VistaGen Therapeutics, Inc.
Form 10-K
July 18, 2013

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: March 31, 2013

or

[ ] Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Commission file number: 000-54014

VISTAGEN THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Nevada	20-5093315
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

384 Oyster Point Boulevard, No. 8
South San Francisco, California 94080
(650) 244-9990
(Address, including zip code, and telephone number, including area code, of registrant's principal executive office)

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

None

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

Common Stock, par value $0.001 per share

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 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 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 [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 [X] 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 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. [ ]

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 [ ] (Do not check if a smaller reporting company)	Smaller reporting company [ ]

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

The aggregate market value of the common stock of the registrant held by non-affiliates of the registrant on September 30, 2012, the last business day of the registrant’s second fiscal quarter was: $8,317,414.

As of July 12, 2013 there were 21,265,967 shares of the registrant’s common stock outstanding.

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Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K report contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as Amended (the "Exchange Act") and Section 27A of the Securities Act of 1933 (the "Securities Act") which involve risk and uncertainties . All statements other than statements of historical information provided herein may be deemed to be forward-looking statements. VistaGen Therapeutics, Inc. (the "Company") intends that such statements be protected by the safe harbor created under the Exchange Act and the Securities Act. Forward-looking statements involve risks and uncertainties and the Company's actual results and the timing of events may differ significantly from the results or timing discussed in the forward-looking statements. Statements about our current and future plans, expectations and intentions, results, levels of activity, performance, goals or achievements or any other future events or developments constitute forward-looking statements. Without limiting the foregoing, the words "may", "will", "would", "should", "could", "expect", "plan", "intend", "trend", "indicatio "believe", "estimate", "predict", "likely" or "potential", or the negative or other variations of these words or other compara words or expressions, are intended to identify forward-looking statements. Discussions containing forward-looking statements in this report may be found, among other places, under "Business", "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations". Forward-looking statements are based on estimates and assumptions we make in light of our experience and perception of historical trends, current conditions and expected future developments, as well as other factors that we believe are appropriate and reasonable in the circumstances.

Many factors could cause our actual results, level of activity, performance or future events to differ materially from those expressed in or implied by the forward-looking statements, including, but not limited to, the factors which are discussed in greater detail in this report under the section entitled "Risk Factors". However, these factors are not intended to represent a complete list of the factors that could affect us. The purpose of the forward-looking statements is to provide the reader with a description of management's expectations regarding, among other things, our financial performance and research and development activities and may not be appropriate for other purposes. Readers are cautioned not to place undue reliance on these forward-looking statements, which, unless otherwise stated, are made only as of the date of this report. We have no intention and undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this report, except as required by applicable law. The forward-looking statements contained in this report are expressly qualified by this cautionary statement. New factors emerge from time to time, and it is not possible for us to predict which factors may arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause our actual results to differ materially from those contained in any forward-looking statements.

EXPLANATORY BACKGROUND INFORMATION

VistaGen Therapeutics, Inc. ("VistaGen" or the "Company" or "we") is a biotechnology company with expertise in human pluripotent stem cell technology ("hPSC technology"). We are currently applying our hPSC technology for drug rescue, predictive toxicology and drug metabolism screening.

VistaGen Therapeutics, Inc., a California corporation ("VistaGen California") is a wholly-owned subsidiary of the Company. VistaGen California was incorporated in California on May 26, 1998. Excaliber Enterprises, Ltd. ("Excaliber"), a publicly-held company (formerly OTCBB:EXCA), was incorporated under the laws of the State of Nevada on October 6, 2005. After being unable to generate material revenues based on its original business plan, Excaliber became inactive in 2007. In May 2011, after assessing the prospects associated with its original business plan and the business opportunities associated with a strategic merger with an established, privately-held biotechnology company seeking the potential advantages of being a publicly-held company, Excaliber's Board of Directors agreed to pursue a strategic merger with VistaGen California, as described in more detail below.

