Capnia, Inc.
Form 10-K
March 15, 2017

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

FORM 10-K

(Mark One)
x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2016
.. TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to .
Commission File No.: 001-36593

Capnia, Inc.
(Exact name of Registrant as specified in its charter)

Delaware	77-0523891
(State or other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
1235 Radio Road, Suite 110 Redwood City, California	94065
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: (650) 213-8444
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 $0.001 per share	The NASDAQ Capital Market
Series A warrants to purchase Common Stock	The NASDAQ Capital 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 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 (§ 229.405 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 (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 Rule 12b-2 of the Act). Yes ¨ No x

The aggregate market value of voting stock held by non-affiliates of the registrant on June 30, 2016, based on the closing price of $1.16 for shares of the registrant's common stock as reported by the NASDAQ Capital Market, was approximately $7.7 million. Shares of Common Stock beneficially held by each executive officer, director and holder of 5% or more of the outstanding Common Stock have been excluded in that such persons may be deemed affiliates. As of March 10, 2017 there were 47,479,879 shares of the registrant's Common Stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement to be filed with the Commission pursuant to Regulation 14A in connection with the registrant's 2016 Annual Meeting of Stockholders, to be filed subsequent to the date hereof, are incorporated by reference into Part III of this Report. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission not later than 120 days after the conclusion of the registrant's fiscal year ended December 31, 2016. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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PART IV

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The following discussion and analysis should be read in conjunction with our audited consolidated financial statements and the related notes that appear elsewhere in this Annual Report on Form 10-K. This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, particularly in Part I, Item 1: "Business," Part I, Item 1A: "Risk Factors" and Part 2, Item 7: "Management's Discussion and Analysis of Financial Condition and Results of Operations." These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "estimate," "plan" or "continue," and similar expressions or variations. All statements other than statements of historical fact could be deemed forward-looking, including, but not limited to: any projections of financial information; any statements about historical results that may suggest trends for our business; any statements of the plans, strategies, and objectives of management for future operations; any statements of expectation or belief regarding future events, technology developments, our products, product sales, expenses, liquidity, cash flow, market growth rates or enforceability of our intellectual property rights and related litigation expenses; and any statements of assumptions underlying any of the foregoing. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Accordingly, we caution you not to place undue reliance on these statements. Particular uncertainties that could affect future results include: our ability to achieve or maintain profitability; our ability to obtain substantial additional capital that may be necessary to expand our business; our ability to maintain internal control over financial reporting; our dependence on, and need to attract and retain, key management and other personnel; our ability to obtain, protect and enforce our intellectual property rights; potential advantages that our competitors and potential competitors may have in securing funding or developing products; business interruptions such as earthquakes and other natural disasters; our ability to comply with laws and regulations; potential product liability claims; and our ability to use our net operating loss carryforwards to offset future taxable income. For a discussion of some of the factors that could cause actual results to differ materially from our forward-looking statements, see the discussion on risk factors that appear in Part I, Item 1A: "Risk Factors" of this Annual Report on Form 10-K and other risks and uncertainties detailed in this and our other reports and filings with the Securities and Exchange Commission, or SEC. The forward-looking statements in this Annual Report on Form 10-K represent our views as of the date of this Annual Report on Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report on Form 10-K.

PART I

ITEM 1. BUSINESS

BUSINESS

Company Overview

We are a diversified healthcare company that develops and commercializes innovative diagnostics, devices and therapeutics addressing unmet medical needs. We have a number of commercial products based on our proprietary technologies, including those which utilize precision metering of gas flow. Our most recent product to launch commercially is Serenz® Allergy Relief, or Serenz, which has a CE Mark certification for sale in the European Union, or E.U. Serenz is a proprietary handheld device that delivers non-inhaled CO2 topically to the nasal mucosa. Serenz is used only when needed, and does not need to be used on a regular basis. We are also selling the CoSense® End-Tidal Carbon Monoxide (ETCO) Monitor, or CoSense, measures ETCO and aids in the detection of excessive hemolysis, a condition in which red blood cells degrade rapidly. When present in neonates with jaundice, excessive hemolysis is a dangerous condition which can lead to adverse neurological outcomes. CoSense is 510(k) cleared for sale in the U.S. and received CE Mark certification for sale in the E.U.

We also develop and market innovative pulmonary resuscitation solutions for the inpatient and ambulatory neonatal markets through our wholly owned subsidiary NeoForce, Inc., or NFI. NFI's primary product is the NeoPip T-piece resuscitator and related consumable, which delivers consistent pre-set inspiratory pressure and positive end-expiratory pressures. Other products include temperature probes, scales, surgical tables and patient surfaces.

Our therapeutic technology involves the use of precisely metered nasal carbon dioxide, or CO2, for the potential relief of symptoms related to various diseases. Several randomized placebo controlled trials have shown its efficacy in the symptomatic treatment of allergic rhinitis, and we continue to evaluate our options to further develop this product. In addition, we are pursuing new initiatives for the development of this technology for the treatment of trigeminally-mediated pain disorders such as cluster headache and trigeminal neuralgia, or TN. We also have orphan drug designation for our nasal, non-inhaled CO2 technology for the treatment of TN. We have filed an investigational new drug, or IND, application with the U.S Food and Drug Administration, or FDA, and started enrolling TN patients in a pilot clinical trial in 2016.

Our research and development efforts are primarily focused on additional products based on our Sensalyze Technology Platform, a portfolio of proprietary methods and algorithms which enables CoSense and can be applied to detect a variety of analytes in exhaled breath, as well as other products for the neonatology market. Our current development pipeline includes proposed diagnostic devices for asthma in children, assessment of blood CO2 concentration in neonates and malabsorption. We may also license elements of our Sensalyze Technology Platform to other companies that have complementary development or commercial capabilities.

Serenz Allergy Relief

Allergic rhinitis, or AR, which is commonly and colloquially referred to as "allergies," is characterized by symptoms that are often episodic and include nasal congestion, itching, sneezing and runny nose. It is one of the most common ailments in the western world and is growing rapidly, making AR one of the largest potential pharmaceutical markets. There are approximately 39 million sufferers in the U.S. and 48 million in France, Germany, Italy, Spain and the United Kingdom, and an additional 36 million in Japan, according to research firm GlobalData. Prevalence of AR is growing rapidly in the developed world. The most common AR drug therapies include antihistamines and intranasal steroids. Leukotriene inhibitors and other drugs are also currently prescribed to AR patients. Several of these drugs have generated sales in excess of $1 billion per year as branded products. However, these products have significant limitations and AR sufferers remain dissatisfied with the available treatments. Thus, there is a need for a more effective treatment with a faster onset of action and improved safety profile.

AR is a cause of significant morbidity in spite of available treatments. According to the Allergies In America Survey conducted in 2006, most AR sufferers reported themselves to be less than "very satisfied" with the products they were taking for allergy relief. Fifty-two percent reported they had suffered from impaired work performance or missed

work due to their AR symptoms even though 69% had used medication at some point in the prior four weeks. Current treatments provide incomplete relief from symptoms and have significant side effects such as drowsiness.

Serenz is based upon the observation that non inhaled CO2 delivered at a low-flow rate into the nasal cavity, alleviates the symptoms of AR by cleansing the nasal mucosa. Serenz is a convenient, hand-held device that delivers low-flow CO2 to the nasal mucosa. It contains a pressurized canister of gas, with approximately enough gas to dose as-needed for one to two weeks. The device is disposable and engineered for ease of use. Our proprietary technology ensures very precise control of aspects such as flow rate and volume, which we believe are both critical to achieve the desired clinical performance.

In our clinical trials to date, Serenz has shown a statistically significant effect within 30 minutes and is well tolerated. We believe that such a therapeutic benefit will position Serenz to be a potential first-line treatment for any AR sufferer. Contrary to dosing with commonly used medications such as antihistamines and nasal steroids, which must be dosed on a regular basis regardless of the presence of symptoms, Serenz is used on an as-needed basis and only when symptoms are present.

One Serenz device contains enough gas for approximately 20 doses, which we believe will treat AR for an average of one to two weeks, depending on frequency of use. We have not determined final pricing for Serenz, but expect to price it at a premium to existing therapies for AR due to the benefits we believe the product provides to patients over such therapies.

Based on clinical trials to date, we believe Serenz exhibits the ideal characteristics of an AR therapeutic, including:

- Rapid relief
- Relief from all nasal symptoms
- Mild side effect profile
- No known long-lasting side effects
- Locally acting
- Non-sedating
- Non-steroidal
- Usable on an as-needed basis

Clinical Trials of Serenz in Allergic Rhinitis

We have conducted six randomized, controlled clinical trials involving 975 patients, testing the safety and effectiveness of nasal CO_2 in treating the symptoms of AR. Four of these clinical trials were in patients with seasonal AR, or SAR, and two of these clinical trials was in patients with perennial AR, or PAR. In addition, GlaxoSmithKline conducted a trial in 147 patients to assess the consumer appeal of Serenz for patients with nasal congestion. The trials using the as-needed approach showed statistically significant and clinically meaningful effects in both SAR and PAR. The effect is seen on each of the individual nasal and non-nasal symptoms, with as little as a 10 second per nostril application of Serenz. Given the rapid onset and generally mild side effect profile, we believe Serenz is ideally suited for marketing to patients for use on an as-needed basis.

These studies show statistically significant and clinically meaningful effects in both SAR and PAR. The effect is seen on each of the individual nasal and non-nasal symptoms, with as little as a 10 sec/nostril application. The magnitude of the effect appears to be substantially larger than that of antihistamines and in the range of that seen with intranasal corticosteroids. Given the rapid onset and benign side effect profile, Serenz is ideally suited for use on an as-needed basis.

The As-Needed Only Treatment Paradigm

The traditional therapeutics used for the symptomatic treatment of AR have left a significant unmet need in this population. These agents (mostly antihistamines and nasal steroids) are approved for use on a scheduled basis (once a day, twice a day, etc.). This is counter-intuitive given that the symptoms of AR are typically episodic (such as when a subject is exposed to a pollen when they step outdoors in allergy season). The reason for chronic treatment of this

episodic disorder is that the available treatments for AR take too long to act. Antihistamines typically take hours to have an effect. They are not very effective and the efficacy decreases further over time for patients and as exposure to allergens continues (whether seasonal or perennial). In addition, antihistamines in general do not have any effect on congestion. Nasal steroids can take days before onset of effect. While they are more efficacious than antihistamines, they must be taken regularly during the allergy season (or indefinitely for perennial allergies). In addition, they have bothersome side effects and are associated with the perception issues

that relate to steroid use in general. What is needed is a treatment that can act rapidly – so that it can be taken only when needed. In addition, it should not have any lasting or significant side effects. Serenz has the characteristics of such a treatment.

Serenz as an As-Needed Only Application

The targeted indication as-needed use is supported by the following studies:

- SAR-2005—This was the first randomized, placebo-controlled trial in subjects with SAR. Symptomatic subjects were treated with a single application of active (nasal CO_2) or placebo 60 sec/nostril one time. Symptoms were measured just before and at several time points after the treatment. Statistically significant improvements in symptoms were noted as early as 10 minutes, lasting for as long as 24 hours.
- C211 (PAR)—This was a randomized, placebo-controlled trial in subjects with PAR. Symptomatic subjects were treated with a single application of active or placebo. Subjects were assigned to one of six treatment groups: CO_2 at 5 mL/sec for 10 sec/nostril, CO_2 at 10 mL/sec for 10 sec/nostril, CO_2 at 5 mL/sec for 30 sec/nostril, CO_2 at 10 mL/sec for 30 sec/nostril, placebo for 10 sec/nostril, and placebo for 30 sec/nostril in a 2:2:2:2:1:1 ratio. Symptoms were measured just before and at several time points after the treatment. Statistically significant improvements in symptoms were noted at 30 minutes in the CO_2 at 10 mL/sec for 10 sec/nostril group. There was sustained (4-6 hours) relief of symptoms in this group.
- C216 (SAR)—This was the first multi-application, randomized, placebo-controlled trial in which the nasal CO_2 device was used as needed in subjects with SAR. Subjects applied active or placebo 10 sec/nostril only as needed up to six times a day for 14 days. Symptoms were measured just before and at 30 minutes after each treatment during the 14-day treatment period. Statistically significant improvements ($p<0.0001$) in symptoms were noted at 30 minutes after each treatment during the 14-day treatment period. These results show that the nasal CO_2 device is effective for the prn treatment of SAR symptoms. The effect is rapid and the effect size is large.

