.2 million, which extended the initial date by which we could exercise our option to acquire the remainder of Aeson to September 30, 2002. We also received additional equity securities of Aeson as a result of this payment. We elected not to exercise the option to acquire the remainder of Aeson by September 30, 2002. On June 7, 2006, we acquired substantially all of the assets of Aeson. As consideration for Aeson s assets, we agreed (i) to issue a total of 35,000 shares of our common stock to Aeson at the closing of the acquisition and (ii) to issue to Aeson s stockholders up to a total of 165,000 additional shares of our common stock if certain development milestones are achieved. We have not achieved any of the development milestones to date.

Employees

As of March 27, 2010, we had 19 full-time equivalent, non-union employees. We believe that our relations with our employees are good.

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Executive Officers and Senior Management

Our executive officers and senior management and their ages as of March 27, 2010 are as follows:

Name	Age	Position
James M. Frincke, Ph.D.	59	Chief Executive Officer
Christopher L. Reading, Ph.D.	62	Chief Scientific Officer
Dwight R. Stickney, M.D.	67	Chief Medical Officer
Robert W. Weber	59	Chief Financial Officer and Secretary

James M. Frincke, Ph.D. joined Harbor BioSciences, Inc., as Vice President, Research and Development in November 1997, was promoted to Executive Vice President in March 1999, to Chief Scientific Officer in December 2001, to Chief Operating Officer in February 2008 and to Chief Executive Officer in 2009. Dr. Frincke joined Harbor BioSciences, Inc. from Prolinx, Inc., where he served as Vice President, Therapeutics Research and Development from 1995 to 1997. During his 29 years in the biotechnology industry, Dr. Frincke has managed major development programs including drugs, biologicals, and cellular and gene therapy products aimed at the treatment of cancer, infectious diseases, organ transplantation, autoimmune disease and type 2 diabetes. Since joining the biotechnology industry, Dr. Frincke has held vice president, research and development positions in top tier biotechnology companies including Hybritech/Eli Lilly and SyStemix Inc. (acquired by Novartis). In various capacities, he has been responsible for all aspects of pharmaceutical development including early stage research programs, product evaluation, pharmacology, manufacturing, and the management of regulatory and clinical matters for lead product opportunities. Dr. Frincke has authored or co-authored more than 100 scientific articles, abstracts and regulatory filings. Dr. Frincke received his B.S. in Chemistry and his Ph.D. in Chemistry from the University of California, Davis. Dr. Frincke performed his postdoctoral work at the University of California, San Diego.

Christopher L. Reading, Ph.D. became Vice President of Scientific Development in January 1999, was promoted to Executive Vice President, Scientific Development in March 2002 and to Chief Scientific Officer in February 2008. Before Harbor BioSciences, Inc., Dr. Reading was Vice President of Product and Process Development at Novartis Inc.-owned SyStemix Inc. During this time, he successfully filed three investigational new drug applications (INDs) in the areas of stem cell therapy technology and stem cell gene therapy for HIV/AIDS. Prior to joining SyStemix, Dr. Reading served on the faculty of the M.D. Anderson Cancer Center in Houston for nearly 13 years. His positions there included Associate and Assistant Professor of Medicine in the Departments of Hematology and Tumor Biology. During his career, Dr. Reading has given more than 25 national and international scientific presentations, published more than 100 peer-reviewed journal articles and 15 invited journal articles as well as written nearly 20 book chapters, and received numerous grants and contracts which supported his research activities. Dr. Reading has served on the National Science Foundation Advisory Committee for Small Business Innovative Research Grants (SBIR) as well as on the editorial boards of *Journal of Biological Response Modifiers* and *Molecular Biotherapy*. He holds a number of patents for his work with monoclonal antibodies and devices. Dr. Reading received his Ph.D. in Biochemistry at the University of California at Berkeley and completed postdoctoral study in tumor biology at The University of California at Irvine. He earned his B.A. in cell biology at the University of California at San Diego.