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On May 11, 2011, pursuant to a strategic merger transaction with VistaGen California, Excaliber acquired all outstanding shares of VistaGen California in exchange for 6,836,452 restricted shares of Excaliber's common stock (the "Merger"), and Excaliber assumed all of VistaGen California's pre-Merger obligations to contingently issue restricted shares of common stock in accordance with VistaGen California's stock option agreements, warrant agreements, and a convertible promissory note. In connection with the Merger, Excaliber repurchased 5,064,207 shares of Excaliber common stock from two of its stockholders for a nominal amount, resulting in a total of 784,500 shares of Excaliber common stock outstanding at the date of the Merger. The 6,836,452 restricted shares of common stock issued to VistaGen California stockholders in connection with the Merger represented approximately 90% of Excaliber's outstanding shares of common stock after the closing of the Merger. As a result of the Merger, the biotechnology business of VistaGen California became the operating business of Excaliber. Shortly after the Merger:

Each of the pre-Merger directors of VistaGen California was appointed as a director of Excaliber;
The pre-Merger directors and officers of Excaliber resigned as officers and directors of Excaliber;
Each of VistaGen California's pre-Merger officers was appointed an officer of like tenor of Excaliber;
The post-Merger directors of Excaliber (consisting of the pre-Merger directors of VistaGen California) approved a two-for-one (2:1) stock split of Excaliber's common stock;
The post-Merger directors of Excaliber approved an increase in the number of shares of common stock Excaliber was authorized to issue from 200 million to 400 million shares, (see Note 9, Capital Stock, to the Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K);
Excaliber's name was changed to "VistaGen Therapeutics, Inc."; and
VistaGen California's fiscal year-end of March 31 was adopted as Excaliber's fiscal year-end.

VistaGen California, as the accounting acquirer in the Merger, recorded the Merger as the issuance of stock for the net monetary assets of Excaliber, accompanied by a recapitalization. This accounting for the Merger was identical to that resulting from a reverse acquisition, except that no goodwill or other intangible assets were recorded. Since June 21, 2011, VistaGen's common stock has traded on the OTC Bulletin Board under the symbol VSTA.

PART I

Item 1. Business

We are a biotechnology company with expertise in human pluripotent stem cell technology ("hPSC technology"). We are applying our hPSC technology for drug rescue, predictive toxicology and drug metabolism screening. Our primary goal is to generate novel, proprietary, safer variants of once-promising small molecule drug candidates discovered, developed and ultimately discontinued by pharmaceutical and biotechnology companies prior to regulatory approval due to unexpected safety concerns relating to the heart and/or liver. We refer to these new, safer variants as Drug Rescue Variants. Our strategy leverages our hPSC technology platform, Human Clinical Trials in a Test Tube™, our next generation hPSC-based bioassay systems, CardioSafe 3D™ and LiverSafe 3D™, our network of strategic relationships, and the substantial prior third-party investment in drug discovery and development of the once-promising drug candidates we plan to include in our drug rescue programs.

We believe the U.S. pharmaceutical industry is facing a drug discovery and development crisis. In 2012, the U.S. pharmaceutical industry invested nearly $49 billion in research and development and the Center for Drug Evaluation and Research (CDER) of the U.S. Food and Drug Administration (FDA) approved a total of only 39 novel drugs, known as New Molecular Entities (NMEs). Despite this investment by the pharmaceutical industry, since 2003, the FDA has approved an average of approximately 26 NMEs per year. We believe the high cost of drug development and relatively low annual number of FDA-approved NMEs over the past decade is attributable in large part to the cost of failure due to unexpected safety issues related to the heart and/or liver. In turn, we believe the unexpected safety issues related to the heart and liver result from limitations of the major toxicological testing systems currently used in

the pharmaceutical industry, namely animal models involving live animals or animal cells and cellular assays based on transformed cell lines and human cadaver cells, all of which, at best, are capable only of approximating human biology. We believe better cells, human cells derived from our hPSC technology, can help develop better medicine by providing clinically relevant human biological information about a new drug candidate early in the drug development process, long before costly and time-consuming clinical trials.

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With our mature human heart cells derived from pluripotent stem cells, we have developed CardioSafe 3D™, a novel three-dimensional (3D) in vitro bioassay system for predicting in vivo cardiac effects, both toxic and non-toxic, of small molecule drug candidates long before they are tested in animals or humans. With our mature human liver cells derived from pluripotent stem cells, we are developing and now validating LiverSafe 3D™, a novel three-dimensional (3D) in vitro bioassay system for assessing liver toxicity and drug metabolism issues. Our primary near term goal is to use CardioSafe 3D™, and eventually LiverSafe 3D™, for drug rescue, to recapture substantial potential value associated with the pharmaceutical industry's prior investment in drug discovery and development of once-promising small molecule drug candidates discontinued due to safety issues related to unexpected heart or liver toxicity or drug metabolism issues.