Scheduled Dosing Studies with Serenz

Other studies conducted for AR have evaluated the more traditional paradigm of scheduled dosing. Effectiveness measurements in these studies, based on a Guidance Document published by the FDA, are recorded in the morning and evening, regardless of the time of the treatment or pre-treatment symptoms. These measurements therefore reflect the overall symptomatic relief during the day as opposed to measuring the true effect of a treatment. Measurement of post-treatment scores in this scheduled dosing paradigm show the efficacy to be predictably lacking since pretreatment scores are low (subjects treat when they are scheduled to, regardless of whether they need to based on worse symptoms). The following two studies evaluated twice a day and four times a day scheduled dosing in subjects with SAR:

- C215 (SAR)—This was the first multi-application, randomized, placebo-controlled trial in subjects with SAR.Significantly symptomatic subjects were treated with a multi-application of active or placebo 10 sec/nostril two times a day for 14 days. Symptoms were measured just before the treatment. Prior to initiating the 14-day treatment period, subjects applied either active or placebo 10 sec/nostril in the clinic. Symptoms were measured just before and at several time points after this initial application. There were no statistically significant improvements in TNSS during the 14-day treatment period. However, a statistically significant improvement in symptoms was noted at 30 minutes and persisted for 6 hours after the first application, once again supporting the paradigm of as needed only use.
- C218 (SAR)—This was a multi-application, randomized, placebo-controlled trial in which the nasal CO2 device was used four times a day in subjects with SAR. Significantly symptomatic subjects applied active or placebo 10 sec/nostril four times a day for 14 days. Symptoms were measured just before and at 30 minutes after the treatment during the 14-day treatment period. There were no statistically significant improvements in TNSS during the 14-day treatment period. Predictably, the average pre-treatment symptoms were low in this study- which may have been the primary driver of the lack of response.

Safety of Serenz

There were no application-related or device-related serious adverse events in any of the clinical trials conducted. Adverse events were generally mild and application-related, and resolved immediately upon cessation of application. The most common adverse events were transient nasal sensation and tearing of the eyes, or lacrimation, that lasted for the duration of the application only.

The nasal sensation commonly encountered during these clinical trials was described by patients differently, and ranges from tingling to burning to pain. We also observed that these sensations were generally not severe enough for patients to discontinue use of nasal CO_2, and for more than 1,000 patients treated in all of the AR clinical trials, only six patients discontinued use of nasal CO_2 due to an adverse event. We believe that these clinical trials provide evidence that gentle cleansing of the nasal mucosa with Serenz is safe, acts locally and provides rapid relief of allergy symptoms.

Serenz Regulatory Status

We have CE Mark certification for Serenz.

The approval route for Serenz in the U.S. may be through a drug-device combination approval or a device approval. In the case of a drug-device combination, a new drug application, or NDA, filing with the FDA will be required. Additional randomized, controlled clinical trials may be necessary to obtain approval. If it is a device approval pathway, it may be either via the premarket approval application process, a de novo 510(k) pathway, or traditional 510(k). We are currently reviewing regulatory pathway options including the possibility of marketing Serenz as a Class I, 510(k) exempt device in the U.S.

Market opportunity

Independent market research has confirmed that nearly 23% of the population in the U.K., France, Germany, Italy and Spain suffers from AR. An estimated 9% of the population is being treated by their physician, and 2% self-treats for allergies. Greater than 75% of physician-treated patients and 100% of self- treated individuals use over the counter, or OTC, allergy products as part of their regimen, resulting in the OTC market segment for adults aged 18 or older at approximately 25 million people in these five countries. Quantitative market research in three major European countries was conducted to determine the level of consumer interest in an OTC allergy relief product with the benefits of Serenz. Despite many lower priced treatment options available to consumers, approximately 27% of those surveyed indicated a willingness to pay a premium for a product like Serenz. We believe that the population of consumers willing to pay a premium for an OTC allergy product to be the market opportunity for Serenz.

The length of allergy season varies across Europe, but on average, it ranges from April to September. Allergy season is weather dependent, and a cold, rainy season can naturally improve symptoms for many sufferers, reducing the need for OTC
treatments. Based on our research, we expect that consumers will treat themselves two to three times per day during the course of allergy season. Both previous market research and current experience with our U.K. pilot test market show strong product satisfaction and repurchase rates. We expect approximately 75% of individuals who try Serenz to repurchase the product throughout the duration of allergy season.

Although some allergy sufferers experience symptoms throughout the year, we plan to focus our sales and marketing efforts on seasonal AR which represents the vast majority of treatment needs. We plan to generate awareness through direct to consumer, or DTC, marketing through internet and social media advertising campaigns and through pharmacy marketing channels. We do not have plans for physician marketing in 2017, which may limit our ability to create demand with physician-treated patients. We have seen positive feedback from DTC customers in the U.K. who value the format and delivery system of Serenz for rapid allergy relief, and we believe we can reach a significant portion of the OTC audience through the DTC and pharmacy channels.

Sales and Marketing

In the second quarter of 2016, we initiated a pilot launch of Serenz in the U.K and Ireland. We entered into distribution
agreements with UK-based pharmacy chains, Paydens Group and Weldricks Pharmacy Limited, providing access to more than
retail pharmacy locations in the UK, as well as through their respective online website sales channel.

In Ireland, we entered into a distribution agreement with Medinutrix, a leading developer of OTC health products and natural therapies. Under the terms of the agreement, Medinutrix is initially providing Serenz to 25 community pharmacies as part of the pilot launch in Ireland.

Serenz market segmentation will focus on allergy sufferers who wish to try a solution that is:

- Local topical and safe treatment
- Only used as needed

- Well-tolerated side effect profile (side effects, if they occur, are transient and resolve once cleansing is done
- Rapid relief
- Portable and convenient
- Affordable

We plan to pursue additional pilot sales launches in select geographies through leading local and regional distributors and retailers. We also plan to engage consumers with geography-focused, direct to consumer marketing efforts utilizing digital and traditional media to optimize our media mix and consumer messaging.

Pricing

Since Serenz offers a number of benefits to allergy sufferers over existing treatment regiments, we plan to price the product at a premium relative to other OTC therapies. Our market research has identified a large segment of allergy sufferers who are willing to pay a premium for rapid, as needed relief with convenient, no-mess delivery. Our marketing efforts will focus on targeting and growing awareness with the segment of allergy sufferers willing to pay a premium. In some of the E.U. markets such as the U.K., consumers pay very little out-of-pocket for allergy medication, which may slow our ability to grow uptake with a premium price. Our commercial strategy will focus on out-of-pocket OTC sales, with no plans to apply for reimbursement until 2018.

Competition

The main competitors in the space are oral and nasal antihistamines and nasal steroids. Oral antihistamines (such as Claritin, Clarinex, Cetrizine, etc.) account for a substantial proportion of the OTC market. Prescription as well as OTC nasal steroids (Rhinocort, Budesonide, Nasocort, etc.) are commonly used as well. Other pharmaceutical products such as leukotriene inhibitors are also prescribed and nasal saline rinses are are also widely available OTC.

CoSense

CoSense is our first Sensalyze Technology Platform product to receive 510(k) clearance from the FDA and CE Mark certification. CoSense measures ETCO, which can be elevated due to endogenous causes such as excessive breakdown of red blood cells, or hemolysis, or exogenous causes such as CO poisoning and smoke inhalation. Our first target market is for the use of ETCO measurements to aid in detection of hemolysis in neonates, a disorder in which CO and bilirubin are produced in excess as byproducts of the breakdown of red blood cells. Hemolysis can place neonates at high risk for hyperbilirubinemia and resulting neurodevelopmental disability. The AAP recommends the use of ETCO monitoring to evaluate neonates for hemolysis, but, other than CoSense, there is no device currently on the market as accurate as CoSense for physicians to effectively monitor ETCO in clinical practice.

Hemolysis and Bilirubin

We estimate that approximately one third of the 9.2 million newborns in the U.S. and E.U. each year are at risk for hemolysis under current practice, representing approximately 3.1 million newborns. We believe that many of these newborns are tested for hemolysis, but using relatively inaccurate and/or invasive diagnostic methods. Retrospective analysis of data, including data from over 54,000 newborns compiled by the Collaborative Perinatal Project sponsored by the National Institutes of Health, or NIH, suggests that the only factor that predisposes newborns with jaundice to adverse neurodevelopmental outcomes is the concurrent presence of hemolysis. Hemolysis can be caused by a number of factors, including physical trauma and bruising, blood group incompatibility, autoimmune disorders, and genetic causes such as sickle cell disease and glucose-6-phosphate dehydrogenase (G6PD) enzyme deficiency. Because bilirubin is the chemical byproduct of the destruction of hemoglobin from red blood cells, hemolysis causes bilirubin production to spike. Bilirubin is yellow in color, and if present in excessive amounts in the body, known as hyperbilirubinemia, it can be deposited in tissues such as the skin and conjunctiva. The condition manifests as a

yellowing of skin and conjunctiva and is called jaundice. Elevated levels of bilirubin are particularly dangerous to neonates, who have immature livers and lack the adult ability to excrete bilirubin. Neonates also lack a well-formed blood-brain barrier to prevent bilirubin from entering the central nervous system, or CNS, where bilirubin is known to be toxic to neuronal tissue.

Adverse Effects of Jaundice and Hyperbilirubinemia

Every year approximately 143 million babies are born world-wide, of which 4.0 million are in the U.S. and 5.2 million in the E.U. It is estimated that up to 60% of term neonates and 80% of preterm neonates may have jaundice. Many neonates have jaundice, which is related to a decreased capacity of the neonate to excrete bilirubin into the intestinal tract for elimination from the body, or from a decreased capacity of the liver to conjugate bilirubin for excretion. These neonates will often normalize their bilirubin levels without a need for treatment. When treatment is required, it is usually via phototherapy, which typically involves isolating the baby in a chamber that directs blue-wavelength light to the baby's skin. The light penetrates the skin and breaks down bilirubin via a photochemical reaction over a period of several hours. When treatment is performed in a timely fashion, adverse outcomes can be avoided. Some neonates with jaundice, however, will develop adverse neurodevelopmental outcomes related to hyperbilirubinemia if not properly treated.

According to the Agency for Healthcare Research and Quality, part of the U.S. Department of Health and Human Services, neonatal jaundice is the single largest cause for hospital readmission of neonates in the U.S. This results in inefficient care and can also be highly stressful and disruptive for the parents and neonate.

Exposure to excess bilirubin in the central nervous system as a result of hyperbilirubinemia is toxic and may cause long-term developmental disabilities. These abnormalities may be subtle, and include hearing problems and low IQ. Subtle forms of disability are known as Bilirubin-Induced Neurological Dysfunction, or BIND. More severe bilirubin-induced disabilities, including respiratory failure and resulting death, can be referred to as Acute Bilirubin Encephalopathy, or ABE. Bilirubin toxicity can ultimately result in a chronic, severe, and disabling condition called kernicterus. Kernicterus is a cerebral palsy-like condition in which the patient lacks muscle tone and motor control, cannot operate self-sufficiently, and typically requires long-term care. The National Quality Forum has in the past described kernicterus as a "never event," one which physicians should ensure never occurs in their practice.