Dwight R. Stickney, M.D. joined Harbor BioSciences, Inc., as Medical Director, Oncology in May 2000, was appointed Vice President, Medical Affairs in March 2003 and was promoted to Chief Medical Officer in February 2008. Dr. Stickney joined Harbor BioSciences, Inc. from the Radiation Oncology Division of Radiological Associates of Sacramento Medical Group, Inc., in Sacramento, California, where he served as a Radiation Oncologist since 1993. While at Radiological Associates, he served as Chairman of the Radiation Oncology Division from 1997 to 1999 and was a member of the Radiation Study section of the National Institute of Health s Division of Research Grants from 1993 to 1997. He also served as the Director of Radiation Research for Scripps Clinic and Research Foundation in La Jolla, California. Dr. Stickney has taught in medical academia as Associate Professor of Radiation Medicine at Loma Linda University School of Medicine and has served as

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Director of the International Order of Forresters Cancer Research Laboratory and on the Board of Directors of the California Division of the American Cancer Society. Earlier in his career, Dr. Stickney held positions with Burroughs Wellcome and the Centers for Disease Control, and academic teaching appointments at The University of California at Los Angeles and The University of California at Riverside. He has also served as a consultant for a number of biotechnology companies on the design and conduct of clinical trials. Dr. Stickney has authored or co-authored over 80 scientific articles, abstracts and book chapters. He is named inventor on numerous issued patents and patent applications. Dr. Stickney holds a Bachelor of Science in Microbiology, a Masters of Science in Immunology, and a M.D. from Ohio State University. In addition, he is certified as a Diplomat of the American Board of Internal Medicine and Hematology and a Diplomat of the American Board of Radiology, Therapeutic Radiology.

Robert W. Weber joined Harbor BioSciences, Inc., in March 1996 and currently serves as the Chief Financial Officer and Secretary. Mr. Weber has over thirty years of experience in financial management. He has been employed at executive levels by multiple start-up companies and contributed to the success of several turnaround situations. He previously served as Vice President of Finance at Prometheus Products, a subsidiary of Sierra Semiconductor (now PMC Sierra), from 1994 to 1996, and Vice President Finance and Chief Financial Officer for Amercom, a personal computer telecommunications software publishing company, from 1993 to 1994. From February 1988 to August 1993, Mr. Weber served as Vice President Finance and Chief Financial Officer of Instromedix, a company that develops and markets medical devices and software. Mr. Weber brings a broad and expert knowledge of many aspects of financial management. In various capacities, he has been responsible for all aspects of finance and accounting including cost accounting, cash management, SEC filings, treasury, investor relations, private and venture financing, corporate legal matters, acquisitions/divestitures as well as information technology, human resources and facilities. Mr. Weber received a B.S. from GMI Institute of Technology (now Kettering University) and a MBA from the Stanford Graduate School of Business.

Item 1A. Risk Factors

In evaluating our business, you should consider the following discussion of risks, in addition to other information contained in this Annual Report on Form 10-K, as well as our other public filings with the Securities and Exchange Commission. Any of the following risks could materially adversely affect our business, financial condition, results of operations and prospects and, as a result, the market price of our common stock could decline, and you may lose all or part of the money you paid to buy our common stock.

We are still a development stage company.

We have never had any revenues from sales of products. None of our drug candidates has been approved for commercial sale and we do not expect that any of our present or future drug candidates will be commercially available for a number of years, if at all. We have incurred losses since our inception and we expect to continue to incur significant additional operating losses for the foreseeable future as we fund clinical trials and other expenses in support of regulatory approval of our drug candidates.

If we do not obtain government regulatory approval for our products, we cannot sell our products and we will not generate revenues.