Our drug rescue activities involve the combination of our human pluripotent stem cell technology with third-party modern medicinal chemistry. Our principal drug rescue goal is to generate new, safe, proprietary chemical variants of once-promising small molecule drug candidates that were initially discovered and developed by pharmaceutical and biotechnology companies but ultimately discontinued before receiving FDA or foreign market approval due to heart toxicity, liver toxicity or drug metabolism issues. We refer to these new, safe, proprietary chemical variants as "Drug Rescue Variants" or "DRVs." With human heart cells and liver cells derived from pluripotent stem cells, we believe that CardioSafe 3D™ and, when developed and validated, LiverSafe 3D™, will allow us to assess the heart toxicity, liver toxicity and/or metabolism profile of new drug candidates with greater speed and precision than traditional animal testing models and cellular assays used in the drug development process.

We plan to monetize Drug Rescue Variants we develop by licensing them to pharmaceutical companies pursuant to development and marketing agreements. Through these agreements, for each lead Drug Rescue Variant we develop, anticipate receiving up front license fees, development and regulatory milestone payments and royalties on commercial sales.

In addition to drug rescue, we are exploring a range of emerging opportunities to advance nonclinical development of selected pilot regenerative cell therapy programs focused on blood, cartilage, heart, liver and pancreas cells, each based on the proprietary stem cell differentiation and production capabilities of our Human Clinical Trials in a Test Tube™.

AV-101 is our orally available small molecule prodrug candidate aimed at the multi-billion dollar neurological disease and disorders market. AV-101 has successfully completed Phase I development in the U.S. for treatment of neuropathic pain, a serious and chronic condition causing pain after an injury or disease of the peripheral or central nervous system. Neuropathic pain affects approximately 1.8 million people in the U.S. alone. To date, we have been awarded over $8.3 million of grant funding from the National Institutes of Health ("NIH") to support preclinical and Phase I clinical development of AV-101. We believe AV-101 may also be a candidate for development as a therapeutic alternative for depression, epilepsy and Parkinson's disease. To advance further clinical development, manufacturing and commercialization of AV-101, we plan to pursue a strategic licensing arrangement with a pharmaceutical or biotechnology company.

Stem Cell Basics

Human stem cells have the potential to develop into mature cells in the human body. Human pluripotent stem cells ("hPSCs") can differentiate into any of the more than 200 types of cells in the human body. In addition, hPSCs can be expanded readily and have diverse medical research, drug development and therapeutic applications. We believe hPSCs can be used to develop numerous cell types and tissues that can mimic complex human biology, including heart and liver biology, for our proposed drug rescue applications.

Pluripotent stem cells are either embryonic stem cells (“ES Cells”) or induced pluripotent stem cells (“iPS Cells”). Both ES Cells and iPS Cells can be maintained and expanded in an undifferentiated (undeveloped) state indefinitely. We believe these features make them useful research tools and a reliable source of normal cell populations for creating bioassays to test potential efficacy and toxicity of drug candidates. In addition, these normal human cells have a wide range of potential applications for regenerative cell therapy.

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Embryonic Stem Cells (ES Cells)

ES Cells are derived from excess fertilized eggs produced during clinical in vitro fertilization ("IVF") procedures. The excess fertilized eggs are donated for research purposes with the informed consent of the donors after a successful IVF procedure. ES Cells are not derived from eggs fertilized in a woman's body. Such donated fertilized eggs are cultured in vitro and ES Cells are isolated when the embryo is approximately 100 cells, thus long before organs, tissues or nerves have developed.

ES Cells have the most documented potential to both self-renew (create large numbers of cells identical to themselves) and differentiate (develop) into any of the over 200 types of cells in the body. ES Cells undergo increasingly restrictive developmental decisions during their differentiation. These "fate decisions" commit the ES Cells to becoming only certain types of mature cells and tissues. At one of the first fate decision points, ES Cells differentiate into epiblasts. Although epiblasts cannot self-renew, they can differentiate into the major tissues of the body. This epiblast stage can be used as the starting population of cells that develop into millions of blood, heart, muscle, liver and pancreas cells, as well as neurons. In the next step, the presence or absence of certain growth factors, together with the differentiation signals resulting from the physical attributes of the culture techniques, induce the epiblasts to differentiate into neuroectoderm or mesendoderm cells. Neuroectoderm cells are committed to developing into cells of the skin and cells of the nervous system. Mesendoderm cells are precursor cells that differentiate into mesoderm and endoderm. Mesoderm cells develop into muscle, bone and blood, among other cell types. Endoderm cells develop into the internal organs such as the heart, liver, pancreas and intestines, among other cell types.