Limitations of Current Diagnostic Methods

It has been reported in peer-reviewed publications that the presence of hemolysis in a neonate with jaundice is a predictor of adverse neurodevelopmental outcomes. If neonates with high rates of hemolysis could be identified before they are discharged from the hospital, treatment could begin earlier, exposure to excessive bilirubin would be minimized and readmissions for jaundice would be reduced. Prior to the introduction of CoSense accurate tools for diagnosing hemolysis in neonates were not available in the market. Tests that are commonly performed to assess hemolysis such as serial hematocrit levels, reticulocyte counts, Coombs test and peripheral smear, are all invasive blood tests, involving painful heel sticks to draw the blood and are less useful in neonates due to physiologic changes resulting from childbirth. For example, hematocrit levels and reticulocyte counts may be elevated in neonates unrelated to pathological conditions and may therefore confound the diagnosis of hemolysis, which typically involves low hematocrit and high reticulocyte counts. The Coombs test is a blood test that detects antibodies that can cause hemolysis, is used extensively as a measure of hemolysis; however, it often requires a painful heel stick to draw a blood sample, and other conditions besides hemolysis may trigger a false positive or false negative Coombs test. In spite of this limitation, we believe that the Coombs test remains the most frequently used diagnostic for hemolysis by physicians.

Today, the AAP recommends that all neonates be routinely tested for bilirubin levels at some point prior to being discharged from the hospital, although other organizations such as the United States Preventive Services Task Force, or USPSTF, have not made similar recommendations. In many hospitals this is done via a blood test, although transcutaneous bilirubin meters are now available to test bilirubin levels non-invasively through the skin. Inaccurate results with use of these devices have been reported based on serum bilirubin level, measurement site, race, and ethnicity. In addition, bilirubin levels reflect only a point in time rather than the rate of increase, and therefore, may not address the risk of subsequent adverse outcomes. These tests do not capture the rate of bilirubin production or the presence/absence of hemolysis, leaving the

physician uncertain as to the patient's level of risk. Since many babies have bilirubin levels in a range described as "low and high intermediate risk" by current treatment guidelines, it is difficult for physicians to decide whether to treat aggressively or more conservatively.

Phototherapy is widely used to treat jaundice, and is applied to approximately 8% of all births in the U.S. However, phototherapy treatment disrupts the opportunity for parent-newborn bonding and is often highly stressful for infants and new parents. In some cases, particularly among low-risk newborns who are jaundiced, but not hemolyzing, phototherapy may not be necessary. In other cases, observation of jaundice and early testing for hemolysis may accelerate diagnosis and treatment with phototherapy. In all cases, understanding the rate of hemolysis is a critical part of providing timely and effective care. There is a significant need for a test to aid in the detection of hemolysis that is rapid, accurate, and easy to use across all acuity levels within neonatal care.

Also, neonates are typically discharged from the hospital at approximately 48 hours of normal birth in the U.S. and hospitals are under pressure to discharge even earlier, in order to reduce costs and manage inpatient capacity. Bilirubin levels, however, typically peak more than 72 hours post birth. We believe that neonates with hemolysis can experience bilirubin levels in the intermediate risk range at time of discharge, but can spike rapidly to neurotoxic levels in the post-discharge period, out of the range expected based on the "Bhutani nomogram."

Physicians need to identify the cause of the jaundice and, based upon these findings, determine whether the infant is at serious risk for BIND, ABE, or kernicterus. However, physicians often have a diagnostic dilemma as to what is causing the jaundice. It is often not possible, with current diagnostic techniques and clinical workflow, to test whether it is merely a physiologic jaundice that poses little risk, or some other process that presents a serious risk to the neonate. Risk arises primarily from the presence of hemolysis, which leads to hyperbilirubinemia that persists rather than resolving spontaneously. As a result of the serious consequences of hyperbilirubinemia, the AAP recommends that all neonates be closely monitored for jaundice, and has called for physicians to determine the presence or absence of hemolysis in order to make appropriate treatment decisions. As a result, there are both clinical need and physician interest in the development of accurate and non-invasive methods for detecting hemolysis. CoSense addresses this need by serving as a tool to measure a baby's exhaled CO to detect the rate of hemolysis accurately, and does so via a point-of-care measurement that does not require a heel stick. CoSense delivers results within minutes, which may enable more timely treatment than the current standard of care.

CoSense: FDA 510(k) Clearance and CE Mark Certification

CoSense, our first Sensalyze Technology Platform product to receive 510(k) clearance from the FDA and CE Mark certification, is a monitor of ETCO. CO is a direct byproduct of hemolysis, and based on extensive published data such as that from Stanford University, the rate of bilirubin production can be measured by analyzing the concentration of CO in a neonate's exhaled breath.

CoSense is a point-of-care device that consists of a light-weight, portable monitoring device and a single-use nasal cannula, which we refer to as our Precision Sampling Set, or PSS. The PSS is placed just inside the nostril of the patient and is connected to the device. The CoSense device is turned on and acquires the breath signal while the patient breathes. Appropriate sample acquisition takes an average of 30 seconds. The PSS can then be removed from the patient and the device takes another four minutes to report the test result.

The AAP recommends the use of ETCO monitoring for the detection of hemolysis. We believe ETCO monitoring will enable more rapid and appropriate treatment decisions and reduce overall costs of patient care. However, there is currently no device on the market other than CoSense that effectively measures ETCO in neonates.

With CoSense data, physicians may be able to quickly identify neonates with jaundice who are at risk of adverse neurological outcomes or other disability due to a high rate of hemolysis. The physician may then initiate earlier treatments for jaundice, such as phototherapy, when necessary. We believe the potential impact of CoSense should result in reduced neurodevelopmental abnormalities in neonates. In addition, CoSense may also help identify neonates who do not have excessive hemolysis, and therefore may not require phototherapy or serial bilirubin measurements. As a result, these neonates may be discharged from the hospital earlier, or with less intensive clinical follow-up. We believe this will reduce the total number of blood draws that are necessary. We also believe this will reduce the rate of readmissions, resulting in significant cost savings for the hospital.

CoSense has the following advantages that we believe will drive its adoption by hospitals, other medical institutions and physicians:

- rapid administration at the point-of-care, yielding results in approximately five minutes;
- non-invasive and minimally disruptive to the neonate;

- no requirement for specific breath maneuver;
- simple user interface that allows the healthcare professional to use it correctly with minimal training;
- no on-site calibration necessary; and
- accuracy and precision over a range of CO concentrations clinically relevant (less than 10 parts per million, or ppm, with 0.1ppm resolution) to detect the rate of hemolysis.

In addition, we believe the CoSense device is priced at a level that falls below the typical capital equipment purchasing threshold for a hospital or other medical institution in the U.S.

Clinical Trials

Seven investigator-sponsored clinical trials have been performed to validate the ability of CoSense to detect the presence of hemolysis. Four of these were performed in neonates. One was performed in neonates and children up to 17 years old. Two were performed in children with sickle cell anemia, or SCA, a disease which results in chronic hemolysis.

In a pilot clinical trial at Stanford University, a bench to bedside evaluation of CoSense was undertaken to identify hemolysis in neonates, and to correlate ETCO levels with bilirubin production as defined by levels of carboxyhemoglobin, or COHb, in the blood. When red blood cells are broken down, the pigment heme is released from the red blood cells. In turn, when heme is broken down, CO and biliverdin are produced in equimolar amounts. Biliverdin is a precursor of bilirubin, and is converted into bilirubin. CO combines with hemoglobin in the blood with high affinity to form carboxyhemoglobin, or COHb. Therefore, the level of COHb provides an accurate measurement of bilirubin production, or hemolysis. CO from COHb is released when the blood circulates through the lungs and as a result, levels of ETCO correlates to levels of COHb, bilirubin production and hemolysis. For accurate measurements of low levels of CO, gas chromatography is the method of choice.

In bench studies, inter-device accuracy and intra-device imprecision were evaluated in three different CoSense devices. In the clinical setting, 83 neonates who all had a gestational age, or GA, of more than 30 weeks and had birth weights of at least 1500 grams were tested. ETCO measurements, in triplicate, were compared to COHb levels measured by gas chromatography in the subset of 24 of the 83 neonates who consented to testing for COHb and were suspected of having hemolysis. Gas chromatography is a technique better suited to the laboratory than to high-volume clinical use, particularly in the point-of-care neonatal diagnostic setting. It requires a large, complicated chromatography instrument and highly trained staff.

A strong linear correlation between COHb and ETCO was seen (r= 0.93), confirming that ETCO values with CoSense accurately measure bilirubin production and therefore hemolysis. The results of this study were published in an article titled, “Evaluation of a new end-tidal carbon monoxide monitor from the bench to the bedside,” in Acta Paediatrica 2015.

The ability of CoSense to identify hemolysis in neonates with significant hyperbilirubinemia was evaluated at The Children’s Hospital of Zhejiang University School of Medicine in Hangzhou, China. Significant hyperbilirubinemia was defined as total serum bilirubin, TSB, levels that require phototherapy according to AAP guidelines. Investigators compared ETCO, as measured with CoSense, with current blood tests for hemolysis, such as hematocrit, or Hct, which measures the number of red blood cells, reticulocyte count, or Retic, which measures new red cell production levels, serum bilirubin test, and the Coombs Test. While these tests are often performed to detect hemolysis in neonates, they are not considered to be reliable in
the neonatal setting. The information that is gained from a combination of all these tests is therefore used to inform a determination of the presence or absence of hemolysis. Certain tests may be better than others for a given type of hemolysis, whereas ETCO levels are elevated due to hemolysis regardless of the cause.

Fifty-six neonates with significant hyperbilirubinemia participated in this non-randomized open-label trial. These data from the study showed that ETCO measurement with CoSense can provide the physician with similar information to that currently provided by invasive blood tests regarding the patient’s hemolytic status, but with a simple, non-invasive breath test.

In a clinical trial at Children’s Hospital & Research Center in Oakland, California, ETCO concentration was measured in children with SCA, who are known to have chronic hemolysis, using CoSense. Children between five and fourteen years old with SCA, who were not on regular transfusions, were eligible to participate in the trial. Children with exposure to second-hand smoke, acute respiratory infection or symptomatic asthma were excluded. Healthy children between five and fourteen years old served as matched controls. Up to three measurements were taken for each subject using CoSense, and the highest ETCO value was used. One control subject had a high ETCO value and was excluded

from the analysis since the subject was found to have asthma and was on anti-epileptic medication. The data from this trial showed that CoSense may be useful to monitor the rate of hemolysis in children with SCA. This results from this study were published in an article titled, “Point-of-care end-tidal carbon monoxide reflects severity of hemolysis in sickle cell anemia,” in Pediatric Blood & Cancer 2015.

Recently, another clinical trial was conducted at Children’s Hospital & Research Center in Oakland, California and UCSF Benioff Children’s Hospital, in sickle cell disease, or SCD, subjects ages 2 to18 years old and age-matched controls to validate the accuracy of a CoSense device that had an extended temperature operating range and to determine if the modified device could differentiate between children with sickle cell disease and healthy controls. Eleven SCD subjects and ten healthy age-matched controls were enrolled. The mean ETCO for SCD subjects was statistically significant. Thus, this study showed

that the modified CoSense device provided a reliable detection of hemolysis in the sickle cell subjects. Capnia would like to continue to develop this modified device to be used as a screening tool in countries with limited resources, the greatest amount of SCD births and where early mortality due to SCD is observed.