Our principal development efforts are currently centered around a proprietary class of small compounds that we believe shows promise for the treatment of several diseases and disorders. However, all drug candidates require approval by the U.S. Food and Drug Administration (FDA) before they can be commercialized in the United States as well as approval by various foreign government agencies before they can be commercialized in other countries. These regulations change from time to time and new regulations may be adopted. While limited clinical trials of our drug candidates have been conducted to date, significant additional trials are required, and we may not be able to demonstrate that our drug candidates are safe or effective. In addition, success in early development does not mean that later development will be successful because,

for example, drug candidates in

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later-stage clinical trials may fail to demonstrate sufficient safety and efficacy despite having progressed through initial clinical testing. Our clinical experience with our drug candidates is limited, and to date our drug candidates have been tested in less than the number of patients that will likely need to be studied to gain regulatory approval. The data collected from clinical trials with larger patient populations may not demonstrate sufficient safety and efficacy to support regulatory approval of these drug candidates. In addition, we do not know whether early results from any of our ongoing clinical trials will be predictive of final results of any such trial. If we are unable to demonstrate the safety and effectiveness of a particular drug candidate to the satisfaction of regulatory authorities, the drug candidate will not obtain required government approval and we will experience potentially significant delays in, or be required to abandon, development of the drug candidate. If we do not receive FDA or foreign approvals for our drug candidates, we will not be able to sell products and will not generate revenues. If we receive regulatory approval of one of our drug candidates, such approval may impose limitations on the indicated uses for which we may market the resulting product, which may limit our ability to generate significant revenues. Further, U.S. or foreign regulatory agencies could change existing, or promulgate new, regulations at any time, which may affect our ability to obtain approval of our drug candidates or require significant additional costs to obtain such approvals. In addition, if regulatory authorities determine that we or a partner conducting research and development activities on our behalf have not complied with regulations in the research and development of one of our drug candidates, then they may not approve the drug candidate and we will not be able to market and sell it. If we were unable to market and sell our drug candidates, our business and results of operations would be materially and adversely affected.

Recent publicity concerning the safety of certain drug products has resulted in heightened scrutiny by the FDA in the process of approving new drugs, which could delay or limit any regulatory approvals we may obtain for our drug candidates.

In light of widely publicized events concerning the safety risk of certain drug products, the FDA, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products after approval. In addition, the Food and Drug Administration Amendments Act of 2007, or FDAAA, grants significant expanded authority to the FDA, much of which is aimed at improving the safety of drug products before and after approval. In particular, the new law authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require risk evaluation and mitigation strategies for certain drugs, including certain currently approved drugs. It also significantly expands the federal government s clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FDAAA, companies that violate these and other provisions of the new law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties. The increased attention to drug safety issues may result in a more cautious approach by the FDA in its review of data from our clinical trials. Data from clinical trials may receive greater scrutiny, particularly with respect to safety, which may make the FDA or other regulatory authorities more likely to require additional preclinical studies or clinical trials by drug development companies. As a result, the FDA may require us to conduct additional preclinical studies or clinical trials during the clinical development of one or more of our drug candidates as a condition precedent to approval which could potentially delay our development plans, limit the indications for which our drug candidates are ultimately approved, and otherwise adversely impact us.

If we do not successfully commercialize our products, we may never achieve profitability.

We have experienced significant operating losses to date because of the substantial expenses we have incurred to acquire and fund development of our drug candidates. We have never had significant operating revenues and have never commercially introduced a product. Our accumulated deficit was approximately $251.8 million as of December 31, 2009. Our net losses for fiscal years 2009, 2008 and 2007 were approximately $15.6 million, $21.6 million and $23.1 million, respectively. Many of our research and development programs are at an

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early stage. Potential drug candidates are subject to inherent risks of failure. These risks include the possibilities that no drug candidate will be found safe or effective, meet applicable regulatory standards or receive the necessary regulatory clearances. Even if we were ultimately to receive regulatory approval for one or more of our drug candidates, we may be unable to commercialize them successfully for a variety of reasons. These include, for example, the availability of alternative treatments, lack of cost effectiveness, the cost of manufacturing the product on a commercial scale, the effect of competition with other drugs, or because we may have inadequate financial or other resources to pursue one or more of our drug candidates through commercialization. If we are unable to develop safe, commercially viable drugs, we may never achieve profitability. If we become profitable, we may not remain profitable.

As a result of our intensely competitive industry, we may not gain enough market share to be profitable.