Induced Pluripotent Stem Cells (iPS Cells)

Over the past several years, Nobel prize-winning developments in stem cell research by third parties have made it possible to obtain pluripotent stem cell lines from individuals without the use of embryos. Induced pluripotent stem cells ("iPS Cells") are adult cells, typically human skin or fat cells, that have been genetically "reprogrammed" to behave like ES Cells by being forced to express genes necessary for maintaining the pluripotential property of ES Cells. Although researchers are exploring non-viral methods, most iPS Cells are produced by using various viruses to activate and/or express three or four genes required for the immature pluripotential property similar to ES Cells. It is not yet precisely known, however, how each gene actually functions to induce cellular pluripotency, nor whether each of the three or four genes is essential for this reprogramming. Although ES Cells and iPS Cells are believed to be similar in many respects, including their ability to form all cells in the body and to self-renew, scientists do not yet know whether they differ in clinically significant ways or have the same ability to self-renew and make more of themselves.

Although there are remaining questions in the field about the lifespan, clinical utility and safety of iPS Cells, we believe that the biology and differentiation capabilities of ES Cells and iPS Cells are likely to be comparable. There are, however, specific situations in which we may prefer to use iPS technologies based on the relative ease of generating pluripotent stem cells from:

- individuals with specific inheritable diseases and conditions that predispose the individual to respond differently to drugs; or

- individuals with specific variations in genes that directly affect drug levels in the body or alter the manner or efficiency of their metabolism, breakdown or elimination of drugs.

Because they can significantly affect the therapeutic and/or toxic effects of drugs, these genetic variations have an impact on drug development and the ultimate success of the drug. We believe that iPS Cell technologies may allow

the rapid and efficient generation of pluripotent stem cells from individuals with the desired specific genetic variation. These stem cells might then be used to develop stem cell-based bioassays, for both efficacy and toxicity screening, which reflect the effects of these genetic variations, as well as for cell therapy applications.

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Current Drug Development Process

The current drug development paradigm is designed to assess whether a drug candidate is both safe and effective at treating the disease to which it is targeted. A major challenge in that process is that conventional animal and in vitro testing can, at best, only approximate human biology. A pharmaceutical company can spend millions of dollars to discover, optimize and validate the potential efficacy of a promising small molecule drug candidate and advance it through nonclinical development, only to see it fail due to unexpected safety issues relating to heart or liver toxicity or adverse drug-drug interactions. The pharmaceutical company then often discontinues the development program for the once-promising drug candidate, despite positive efficacy data indicating its potential therapeutic and commercial benefits. If discontinued, the pharmaceutical company's significant prior drug discovery and development investment in the drug candidate is lost.

Taking into account the cost of failures, it has been estimated that the drug discovery and development programs of major pharmaceutical companies have required an average investment of approximately $1 billion for each new drug candidate that reaches the market. It is also estimated that about one-third of all potential new drugs candidates fail in preclinical or clinical trials due to safety concerns. In a 2004 white paper entitled "Stagnation or Innovation", the FDA noted that even a 10% improvement in predicting the failure of a drug due to toxicity before the drug enters clinical trials could, when averaged over a pharmaceutical company's drug development efforts, avoid $100 million in development costs per marketed drug.

We believe there is an unmet need for more predictive human cell-based toxicology and drug discovery screening assays that more closely approximate human biology than do current testing systems used in the pharmaceutical industry. By differentiating pluripotent stem cells into mature, functional human cells that can then be used as the basis for our customized in vitro toxicology screening bioassay systems, we have the potential to identify human heart and liver toxicity of new drug candidates early in the drug development process, resulting in efficient focusing of resources on those candidates with the highest probability of success. We believe this has the potential to substantially reduce development costs and substantially improve the economics of our current healthcare system, while enabling us to generate effective and safer drugs.

Our Human Clinical Trials in a Test TubeTM Platform for Drug Rescue

We are focused on leveraging the substantial prior investment by pharmaceutical companies in discovery and development of new drug candidates that ultimately were discontinued due to unexpected safety issues relating to the heart and liver toxicity. By combining our stem cell technology platform, which we refer to as Human Clinical Trials in a Test TubeTM, with modern medicinal chemistry and 3D "micro-organ" culture systems, we are focused on generating, together with our collaborators, new, safer, proprietary chemical variants of failed drug candidates. Our primary drug rescue goal is to use our stem cell technology platform to generate Drug Rescue Variants that retain the efficacy of a large pharmaceutical company's once-promising drug candidate, but with reduced heart and/or liver toxicity or adverse drug-drug interactions. We believe our Drug Rescue Variants will offer to pharmaceutical companies a potential opportunity to rescue substantial value from their prior drug discovery and development investment in once-promising drug candidates which they discontinued due to heart or liver safety concerns.