A study of 20 neonates and children with known hemolytic disorders, such as hereditary spherocytosis or pyruvate kinase deficiency, and 20 age-matched controls was conducted to compare ETCO measurements at Intermountain Healthcare Institutions in Utah (McKay-Dee NICU, McKay-Dee Pediatric Clinics, McKay-Dee Perinatal Research Outpatient Service, and Primary Children's Hospital Hematology Clinic). The known hemolytic disorders subjects were required to have a hemoglobin (Hbg) at least 10 g/dL based on lab tests performed in the last six months and confirmed within six weeks prior to breath sample collection. Neither group of subjects were to have had a blood cell transfusion within four weeks prior to breath sample collection. One ETCOc measurement was collected from each subject. Twelve out of the infants and children enrolled in each group (24 out of 40) were less than 1 year of age at the time of the ETCO measurement. Of these 12 subjects, seven were less than 1 month old at the time of the ETCO measurement (14 out of 40). The ETCO values of the 20 neonates and children with hemolytic diseases were higher than 20 age-matched controls. Thus, this study may show that CoSense can detect the differences in the rate of hemolysis between neonates and children who have known hemolytic anemia and healthy age-matched neonates and children.

In a separate study at Intermountain Healthcare Institutions, ETCO was measured in 30 healthy, term (at least 37 weeks gestational age) newborns within the first hours after birth and again just before discharge from to home to quantify the rate of hemolysis during the first days of life. Testing was 100% successful, whether newborns were awake or asleep. The 95% confidence intervals were 1.4 to 1.7 ppm. No differences were seen in ETCO values between neonates born vaginally versus by Cesarean section, nor between those whose mothers received pitocin during labor or did not receive pitocin to augment labor. This suggests that the hemolysis was not the result of bruising during delivery. This study provides further evidence that low-grade hemolysis occurs normally in the first days after birth.

The results of these two studies were published in an article titled, "End-tidal carbon monoxide as an indicator of hemolytic rate," in Blood Cells, Molecules and Diseases 2015.

In another study conducted at Intermountain Healthcare Institutions, ETCO was measured in 100 neonates with a total bilirubin greater than the 75th percentile on the Bhutani nomogram during birth hospitalization. Thirty-seven had elevated ETCO values (ETCO greater than 2 ppm) and 11 of these 37 were found to be Coombs positive and the remaining 26 had other etiologies. Thirty-six of the 37 with elevated ETCO had repeat total bilirubin monitoring within 24 hours of discharge from the hospital. Of the 100 neonates, none was re-hospitalized for jaundice treatment. In comparison, 3,535 neonates who did not have an ETCO measurement during this period at these hospitals had a total bilirubin, or TB, level greater than the 75th percentile on the Bhutani nomogram. Of these 3,535 neonates, 106 were re-hospitalized for jaundice between 3 and 11 days of life (rate = 2.99 per 100 neonates). This study showed that it is feasible to use CoSense to measure ETCO and, when an elevated ETCO is found during birth hospitalization, parents were likely to comply with advice to have the TB level rechecked within 24 hours of discharge. The results of this study were published in an article titled, "Measuring End-Tidal Carbon Monoxide of Jaundiced Neonates in the Birth Hospital to Identify Those with Hemolysis," in Neonatalogy 2016.

A multi-center investigator-sponsored trial to define the normative data (mean, median, range and interquartile ranges) for all term and late-preterm newborns for CoSense. The investigating institutions include Stanford University School of Medicine, Albert Einstein Medical Center, Beaumont Children's Hospital, University of Pittsburg Medical Center and McKay-Dee Hospital/Intermountain Healthcare. Enrollment in this study was completed in February 2016. Three-hundred sixty-six newborns were enrolled into this study. The data for all subjects enrolled are currently under review and analysis.

Another article titled, "Identification of neonatal hemolysis: an approach to pre-discharge management of neonatal hyperbilirubinemia," was electronically published ahead of print in Acta Paediatr. 2016 Jan 23. This article included results from 79 newborns with a GA greater than 35 weeks and birthweight greater than 2000 grams, who were enrolled at Lucile Packard Children's Hospital. For each newborn, up to four ETCO measurements were taken once per day for up to four days of life in conjunctions with TB levels. This study confirmed that pre-discharge

measurements of TB together with ETCO can be used as an index of increased bilirubin loads due to hemolysis.

Market Opportunity

Independent market research that we conducted has identified a large market opportunity for the CoSense device in the well-baby nursery and labor and delivery units in term neonates (less than 37 weeks), as well as in the neonatal intensive care unit, or NICU, in preterm births (less than 34 weeks) and late preterm births (between 34 and 37 weeks).

In the U.S. and E.U., there are approximately 8.1 million term births and 1.1 million preterm and late preterm births each year. Approximately 60% of term births, or approximately 4.9 million babies, and 80% of preterm and late preterm babies, or approximately 900,000 babies, are jaundiced. These babies who have concurrent hemolysis are at greatest risk for adverse outcomes. We believe that neonates who are at risk for hemolysis and are candidates to receive one or more CoSense tests during their hospital stay.

Today, the presence of jaundice triggers either a transcutaneous or serum bilirubin test. With the availability of CoSense, physicians may complement bilirubin testing with hemolysis testing in order to perform a more complete clinical assessment. Neonates who are jaundiced but not hemolyzing may receive conservative management or phototherapy. Neonates with jaundice found to be hemolyzing will likely receive early phototherapy and also additional testing such as the Coombs test, Hct or Retic to diagnose the underlying cause of hemolysis. We believe that CoSense will allow physicians to reduce the number of neonates that receive these more invasive and more costly tests for hemolysis.

Sales and Marketing

CoSense is indicated for the measurement of ETCO, which can be used for the detection of the rate of hemolysis. The initial target market for CoSense is to measure ETCO levels in neonates to evaluate for the presence, or the rate, of hemolysis. In January of 2016, we entered into a distribution agreement with Bemes to market and distribute CoSense and our consumable PSS exclusively for sales, marketing, distribution and field service activities in the U.S. Under the terms of this agreement, Bemes currently has the exclusive right for sales, marketing, distribution and field service activities for CoSense in the U.S. Bemes relies on a network of subdistributors, which will allow nationwide distribution of CoSense with 52 sales representatives in eight independent territories covering almost every state. Sales training for the distributors was completed at the end of March 2016. While our efforts will continue to focus on establishing an installed base of CoSense devices and building clinical support for the device, we expect sales of the consumable PSS to be the largest component of our revenue over time. In addition, we are currently reviewing whether to terminate this agreement with Bemes and work directly with the network of sub-distributors.

In the rest of the world, we expect to partner with distributors in each country or region, with oversight and marketing assistance from our own personnel. In 2016, we entered into distribution agreements with independent distributors located in China, India and Canada. We continue discussions with distributors in additional geographies.

We expect the majority of our revenues to result from sales of consumables. Because we believe customers will order these repeatedly once they have adopted CoSense as part of their standard procedures, we expect that our sales force can drive higher revenue per salesperson than might otherwise be the case.

Key elements of our sales and marketing strategy include:

- Focus efforts on growing the volume of tests performed and associated consumables used. We plan to focus specifically on sales to the neonatal intensive care unit, or NICU, well-baby nursery, and labor/delivery units within each hospital. Because CoSense is a point-of-care device, each of these units of the hospital is a separate opportunity for CoSense placement.
- Establish and engage a network of distributors in the E.U., as well as elsewhere in the world. We may establish continuing operations at a location in the E.U. to ensure close coordination and effective execution of the CoSense sales and marketing plan in the E.U.
- Price the CoSense device at a level that allows hospitals to purchase it without protracted review via a “capital purchase committee” or analogous body. We believe that the cost of goods of CoSense devices allows us flexibility in setting this price, and we also believe we can offer customer hospitals attractive financing options to smooth out costs associated with the device purchase.
- Price the CoSense consumable sampling set at a price that is competitive with the current costs of performing the Coombs Test and other associated invasive assays. We believe that this cost offset, complemented by potential improvements in readmission rates and clinical outcomes, will provide hospital decision-makers with a compelling

economic case for adoption of CoSense.

- Build awareness of the AAP treatment guidelines, and of the benefits of CoSense, via medical education efforts to key clinical audiences, including neonatologists, pediatricians, obstetricians, and pediatric nurses.

- Collaborate with key specialty societies, including the AAP, Pediatric Academic Societies, American Academy of Family Physicians and patient advocacy groups such as Parents of Infants and Children with Kernicterus, to ensure ongoing support for ETCO testing in clinical guidelines and to identify opportunities for expanding awareness of ETCO among their respective constituencies.
- Support clinical trials and publications that expand the base of evidence supporting broad adoption of CoSense. We expect these efforts will build support for the clinical benefits to patients as well as economic benefits to various stakeholders in the healthcare system.

We expect that we and our distributor will expand our sales efforts to encompass lower-volume birthing centers in the U.S. once a sufficient proportion of the larger hospitals have begun to use CoSense. We may also selectively initiate direct sales to certain countries in the E.U. Furthermore, we see potential to use CoSense to make more rapid assessments of jaundiced babies in the outpatient pediatric setting, where new parents are frequently directed for follow-up care after hospital discharge. We will continue to evaluate expansion opportunities and pursue those where the potential to accelerate our business is deemed sufficient for the investment we put at risk.

Pricing and Reimbursement

We expect to continue to sell the CoSense device at a price below the typical capital expenditure approval threshold levels of most hospitals and other medical institutions in the U.S. The decision to buy, therefore, will likely be driven at the departmental rather than at the institutional level. The primary decision makers are expected be the neonatologists and nurse managers in the pediatrics and neonatology departments. Our initial efforts are focused on expanding the installed base of devices and will be followed by efforts to increase use of the disposable sampling set. The business model anticipates a significant proportion of the revenues coming from the disposable sales, even more so in later years as the number of total CoSense devices in use in the field increases. With manufacturing scale up, we expect to achieve reduced cost of goods that will lead to scaleable future growth.

Since the use of CoSense is almost entirely in the inpatient setting around the time of birth, reimbursement may be in the form of a Diagnosis-Related Group, or DRG. Frequently referred to as a bundled payment, the DRG is a specific flat-fee payment amount for all services performed by a medical institution pursuant to a single diagnosis. We can, therefore, be reimbursed for the cost of a test directly from an institution without the need to approach payors such as insurance companies, or to obtain a separate reimbursement cost code. Hospital decisions to adopt new technologies for inpatient care are usually driven by improved outcomes and reduced costs of patient care. We expect that the use of CoSense will both improve outcomes related to hyperbilirubinemia and reduce the need for certain diagnostic tests in a subset of neonates with jaundice, which, as a result, will reduce overall testing costs. We also believe that positive identification of infants with hemolysis will lead to a reduced rate of readmissions for jaundice, and this array of benefits may support adoption of CoSense by clinicians and their institutions. We also plan to undertake a comprehensive effort to partner with key physician specialty societies, physician opinion leaders and patient advocacy groups to educate and inform payer stakeholders. The AAP guidelines recommend ETCO detection to confirm the presence of hemolysis in neonates requiring phototherapy, neonates unresponsive to phototherapy or readmitted for phototherapy, and neonates with bilirubin levels approaching transfusion levels. In general, payor policies related to the care of neonates with jaundice reflect third-party treatment guidelines, and in this case the AAP guidelines favor use of ETCO testing, which CoSense is able to perform.

Competition for CoSense

Currently CoSense is the only device commercially available with the sensitivity and accuracy necessary to detect ETCO levels that are meaningful for monitoring the rate of hemolysis in neonates, and we do not know of any such device that is under development by any party. From 2001 to 2004, Natus Medical marketed the CO-Stat device for detection of ETCO in neonates. The Natus product was withdrawn from the market due to poor sales. We believe Natus' CO-Stat did not achieve commercial success due to several disadvantages that we have overcome with our product, including a lack of consistent accuracy, limited ability to compensate for environmental factors such as humidity and heat, high price, and poor ease of use, including a requirement for frequent calibration.

In addition, devices are commercially available to measure CO poisoning from external sources, but these are less-sensitive devices that are not appropriate for detecting ETCO in the low concentrations (less than 10 ppm), small volumes and high breath rates that are clinically relevant in neonates. CoSense has the ability to overcome these

problems using our Sensalyze technology. Several companies and academic groups have capabilities sufficient to develop such devices, and these parties may have significant resources to devote to research, development, and commercialization of devices that may compete with CoSense as well as technologies that compete with our Sensalyze Technology Platform generally. Competition within our target market will depend on several factors, including:

- quality and strength of clinical and analytical validation data;
- confidence of health care providers in diagnostic results;
- reimbursement and payment factors;
- inclusion in practice guidelines;
- cost-effectiveness;
- ease of use; and
- the strength of our intellectual property.

Today, physicians primarily diagnose hemolysis via Coombs and other blood tests, and these will represent the primary competition to CoSense initially. These tests do not capture the rate of bilirubin production or the presence/absence of hemolysis, leaving the physician uncertain as to the patient's level of risk. We believe that we can demonstrate compelling advantages over such tests, including faster results, the ability to avoid painful blood draws and greater diagnostic clarity and accuracy. We also believe we will be able to demonstrate economic and workflow advantages over the existing diagnostic practice.

Our Sensalyze Technology Platform

A variety of medical diagnostic testing is performed via measurement of gas concentrations, either from blood samples or from exhaled breath. Examples include capnometry and pulse oximetry, both routinely used in patient monitoring. Devices used for detecting the presence of various analytes in exhaled breath typically rely on the patient performing a specified breath maneuver. Examples of such maneuvers include breath holding, forced expiration, or breathing at a specified rate. The use of these devices is limited to those who can perform such maneuvers, such as adults and older children.

The limitations of existing breath-based technologies are particularly problematic in neonates. Neonates typically have very rapid and irregular breathing patterns. They also inhale and exhale relatively small volumes, which limits the accuracy of devices that require the larger-volume sample sizes exhaled by older patients. In addition, they are not able to perform specified breath maneuvers. Our Sensalyze Technology Platform allows the measurement of analytes in all patients, from neonates to adults, regardless of their ability to actively perform a breath maneuver.

Our Sensalyze Technology Platform combines hardware, sensors, and software to provide the following novel capabilities:

- Identification of full breaths that follow a normal pattern, also known as "physiologic" breaths. Our platform can identify physiologic breaths even if the patient is breathing very rapidly, a capability that is particularly relevant in infants.
- Capture of individual exhaled breaths, and segmentation of the breath into different components such as "end-tidal", "upper airway", and "lower airway". This may allow the localization of the source of a given analyte to a specific anatomic area.
- Ability to move a specific micro-liter component of breath to a sensor module. When combined, these capabilities provide a novel patent protected platform for non-invasive detection of various analytes.

Sensalyze Technology Platform — Research and Development of Additional Diagnostic Products

Our primary focus is currently on the commercialization of CoSense. Once the CoSense business is generating adequate revenue, we intend to utilize our research and development expertise to develop devices that leverage the capabilities of our Sensalyze Technology Platform. We expect to introduce additional products of our own over time and intend to develop additional diagnostic tests for analytes that might be found in the exhaled breath. These include the following diagnostic opportunities:

- Nitric oxide or NO, for assessment and management of asthma in infants and young children;
- End-tidal CO_2 for neonates;
- Hydrogen breath testing for infants with malabsorption problems;

- Carbon monoxide levels for hemolysis, CO poisoning or Sickle Cell Screening;
- Acetone, nitrites for diabetes;
- Volatile Organic Compounds, or VOC, for cancer, heart failure and multiple sclerosis; and
- Alkanes, transplant rejection. We may also license elements of our Sensalyze Technology Platform to other companies that have complementary development or commercial capabilities.

NeoForce Pulmonary Solutions

Approximately 10% of newborns require some assistance to begin breathing at birth and represents the number of patients that would benefit from our products. Of this 10%, approximately 1% requires extensive resuscitative measures. Although the vast majority of newly born infants do not require intervention to make the transition from intrauterine to extra uterine life, because of the large number of births, a sizable number will require some degree of resuscitation.

Respiratory adaptation

In utero, most of the blood flow is shunted away from the lungs and directed to the placenta where fetoplacental gas exchange occurs. After birth, the airways and the alveoli must be cleared of fetal lung fluid so that the lungs can operate as a functional respiratory unit providing adequate gas exchange. Pulmonary blood flow must increase, and spontaneous respirations must be established.

NeoForce T-Piece Resuscitation Platform

A T-piece resuscitator is a manually operated resuscitation delivery device used for infants and small children (less than 10 kg) to effectively deliver inhalation breaths at preset peak inspiratory pressures, or PIP, and a small back pressure to keep the lungs from collapsing on exhalation, known as positive end expiratory pressures, or PEEP, at a preset Fi02, or percent oxygen. There are two components to T-piece Resuscitation, the “Box or T-piece Resuscitator” and a single patient use circuit. The circuit connects to the box on one end and the patient on the other through a mask. The box controls the PIP, and the circuit controls the PEEP through an adjustable valve. In general, it is a modern replacement for the traditional bag and mask which requires significant user training and experience to deliver breaths to infants with tiny and very delicate lungs and may result in injury due to inappropriately high pressure and/or larger volumes.

Resuscitation and the First Breaths of Life

Neonatal resuscitation skills are essential for all health care providers who are involved in the delivery of newborns. The transition from fetus to newborn requires intervention by a skilled individual or team in approximately 10% of all deliveries. In the U.S., 81% of all babies are born in nonteaching level I or II hospitals. In these hospitals, the volume of delivery service may not provide sufficient economic justification for the continuous in-hospital presence of specialists with high-risk delivery room experience, as recommended by the AAP Neonatal Resuscitation Guidelines and the American College of Obstetricians and Gynecologists. Perinatal asphyxia and extreme prematurity are the 2 complications of pregnancy that most frequently necessitate complex resuscitation by skilled personnel. However, only 60% of asphyxiated newborns can be predicted ante partum. The remaining newborns are not identified until the time of birth. Additionally, approximately 80% of low-birth-weight infants (infants less than 2kg) require resuscitation and cardio pumonary stabilization at post delivery.

Nearly one half of newborn deaths (many of which involve extremely premature infants) occur during the first 24 hours after birth. Many of these early deaths also have a component of asphyxia or respiratory depression as an etiology. For the surviving infants, effective management of asphyxia in the first few minutes of life can influence long-term outcome.

Even though prenatal care can identify many potential fetal difficulties ante partum, allowing maternal transfer to a referral center for care, many women who experience preterm labor are not identified prospectively and therefore are not appropriately transferred to a tertiary perinatal center. Consequently, many deliveries of extremely premature infants occur in smaller hospitals.

For these reasons, all personnel involved in delivery room care of the newborn should be trained adequately in all aspects of neonatal resuscitation. Additionally, equipment that is appropriately sized to resuscitate infants of all gestational ages should be available in all delivering institutions, even if the institution does not care for preterm or

intensive care infants.

Market Opportunity

The United Nations estimates the annual number of births worldwide to be approximately 143 million. Of these births, the number requiring assisted ventilation is approximately 10% of all births which represents the theoretical maximum addressable market potential. The addressable market is however much lower since a large number of infants are born in regions that do not have access to advanced resuscitation facilities, people or equipment. In general the market can be segmented along the economic development status of the country region where the infant is born and our current solutions are aligned to more developed regions such as the U.S., E.U., and portions of the Middle East.

In the U.S. and E.U., there are approximately 8.1 million term births and 1.1 million preterm and late preterm births each year. Approximately 10% of term births, or approximately 800,000 babies, and 80% of preterm and late preterm babies, or approximately 88,000 babies, will need assisted ventilation during the birthing process or later in the NICU as a supplement to long term ventilation management,

In the U.S. approximately the majority of all birthing hospitals have or use some form of T-piece resuscitation and are potential consumers of our T-piece solutions which include a delivery device (NeoPiP T-piece Resuscitator) or our universal T-piece single patient use circuit (NeoPiP Circuit).

Sales and Marketing

We intend to leverage the existing channels that we have in place to sell the products through NFI. NFI has a well-established and efficient telemarketing presence that will supplement and extend our current distribution channel.

In the U.S., we will continue to sell via a direct sales force, with potential augmentation of our reach via distributors.

In the E.U., we expect to partner with distributors in each country, with oversight and marketing assistance from our personnel.

Our U.S. direct sales efforts will continue to focus on large hospital systems with high volumes of births as the call points and decision makers for both NFI and CoSense customers are nearly identical. NFI has an installed base of over 300 customers and the existing relationships are anticipated to have a positive impact on creating interest in CoSense.

The majority of NFI revenues will continue to be sales of our consumable T-piece circuits.

Key elements of our sales and marketing strategy include:

- Focus efforts on growing the volume of consumables used as our universal circuit will work with all installed base devices of NFI and its competitors.
- Establish and engage a network of distributors in the E.U. and other international markets as conditions warrant.

We will continue to evaluate expansion opportunities and pursue those where the potential to accelerate our business is deemed sufficient for the investment we put at risk.

Pricing and Reimbursement

NFI sells its products into a relatively mature market with established pricing and acquisition methods in place where the hospital focuses on price, clinical utility and improved safety as measures to “switch”. The decision to buy, therefore, will continue be driven at the departmental level controlled by the nursing management team overseeing the newborn areas of the institution, in conjunction with respiratory therapy.

NFI is under contract with MedAssets, a GPO that represents approximately 35% of all hospitals in the US and sets fixed pricing as a function of volume. We will continue to utilize this contract to help expand sales of our neonatology products and will assess other GPO organizations as conditions warrant.

There are no reimbursement issues for the NFI line of products as the devices and consumables for resuscitation are considered mission critical and covered under the hospitals operating budget at the department level.

Competition for NeoForce Recitation Solutions

T-piece resuscitation has been around since the early 1900’s but only became mainstream in the past 30 years mostly due to the efforts of Fisher and Paykel and their NeoPuff ® line of resuscitation devices. Their efforts in conjunction with the widespread integration of T-piece devices built into the radiant warmers used in the delivery room has created a substantial installed base of units that can use our consumable circuit.

Companies that currently produce a T-piece solution include; GE Health Care, Fisher and Paykel, Drager Medical, Mercury Medical and CarFusion. Many of our competitors are part of large companies where T-piece is treated as an accessory or an extension of a larger portfolio of unrelated adult and pediatric solutions. Our focus on this market combined with our small size allows us to be nimble and responsive to changing market dynamics.

Nasal CO_2 Technology

Trigeminal Neuralgia

TN is a clinical condition characterized by debilitating pain in regions innervated by one or more divisions of the trigeminal nerve. The pain is typically described as intense, sharp and stabbing, and is often described as one of the most painful conditions known to humans. It may develop without apparent cause or be a result of another diagnosed disorder. Peripheral TN is caused by a variety of diseases, including multiple sclerosis and herpes zoster.

The International Headache Society describes TN as a disorder characterized by recurrent unilateral brief electric shock-like pains, abrupt in onset and termination, limited to the distribution of one or more divisions of the trigeminal nerve and triggered by innocuous stimuli. There may be persistent background facial pain of moderate intensity. Based on extensive review of literature, we currently estimate that approximately 180,000 people are afflicted with TN in the U.S.

We have orphan drug designation for our nasal, non-inhaled CO_2 technology for the treatment of TN. We filed an IND with the FDA and started enrolling patients in a pilot clinical trial in early 2016.

Cluster Headache

Cluster headaches affect approximately 0.2% of the population, and are characterized by recurring bouts of excruciating pain in one side of the head. In episodic cluster headaches, episodes of pain typically last from 15 minutes to three hours and can occur several times a day over several months before remitting. The same pattern often recurs multiple times over a patient's lifetime. Approximately 10% to 15% of cluster patients have chronic cluster headaches, which are characterized by continuing pain with no remission. The pain of cluster headache may be significantly greater than other conditions, such as severe migraine.