Proprietary Pluripotent Stem Cell Differentiation Protocols

Through several years of research, together with our co-founder, Dr. Gordon Keller, we have developed proprietary differentiation protocols covering key conditions involved in the differentiation of pluripotent stem cells into multiple types of human cells. The human cells generated by following these proprietary differentiation protocols are integral to our Human Clinical Trials in a Test TubeTM platform. We believe they support more clinically predictive in vitro bioassay systems than animal testing or cellular assays currently used in drug discovery and development. Our

exclusive licenses with National Jewish Health and Mount Sinai School of Medicine and University Health Network relate to proprietary stem cell differentiation protocols developed by Dr. Keller and cover, among other things, the following:

- specific growth and differentiation factors used in the tissue culture medium, applied in specific combinations, at critical concentrations, and at critical times unique to each desired cell type;

- modified developmental genes and the experimentally controlled regulation of developmental genes, which is critical for determining what differentiation path a cell will take; and

- biological markers characteristic of precursor cells, which are committed to becoming specific cells and tissues, and which can be used to identify, enrich and purify the desired mature cell type.

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We believe our Human Clinical Trials in a Test TubeTM platform will allow us to assess the heart and liver toxicity profile of new, small molecule drug candidates for a wide range of diseases and conditions, with greater speed and precision than animal testing and cellular assays currently used by pharmaceutical companies in the drug development.

Growth Factors that Direct and Stimulate the Differentiation Process

The proprietary and licensed technologies underlying our Human Clinical Trials in a Test TubeTM platform allow us to direct and stimulate the differentiation process of human pluripotent stem cells. As an example, for pluripotent ES Cells, the epiblast is the first stage in differentiation. One biological factor that controls the first fate decision of the epiblast is the relative concentrations of serum growth factors and activin, a protein involved in early differentiation and many cell fate decisions. Eliminating serum growth factors and adding the optimal amount of activin is an important step in inducing the reproducible development of functional cells and, in our view, is essential for the development of a robust, efficient, and reproducible model of human biological systems suitable for drug rescue applications. The use of activin in these applications is core to many of the claims in the patent applications underlying our licensed technology. Replacing activin with continuous exposure to serum factors results in an inefficient and variable differentiation into cells of the heart, liver, blood and other internal organs. See “Intellectual Property – Mount Sinai School of Medicine Exclusive Licenses.”

In addition to activin, Dr. Keller’s studies have identified a number of other growth and serum-derived factors that play important roles in the differentiation of ES Cells. Some of the patents and patent applications underlying our licensed technology are directed to the use of a variety of specific growth factors that increase the efficiency and reproducibility of the pluripotent stem cell differentiation process. We have exclusive rights to certain patents and patent applications for the use of growth factor concentrations for ES Cell differentiation that we believe are core and essential for our drug rescue and development applications. See “Intellectual Property - Licenses - Mount Sinai School of Medicine Exclusive Licenses,” “National Jewish Health Exclusive Licenses” and “University Health Network Exclusive License.”

Developmental Genes that Direct and Stimulate the Differentiation Process

For the purpose of creating our Human Clinical Trials in a Test TubeTM platform, we further control the differentiation process by controlling regulation of key developmental genes. By studying natural organ and tissue development, researchers have identified many genes that are critical to the normal differentiation, growth and functioning of tissues of the body. We engineer ES Cells in a way that enables us to regulate genes that have been identified as critical to control and direct the normal development of specific types of cells. We can then mimic human biology in a way that allows us to turn on and off the expression of a selected gene by the addition of a specific compound to a culture medium. By adding specific compounds, we have the ability to influence the expression of key genes that are critically important to the normal biology of the cell.

Cell Purification Approaches

The proprietary protocols we have licensed for our Human Clinical Trials in a Test TubeTM platform also establish specific marker genes and proteins which can be used to identify, enrich, purify, and study important populations of intermediate precursor cells that have made specific fate decisions and are on a specific developmental pathway towards a mature functional cell. These protocols enable a significant increase in the efficiency, reproducibility, and purity of final cell populations. For example, we are able to isolate millions of purified specific precursor cells which, together with a specific combination of growth factors, develop full culture wells of functional, beating human heart cells. Due to their functionality and purity, we believe these cell cultures are ideal for supporting our drug rescue activities.