We have an agreement with Clinvest, a division of Banyan Group, Inc., to conduct an investigator-sponsored clinical trial evaluating our nasal, non-inhaled carbon dioxide on up to 25 patients with episodic cluster headaches.

We have also commenced enrollment in a pilot, single-center, investigator-sponsored clinical trial evaluating our proprietary nasal, non-inhaled CO_2 technology for the treatment of cluster headaches. The primary efficacy endpoint of the trial is the greatest change from pre-treatment headache pain intensity to post treatment.

Manufacturing

We currently manufacture CoSense monitors at our facility in Redwood City, California. We assemble components from a variety of original equipment manufacturer, or OEM, sources. Our manufacturing facility is registered with the FDA and certified to the ISO 13485 standard, the internationally harmonized regulatory requirement for quality management systems of medical device companies. We may, depending on sales volume and ongoing requirements in specific sales geographies, outsource manufacturing of components, or finished goods, to various OEMs in the future. We have manufactured the Serenz device in partnership with an OEM supplier based in Shenzhen, China and intend to manufacture future supply with this same OEM supplier.

NFI has its operations in Ivyland, Pennsylvania and is FDA registered and ISO 13485 certified. NFI assembles and tests the NeoPip resuscitators at its facility in Ivyland. The NeoPiP circuit is manufactured in Taiwan at an FDA registered ISO 13485 facility, with inventory stocked at NFI for distribution.

Intellectual Property

Our Sensalyze Technology Platform Patent Portfolio

Our patent portfolio surrounding our Sensalyze Technology Platform, including CoSense, consists of one issued U.S. patent, four pending U.S. non-provisional patent applications, and eight pending U.S. provisional patent applications. Three of the non-provisional filings have corresponding Patent Cooperation Treaty, or PCT, filings and are still eligible for expansion into other geographies. It is our intent to file these, and future cases, in other major commercial geographies over time. Our

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issued U.S. patent (no. 8,021,308) expires in August 2027. The pending patent applications, if issued, would likely expire on dates ranging from 2023 through 2034.
The issued patent and patent pending applications include:

- detection and storage of discrete portions of a breath;
- methods of diversion and isolation of gases to enable measurement within a breath pattern;
- specific compositions of valving and pumps to route airflow in a tightly controlled manner;
- collection methods for increasing the precision of measurement of small volumes of gas;
- identifying a “physiologically representative” breath, including both algorithm and physical capture; and
- various methods for arrangement and specification of components to enhance precision and compensate for factors that cause inaccurate measurements.

On May 11, 2010, we entered into an Asset Purchase Agreement with BioMedical Drug Development, Inc., or BDDI, pursuant to which BDDI agreed to sell certain technology to us and BDDI received and was entitled to receive, among other consideration, certain royalty payments related to the technology. On June 4, 2012, George Tidmarsh and BDDI entered into an Asset Purchase Agreement, pursuant to which, among other things, the Asset Purchase Agreement was assigned and transferred to Mr. Tidmarsh. On June 30, 2015, we entered into an Agreement and First Amendment to Asset Purchase Agreement with Mr. Tidmarsh and BDDI, whereby, among other things patent was purchased by us and, the royalty payments under the Asset Purchase Agreement were terminated. Pursuant to the Agreement and First Amendment to Asset Purchase Agreement, we (i) entered into a Common Stock Purchase Agreement with Mr. Tidmarsh whereby we issued 40,000 shares of Common Stock to Mr. Tidmarsh and (ii) paid $150,000 to Mr. Tidmarsh and agreed to pay an additional $100,000 on each of the six, twelve and eighteen month anniversary of the Agreement and First Amendment to Asset Purchase Agreement. On December 21, 2016, we paid the last installment of $100,000. We have capitalized the fair value of the patent purchased as an intangible asset on our consolidated balance sheet, and we are amortizing the intangible asset over the remaining useful life of the patent.

Serenz Patent Portfolio
Successful application of therapeutic gases to the nasal mucosa is generally dependent on specific dosing, concentration, and rate of gas outflow. The CO2 gas used in the Serenz product is packaged in small sealed cylinders with relatively high internal pressure; regulating the flow of gas from this high pressure cylinder to the relatively low flow rates required for Serenz presents significant technical challenges. Our Serenz patent portfolio addresses these challenges.
Our Serenz patent portfolio consists of over 30 issued patents and over 40 pending patent applications. In the U.S., twelve issued patents, one allowed non-provisional patent application, and 7 pending non-provisional patent applications cover the Serenz technology. The U.S. patents and patent applications have corresponding issued patents and pending patent applications in developed nations. The expiration dates for the issued patents vary, with the latest being in 2022. Patent term extension due to regulatory review may be requested in the U.S. based upon one or more of the issued U.S. patents under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act.

- Our pending applications, when issued, would likely expire between 2020 and 2033.
- Our issued patents and pending patent applications include claims directed to:
  - gas dispensing devices, including various nosepiece configurations, pressure regulators, and cylinder configurations;
  - methods for delivering therapeutic gases to patients;
  - the treatment of various medical conditions via delivery of therapeutic gases to the nasal cavity; and
  - combined delivery of gases with other therapeutic agents.

NFI Patent Portfolio

NFI has designed and patented a device (Ispira) leveraging its neonatal resuscitation product platform to provide effective rescue breaths to pediatric and adult patients in conjunction with integrated cardiac defibrillators.
Ispira is intended to address a need for improving the efficacy of pulmonary resuscitation in adults and pediatric patients. In the neonatal environment there has been a desire to control manual emergency resuscitation with respect to peak inspiratory pressure, positive end expiratory pressure and breath rate. Ispira brings this capability to the adult and pediatric patient market. The alternative to such a device is the BVM or anesthesia bag. The BVM bag is a device that functions as a bellows or bladder to deliver air to a patient by manual compression of the bag. The volume and pressure of delivered gas using manual compression is a function of many variables that include the size and strength of the person's hand, familiarity with the device and even the level of fatigue of the person providing resuscitation. Each breath delivered by the BVM will be different and in some cases the difference can be significant.
A U.S. utility patent application for the Ispira was filed with the U.S. Patent and Trademark Office on July 17, 2007 and was assigned serial number 11/779,037, or the US Application. Claims 1-25 were accepted and pending in the application. The US Application was published as US 2009/0020127 on January 22, 2009. The patent was subsequently issued in July of 2011 and assigned patent #7,980,244. An international patent application under the PCT was filed on July 17, 2008 and assigned application number PCT/US2008/070332, or the PCT Application. The PCT Application claims priority to the US Application. The PCT Application published as PCT publication WO2009/012386 on January 22, 2009. An International Search Report, or ISR, was issued on January 30, 2009, for the PCT Application. In the ISR, claims 1-25 were found to be novel and to have industrial applicability.
Government Regulation Federal Food, Drug, and Cosmetic Act
In the U.S., diagnostic assays are regulated by the FDA as medical devices under the Federal Food, Drug, and Cosmetic Act, or FFDCA. We received initial FDA 510(k) clearance for CoSense in the fourth quarter of 2012 for the monitoring of CO from endogenous and exogenous sources in exhaled breath, particularly in smoking cessation programs for the screening of CO poisoning and smoke inhalation. In the first quarter of 2014, CoSense received 510(k) clearance for the monitoring of CO from endogenous sources, including hemolysis, and exogenous sources, including CO poisoning and smoke inhalation, in exhaled breath. Serenz has not yet commenced any process for regulatory approval in the U.S. We also plan to seek FDA clearance or approval for other diagnostic products currently under development. There are two regulatory pathways to receive authorization to market diagnostics: a 510(k) premarket notification and a premarket approval application, or PMA. The FDA makes a risk-based determination as to the pathway for which a particular diagnostic is eligible. CoSense was cleared via the 501(k) premarket notification pathway as a Class II medical device.
The information that must be submitted to the FDA in order to obtain clearance or approval to market a new medical device varies depending on how the medical device is classified by the FDA. Medical devices are classified into one of three classes on the basis of the controls deemed by the FDA to be necessary to reasonably ensure their safety and effectiveness. Class I devices are subject to general controls, including labeling, registration and listing and adherence to FDA's quality system regulation, which are device-specific good manufacturing practices. Class II devices are subject to general controls and special controls, including performance standards and postmarket surveillance. Class III devices are subject to most of these requirements, as well as to premarket approval. Most Class I devices are exempt from premarket submissions to the FDA; most Class II devices require the submission of a 510(k) premarket notification to the FDA; and Class III devices require submission of a PMA. Most diagnostic kits are regulated as Class I or II devices and are either exempt from premarket notification or require a 510(k) submission.
510(k) premarket notification. A 510(k) notification requires the sponsor to demonstrate that a medical device is substantially equivalent to another marketed device, termed a "predicate device," that is legally marketed in the U.S. and for which a PMA was not required. A device is substantially equivalent to a predicate device if it has the same intended use and technological characteristics as the predicate; or has the same intended use but different technological characteristics, where the information submitted to the FDA does not raise new questions of safety and effectiveness and demonstrates that the device is at least as safe and effective as the legally marketed device. Under current FDA policy, if a predicate device does not exist, the FDA may make a risk-based determination based on the complexity and clinical utility of the device that the device is eligible for de novo 510(k) review instead of a requiring a PMA. The de novo 510(k) review process is similar to clearance of the 510(k) premarket notification, despite the

lack of a suitable predicate device.

The FDA's performance goal review time for a 510(k) notification is 90 days from the date of receipt, however, in practice, the review often takes longer. In addition, the FDA may require information regarding clinical data in order to make a decision regarding the claims of substantial equivalence. Clinical studies of diagnostic products are typically designed with the primary objective of obtaining analytical or clinical performance data. If the FDA believes that the device is not substantially equivalent to a predicate device, it will issue a "Not Substantially Equivalent" letter and designate the device as a Class III device, which will require the submission and approval of a PMA before the new device may be marketed. Under certain

circumstances, the sponsor may petition the FDA to make a risk-based determination of the new device and reclassify the new device as a Class I or Class II device. Any modifications made to a device, its labeling or its intended use after clearance may require a new 510(k) notification to be submitted and cleared by FDA. Some modifications may only require documentation to be kept by the manufacturer, but the manufacturer's determination of the absence of need for a new 510(k) notification remains subject to subsequent FDA disagreement.

The FDA has undertaken a systematic review of the 510(k) clearance process that includes both internal and independent recommendations for reform of the 510(k) system. The internal review, issued in August 2010, included a recommendation for development of a guidance document defining a subset of moderate risk (Class II) devices to include implantable, life-supporting or life-sustaining devices, called Class IIb, for which additional clinical or manufacturing data typically would be necessary to support a substantial equivalence determination. In the event that such new Class IIb sub-classification is adopted, we believe that most of the tests that we may pursue would be classified as Class IIa devices having the same requirements of the current Class II designation. In July 2011, the Institute of Medicine, or IOM, issued its independent recommendations for 510(k) reform. As the FDA receives public comment on the IOM recommendations and reconciles its plan of action to respond to both the internal and IOM recommendations, the availability of the 510(k) pathway for our diagnostic tests, and the timing and data burden required to obtain 510(k) clearance, could be adversely impacted. We cannot predict the impact of the 510(k) reform efforts on the development and clearance of our future diagnostic tests.

De Novo 510(k). If a previously unclassified new medical device does not qualify for the 510(k) pre-market notification process because there is no predicate device to which it is substantially equivalent, and if the device may be adequately regulated through general controls or special controls, the device may be eligible for de novo classification through what is called the de novo review process. In order to use the de novo review process, a company must receive a letter from the FDA stating that, because the device has been found not substantially equivalent to a legally marketed Class I or II medical device or to a Class III device marketed prior to May 28, 1976 for which the FDA has not required the submission of a PMA application, it has been placed into Class III. After receiving this letter, we, within 30 days, must submit to the FDA a request for a risk based down classification of the device from Class III to Class I or II based on the device's moderate or low risk profile which meets the definition of a Class I or Class II medical device. The FDA then has 60 days in which to decide whether to down classify the device. If the FDA agrees that a lower classification is warranted, it will issue a new regulation describing the device type and, for a Class II device, publish a Special Controls guidance document. The Special Controls guidance document specifies the scope of the device type and the recommendations for submission of subsequent devices for the same intended use. If a product is classified as Class II through the de novo review process, then that device may serve as a predicate device for subsequent 510(k) pre-market notifications.

Premarket approval. The PMA process is more complex, costly and time consuming than the 510(k) process. A PMA must be supported by more detailed and comprehensive scientific evidence, including clinical data, to demonstrate the safety and efficacy of the medical device for its intended purpose. If the device is determined to present a "significant risk," the sponsor may not begin a clinical trial until it submits an investigational device exemption, or IDE, to the FDA and obtains approval from the FDA to begin the trial.

After the PMA is submitted, the FDA has 45 days to make a threshold determination that the PMA is sufficiently complete to permit a substantive review. If the PMA is complete, the FDA will file the PMA. The FDA is subject to a performance goal review time for a PMA of 180 days from the date of filing, although in practice this review time is longer. Questions from the FDA, requests for additional data and referrals to advisory committees may delay the process considerably. Indeed, the total process may take several years and there is no guarantee that the PMA will ever be approved. Even if approved, the FDA may limit the indications for which the device may be marketed. The FDA may also request additional clinical data as a condition of approval or after the PMA is approved. Any changes to the medical device may require a supplemental PMA to be submitted and approved.

Regulation of Pharmaceuticals or Combination Products. In the U.S., the FDA may determine that Serenz should be regulated as a combination product or as a drug. The sales and marketing of pharmaceutical products in the U.S. are subject to extensive regulation by the FDA. The FFDCA and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling,

promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable FDA or other requirements may subject a company to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, a clinical hold, warning letters, recall or seizure of products, partial or total suspension of production, withdrawal of the product from the market, injunctions, fines, civil penalties or criminal prosecution.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the U.S. The process required by the FDA before a drug may be marketed in the U.S. generally involves:

- completion of pre-clinical laboratory and animal testing and formulation studies in compliance with the FDA's current good laboratory practice regulation;
- submission to the FDA of an IND, application for human clinical testing which must become effective before human clinical trials may begin in the U.S.;
- approval by an institutional review board, or IRB, at each clinical trial site before a trial may be initiated at the site;
- performance of adequate and well-controlled human clinical trials in accordance with current good clinical practices, or GCP regulations, to establish the safety and efficacy of the proposed drug product for each intended use;
- satisfactory completion of an FDA pre-approval inspection of the facility or facilities at which the product is manufactured to assess compliance with the FDA's current Good Manufacturing Practices, or cGMP, regulations, and for devices and device components, the FDA's Quality Systems Regulation, or QSR, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- submission to the FDA of an NDA;
- satisfactory review by an FDA advisory committee, if applicable; and
- FDA review and approval of the NDA.

The pre-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our future products will be granted on a timely basis, if at all. Pre-clinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The results of pre-clinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Some pre-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions relating to one or more proposed clinical trials and places a trial on clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Further, an independent IRB, covering each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and informed consent information for subjects before the trial commences at that site and it must monitor the study until completed. The FDA, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk or for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials involve the administration of an investigational drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Sponsors of clinical trials generally must register and report, at the NIH-maintained website ClinicalTrials.gov, key parameters of certain clinical trials. For purposes of an NDA submission and approval, human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

Phase 1: The drug is initially introduced into healthy human subjects or patients and tested for safety, dose tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness.

Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more extensive Phase 3 clinical trials.

Phase 3: These are commonly referred to as pivotal studies. When Phase 2 evaluations demonstrate that a dose range of the product appears to be effective and has an acceptable safety profile, Phase 3 trials are undertaken in large patient populations to further evaluate dosage, to obtain additional evidence of clinical efficacy and safety in an expanded patient

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population at multiple, geographically-dispersed clinical trial sites, to establish the overall risk-benefit relationship of the drug and to provide adequate information for the labeling of the drug.

Phase 4: In some cases, the FDA may condition approval of an NDA for a future product on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after NDA approval. Such post-approval trials are typically referred to as Phase 4 studies.

The results of product development, pre-clinical studies and clinical trials are submitted to the FDA as part of an NDA. NDAs must also contain extensive information relating to the product's pharmacology, CMC and proposed labeling, among other things.

For combination products, the FDA's review may include the participation of both the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health, which may complicate or prolong the review.

Before approving an NDA, the FDA may inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP, and if applicable, QSR, requirements and are adequate to assure consistent production of the product within required specifications. Additionally, the FDA will typically inspect one or more clinical sites to assure compliance with GCP before approving an NDA.

After the FDA evaluates the NDA and, in some cases, the related manufacturing facilities, it may issue an approval letter, or it may issue a Complete Response Letter, or CRL, to indicate that the review cycle for an application is complete and that the application is not ready for approval. CRLs generally outline the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when the deficiencies have been addressed to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Once issued, the FDA may withdraw product approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. In addition, the FDA may require post-approval testing, including Phase 4 studies, and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the authority to prevent or limit further marketing of a product based on the results of these post-marketing programs. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label, and, even if the FDA approves a product, it may limit the approved indications for use for the product or impose other conditions, including labeling or distribution restrictions or other risk-management mechanisms. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the sponsor may be required to submit and obtain FDA approval of a new or supplemental NDA, which may require the development of additional data or conduct of additional pre-clinical studies and clinical trials.

Continuing FDA Regulation

Devices. Under the medical device regulations, the FDA regulates quality control and manufacturing procedures by requiring us to demonstrate and maintain compliance with the quality system regulation, which sets forth the FDA's current good manufacturing practices requirements for medical devices. The FDA monitors compliance with the quality system regulation and current good manufacturing practices requirements by conducting periodic inspections of manufacturing facilities. We could be subject to unannounced inspections by the FDA. Violations of applicable regulations noted by the FDA during inspections of our manufacturing facilities, or the manufacturing facilities of these third parties, could adversely affect the continued marketing of our tests.

The FDA also enforces post-marketing controls that include the requirement to submit medical device reports to the agency when a manufacturer becomes aware of information suggesting that any of its marketed products may have caused or contributed to a death, serious injury or serious illness or any of its products has malfunctioned and that a recurrence of a malfunction would likely cause or contribute to a death or serious injury or illness. The FDA relies on medical device reports to identify product problems and utilizes these reports to determine, among other things,

whether it should exercise its enforcement powers. The FDA may also require postmarket surveillance studies for specified devices.

FDA regulations also govern, among other things, the preclinical and clinical testing, manufacture, distribution, labeling and promotion of medical devices. In addition to compliance with good manufacturing practices and medical device reporting requirements, we will be required to comply with the FDCA's general controls, including establishment registration, device listing and labeling requirements. If we fail to comply with any requirements under the FDCA, we could be subject to, among other things, fines, injunctions, civil penalties, recalls or product corrections, total or partial suspension of production, denial of premarket notification clearance or approval of products, rescission or withdrawal of clearances and approvals, and

criminal prosecution. We cannot assure you that any final FDA policy, once issued, or future laws and regulations concerning the manufacture or marketing of medical devices will not increase the cost and time to market of new or existing tests. Furthermore, any current or future federal and state regulations also will apply to future tests developed by us.

If our promotional activities fail to comply with these FDA regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to issue warning letters or untitled letters, suspend or withdraw a product from the market, require a recall or institute fines or civil fines, or could result in disgorgement of money, operating restrictions, injunctions or criminal prosecution.

Pharmaceuticals. Once an NDA is approved, a product will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug-device listing, recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP or QSR requirements. Changes to the manufacturing process are strictly regulated and generally require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP or QSR and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP or QSR compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market, though the FDA must provide an application holder with notice and an opportunity for a hearing in order to withdraw its approval of an application. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

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

The FDA strictly regulates the marketing, labeling, advertising and promotion of drug and device products that are placed on the market. While physicians may prescribe drugs and devices for off label uses, manufacturers may only promote for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability.

Advertising

Advertising of our neonatology products are subject to regulation by the Federal Trade Commission, or FTC, under the FTC Act. The FTC Act prohibits unfair or deceptive acts or practices in or affecting commerce. Violations of the FTC Act, such as failure to have substantiation for product claims, would subject us to a variety of enforcement actions, including compulsory process, cease and desist orders and injunctions, which can require, among other things, limits on advertising, corrective advertising, consumer redress and restitution, as well as substantial fines or other penalties. Any enforcement actions by the FTC could have a material adverse effect our business.

HIPAA and Other Privacy Laws

The Health Insurance Portability and Accountability Act of 1996, or HIPAA, established for the first time comprehensive protection for the privacy and security of health information. The HIPAA standards apply to three types of organizations, or “Covered Entities”: health plans, healthcare clearing houses, and healthcare providers which conduct certain healthcare transactions electronically. Covered Entities and their Business Associates must have in place administrative, physical, and technical standards to guard against the misuse of individually identifiable health information. Because we are a

healthcare provider and we conduct certain healthcare transactions electronically, we are presently a Covered Entity, and we must have in place the administrative, physical, and technical safeguards required by HIPAA, HITECH and their implementing regulations. Additionally, some state laws impose privacy protections more stringent than HIPAA. Most of the institutions and physicians from which we obtain biological specimens that we use in our research and validation work are Covered Entities and must obtain proper authorization from their patients for the subsequent use of those samples and associated clinical information. We may perform future activities that may implicate HIPAA, such as providing clinical laboratory testing services or entering into specific kinds of relationships with a Covered Entity or a Business Associate of a Covered Entity.

If we or our operations are found to be in violation of HIPAA, HITECH or their implementing regulations, we may be subject to penalties, including civil and criminal penalties, fines, and exclusion from participation in U.S. federal or state health care programs, and the curtailment or restructuring of our operations. HITECH increased the civil and criminal penalties that may be imposed against Covered Entities, their Business Associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions.

Our activities must also comply with other applicable privacy laws. For example, there are also international privacy laws that impose restrictions on the access, use, and disclosure of health information. All of these laws may impact our business. Our failure to comply with these privacy laws or significant changes in the laws restricting our ability to obtain tissue samples and associated patient information could significantly impact our business and our future business plans.

Federal and State Billing and Fraud and Abuse Laws

Antifraud Laws/Overpayments. As participants in federal and state healthcare programs, we are subject to numerous federal and state antifraud and abuse laws. Many of these antifraud laws are broad in scope, and neither the courts nor government agencies have extensively interpreted these laws. Prohibitions under some of these laws include:

- the submission of false claims or false information to government programs;
- deceptive or fraudulent conduct;
- excessive or unnecessary services or services at excessive prices; and
- prohibitions in defrauding private sector health insurers.

We could be subject to substantial penalties for violations of these laws, including denial of payment and refunds, suspension of payments from Medicare, Medicaid or other federal healthcare programs and exclusion from participation in the federal healthcare programs, as well as civil monetary and criminal penalties and imprisonment. One of these statutes, the False Claims Act, is a key enforcement tool used by the government to combat healthcare fraud. The False Claims Act imposes liability on any person who, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. In addition, violations of the federal physician self-referral laws, such as the Stark laws discussed below, may also violate false claims laws. Liability under the False Claims Act can result in treble damages and imposition of penalties. For example, we could be subject to penalties of $5,500 to $11,000 per false claim, and each use of our product could potentially be part of a different claim submitted to the government. Separately, the U.S Department of Health and Human Service, or HHS, office of the Office of Inspector General, or OIG, can exclude providers found liable under the False Claims Act from participating in federally funded healthcare programs, including Medicare. The steep penalties that may be imposed on laboratories and other providers under this statute may be disproportionate to the relatively small dollar amounts of the claims made by these providers for reimbursement. In addition, even the threat of being excluded from participation in federal healthcare programs can have significant financial consequences on a provider.