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3D “Micro-Organ” Culture Systems

In addition to standard two-dimensional (“2D”) cultures which work well for some cell types and cellular assays, the proprietary stem cell technologies underlying our Human Clinical Trials in a Test TubeTM platform enable us to grow large numbers of normal, non-transformed, human cells to produce novel in vitro 3D “micro-organ” culture systems. For example, for CardioSafe 3DTM, we grow large numbers of normal, non-transformed, human heart cells in vitro in 3D micro-organ culture systems. The 3D micro-organ cultures induce the cells to grow, mature, and develop 3D cell networks and tissue structures. We believe these 3D cell networks and structures more accurately reflect the structures and biology inside the human body than traditional flat, 2D, single cell layers grown on plastic, that are widely used by pharmaceutical companies today. We believe that the more representative human biology afforded by the 3D system will yield responses to drug candidates that are more predictive of human drug responses.

Medicinal Chemistry

Medicinal chemistry involves designing, synthesizing, modifying and developing small molecule drugs suitable for therapeutic use. It is a highly interdisciplinary science combining organic chemistry, biochemistry, physical chemistry, computational chemistry, pharmacology, and statistics. The combination of medicinal chemistry with the proprietary and licensed stem cell technologies underlying our Human Clinical Trials in a Test TubeTM platform are core components of our drug rescue business model. Working with our strategic medicinal chemistry partner, Synterys, Inc., we are focused on using our stem cell biology to generate a pipeline of effective and safe Drug Rescue Variants of once-promising pharmaceutical company drug candidates in a more efficient and cost-effective manner than the processes currently used for drug development.

Application of Stem Cell Technology to Drug Rescue

By using CardioSafe 3DTM, we are focused on identifying and optimizing a lead Drug Rescue Variant (generated in collaboration with our medicinal chemistry partner) with reduced heart toxicity compared to the once-promising pharmaceutical company drug candidate. We believe each lead Drug Rescue Variant will be a new drug candidate (to which we expect to have certain intellectual property and commercialization rights) that preserves the therapeutic potential of the original pharmaceutical company drug candidate, and thus retains its potential commercial value to a pharmaceutical company, but substantially reduces or eliminates its heart toxicity risks. We believe that focusing on failed drug candidates that generated positive efficacy data will allow us to leverage a pharmaceutical company’s substantial prior investment in discovery and development of the original drug candidate to develop our new lead Drug Rescue Variant. We anticipate that the positive efficacy data relating to the pharmaceutical company’s original drug candidate will give us and our medicinal chemistry partner a significant “head start” in our efforts to generate a lead Drug Rescue Variant, resulting in faster, less expensive development of our Drug Rescue Variants than drug candidates discovered and developed using only conventional animal testing and cellular testing systems.

CardioSafe 3DTM

We have used the proprietary pluripotent stem cell technology underlying our Human Clinical Trials in a Test TubeTM platform to develop and validate CardioSafe 3DTM, a human heart cell-based toxicity screening system that we believe is stable, reproducible and capable of generating data to allow our scientists to more accurately predict the in vivo cardiac effects, both toxic and non-toxic, of drug candidates. A single CardioSafe 3DTM assay is stable for many weeks and can be used for evaluating the heart toxicity of numerous drug candidates.

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Our initial internal validation study was designed to test the ability of CardioSafe 3DTM to generate data to allow our scientists to predict the in vivo cardiac effects of drug candidates. This study included 10 drugs previously approved for human use by the FDA and one experimental research compound widely accepted for studying cardiac electrophysiological effects. We selected these drugs and the research compound because of their known toxic or non-toxic cardiac effects on human hearts that we believe represent the testing characteristics we expect to encounter during our drug rescue programs. More specifically:

- five of the FDA-approved drugs (astemizole, sotalol, cisapride, terfenadine and sertindole) were withdrawn from the market due to heart toxicity concerns;

- the other five FDA-approved drugs (fexofenadine, nifedipine, verapamil, lidocaine and propranolol) are currently available in the U.S. market and demonstrate certain measurable clinical non-toxic cardiac effects, one of which (fexofenadine) is a non-cardiotoxic drug variant (similar in concept to our planned rescued drug variants) of terfenadine (one of the FDA-approved drugs withdrawn from the market due to heart safety concerns); and

- the research compound (E-4031) failed in a small Phase I human clinical study before being discontinued due to heart toxicity concerns.

In our stud