Numerous federal and state agencies enforce the antifraud and abuse laws. In addition, private insurers may also bring private actions. In some circumstances, private whistleblowers are authorized to bring fraud suits on behalf of the government against providers and are entitled to receive a portion of any final recovery.

Federal and State "Self-Referral" and "Anti-Kickback" Restrictions

Self-Referral law. We are subject to a federal "self-referral" law, commonly referred to as the "Stark" law, which provides that physicians who, personally or through a family member, have ownership interests in or compensation arrangements with a laboratory are prohibited from making a referral to that laboratory for laboratory tests reimbursable by Medicare, and also prohibits laboratories from submitting a claim for Medicare payments for laboratory tests referred by physicians who, personally or through a family member, have ownership interests in or compensation arrangements with the testing laboratory. The Stark law contains a number of specific exceptions which, if met, permit physicians who have

ownership or compensation arrangements with a testing laboratory to make referrals to that laboratory and permit the laboratory to submit claims for Medicare payments for laboratory tests performed pursuant to such referrals.

We are subject to comparable state laws, some of which apply to all payors regardless of source of payment, and do not contain identical exceptions to the Stark law. For example, we are subject to a North Carolina self-referral law that prohibits a physician investor from referring to us any patients covered by private, employer-funded or state and federal employee health plans. The North Carolina self-referral law contains few exceptions for physician investors in securities that have not been acquired through public trading, but will generally permit us to accept referrals from physician investors who buy their shares in the public market.

We have several stockholders who are physicians in a position to make referrals to us. We have included within our compliance plan procedures to identify requests for testing services from physician investors and we do not bill Medicare, or any other federal program, or seek reimbursement from other third-party payors, for these tests. The self-referral laws may cause some physicians who would otherwise use our laboratory to use other laboratories for their testing.

Providers are subject to sanctions for claims submitted for each service that is furnished based on a referral prohibited under the federal self-referral laws. These sanctions include denial of payment and refunds, civil monetary payments and exclusion from participation in federal healthcare programs and civil monetary penalties, and they may also include penalties for applicable violations of the False Claims Act, which may require payment of up to three times the actual damages sustained by the government, plus civil penalties of $5,500 to $11,000 for each separate false claim. Similarly, sanctions for violations under the North Carolina self-referral laws include refunds and monetary penalties.

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. The term “remuneration” is not defined in the federal Anti-Kickback Statute and has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Care Act of 2010, as amended by Health Care and Education Affordability Act, or PPACA, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute and certain criminal healthcare fraud statutes, effective March 23, 2010. Pursuant to the statutory amendment, a person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Sanctions for violations of the federal Anti-Kickback Statute may include imprisonment and other criminal penalties, civil monetary penalties and exclusion from participation in federal healthcare programs.

The OIG has criticized a number of the business practices in the clinical laboratory industry as potentially implicating the Anti-Kickback Statute, including compensation arrangements intended to induce referrals between laboratories and entities from which they receive, or to which they make, referrals. In addition, the OIG has indicated that “dual charge” billing practices that are intended to induce the referral of patients reimbursed by federal healthcare programs may violate the Anti-Kickback Statute.

Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs, and do not contain identical safe harbors. For example, North Carolina has an anti-kickback statute that prohibits healthcare providers from paying any financial compensation for recommending or securing patient referrals. Penalties for violations of this statute include license suspension or revocation or other disciplinary action. Other states have similar anti-kickback prohibitions.

Both the federal Anti-Kickback Statute and the North Carolina anti-kickback law are broad in scope. The anti-kickback laws clearly prohibit payments for patient referrals. Under a broad interpretation, these laws could also prohibit a broad array of practices involving remuneration where one party is a potential source of referrals for the other.

If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in U.S. federal or state health care programs, and the curtailment or restructuring of our operations. To the extent that any product we make is sold in a foreign country in the future, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals. To reduce the risks associated with these various laws and governmental regulations, we have

implemented a compliance plan. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

International Medical Device Regulations

International marketing of medical devices is subject to foreign government regulations, which vary substantially from country to country. The European Commission is the legislative body responsible for directives with which manufacturers selling medical products in the E.U. and the European Economic Area, or EEA, must comply. The E.U. includes most of the major countries in Europe, while other countries, such as Switzerland, are part of the EEA and have voluntarily adopted laws and regulations that mirror those of the E.U. with respect to medical devices. The E.U. has adopted directives that address regulation of the design, manufacture, labeling, clinical studies and post-market vigilance for medical devices. Devices that comply with the requirements of a relevant directive will be entitled to bear the CE conformity marking, indicating that the device conforms to the essential requirements of the applicable directives and, accordingly, can be marketed throughout the E.U. and EEA.

Outside of the E.U., regulatory pathways for the marketing of medical devices vary greatly from country to country. In many countries, local regulatory agencies conduct an independent review of medical devices prior to granting marketing approval. For example, in China, approval by the SFDA, must be obtained prior to marketing an medical device. In Japan, approval by the MHLW following review by the Pharmaceuticals and Medical Devices Agency is required prior to marketing an medical device. The process in such countries may be lengthy and require the expenditure of significant resources, including the conduct of clinical trials. In other countries, the regulatory pathway may be shorter or less costly. The timeline for the introduction of new medical devices is heavily impacted by these various regulations on a country-by-country basis, which may become more lengthy and costly over time.

U.S. Healthcare Reform

In March 2010, the PPACA was enacted, which includes measures that have or will significantly change the way healthcare is financed by both governmental and private insurers. Beginning in August 2013, the Physician Payment Sunshine Act, enacted as part of PPACA, and its implementing regulations requires medical device manufacturers to track certain financial arrangements with physicians and teaching hospitals, including any "transfer of value" made or distributed to such entities, as well as any investment interests held by physicians and their immediate family members. Manufacturers are required to report this information to Centers for Medicare & Medicaid Services, or CMS, beginning in 2014. Various states have also implemented regulations prohibiting certain financial interactions with healthcare professionals or mandating public disclosure of such financial interactions. We may incur significant costs to comply with such laws and regulations now or in the future.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Recent Developments

Merger with Essentialis

On December 22, 2016, we entered into an Agreement and Plan of Merger, or Merger Agreement, with Essentialis, Inc., a Delaware corporation, or Essentialis. On March 7, 2017, we completed the previously announced merger pursuant to the Merger Agreement, with Essentialis as the surviving corporation and becoming our wholly-owned

subsidiary. Under the terms of the Merger Agreement, in connection with the closing of the transactions contemplated by the Merger Agreement, the former holders of Essentialis stock received an aggregate of 18,916,940 shares of our common stock. We held back an 913,379 shares of our common stock as partial recourse to satisfy any indemnification claims made by us under the Merger Agreement, and such shares of our common stock will be issued to Essentialis stockholders on the one year anniversary of the closing (subject

to the limitations set forth in the Merger Agreement). We are also obligated to issue an additional 4,566,948 shares of common stock to Essentialis stockholders upon the achievement of a development milestone associated with Essentialis' product. Assuming that we issues all of the shares of our common stock held back and the development milestone is achieved, we would issue a total of 24,397,306 shares of common stock to Essentialis stockholders. Additionally, upon the achievement of certain commercial milestones associated with the sale of Essentialis' product in accordance with the terms of the Merger Agreement, we are obligated to make cash earnout payments of up to a maximum of $30 million to Essentialis stockholders. The merger consideration described above will be reduced by any such shares of common stock issuable, or cash earnout payments payable, to Essentialis' management carve-out plan participants and other service providers of Essentialis, in each case, in accordance with the terms of the Merger Agreement. Certain stockholders of Essentialis, including Vivo Ventures Fund V L.P. and its affiliated entities ("Vivo"), Technology Partners Fund VII, L.P. and its affiliated entities ("Technology Partners") and Forward Ventures V, L.P. ("Forward"), are affiliated with certain members of our board of directors, including the three directors appointed to the board of directors in connection with the closing of the merger will receive a portion of the merger consideration in their capacities as former stockholders of Essentialis.

Essentialis is a privately held, clinical stage biotechnology company focused on the development of breakthrough medicines forthe treatment of rare metabolic diseases where there is increased mortality and risk of cardiovascular and endocrine complications. To date, Essentialis's efforts have focused primarily on developing and testing product candidates that target the ATP-sensitive potassium channel, a metabolically regulated membrane protein whose modulation has the potential to impact a wide range of rare metabolic, cardiovascular, and CNS diseases. Essentialis has tested Diazoxide Choline Controlled Release Tablet, or DCCR, as a treatment for Prader-Willi syndrome, or PWS, a complex metabolic/neurobehavioral disorder.

Aspire PIPE Financing

On January 27, 2017, we entered into a common stock purchase agreement, or the Purchase Agreement, with Aspire Capital Fund, LLC, an Illinois limited liability company, or Aspire Capital, which provides that, upon the terms and subject to the conditions and limitations set forth therein, Aspire Capital is committed to purchase up to an aggregate of $17.0 million of our shares of common stock over the approximately thirty month term of the Purchase Agreement. In consideration for entering into the Purchase Agreement, concurrently with the execution of the Purchase Agreement, we issued to Aspire Capital 708,333 shares of our common stock as a commitment fee, or the Commitment Shares. Concurrently with entering into the Purchase Agreement, we also entered into a registration rights agreement with Aspire Capital, or the 2017 Registration Rights Agreement, in which we agreed to file one or more registration statements, as permissible and necessary to register under the Securities Act the sale of the shares of our common stock that have been and may be issued to Aspire Capital under the Purchase Agreement. We filed a registration statement on Form S-1 on February 1, 2017 that was declared effective by the United States Securities and Exchange Commission, or SEC, on February 15, 2017 and which covers the shares of common stock issued or issuable to Aspire Capital pursuant to the Purchase Agreement.

Financing

On March 7, 2017, we entered into common stock purchase agreements, or 2017 Financing, with certain new and existing investors who previously delivered non-binding indications of interest to us to participate in a financing of $8 million in connection with the merger with Essentialis. Under the terms of the 2017 Financing we agreed to sell to the purchasers, in a private placement, an aggregate of 8,333,333 shares of our common stock, par value $0.001 per share, at a purchase price of $0.96 per share for gross proceeds of approximately $8 million. This financing closed concurrently with the closing of the merger with Essentialis on March 7, 2017. The 2017 Financing provided for the sale of our common stock to the investors and under the terms of the Financing, we agreed to use commercially reasonable efforts to file a registration statement covering the resale of the shares of our common stock sold to

purchasers in this financing within 45 days of the closing. Certain purchasers, including Vivo Ventures, Technology Partners, and Forward Ventures are affiliated with members of our board of directors, including the three directors appointed to our board of directors in connection with the closing of the merger with Essentialis. The shares issued in this financing will not initially be registered under the Securities Act of 1933, as amended, and will be subject to restrictions and limitations on transfer under U.S. Securities laws.

Employees

As of December 31, 2016, we had 26 full-time employees and 3 full-time or part-time consultants providing services to us. None of our employees is represented by a labor union or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Corporate and Available Information

Our principal corporate offices are located at 1235 Radio Road, Suite 110, Redwood City, California 94065 and our telephone number is (650) 213-8444. We were incorporated in Delaware on August 25, 1999. Our internet address is www.Capnia.com. We make available on our website, free of charge, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after we electronically file such materials with, or furnish it to, the Securities Exchange and Commission. Our Securities Exchange and Commission reports can be accessed through the Investor Relations section of our internet website. The information found on our internet website is not part of this or any other report we file with or furnish to the Securities Exchange and Commission.

ITEM 1A. RISK FACTORS

An investment in our securities has a high degree of risk. Before you invest you should carefully consider the risks and uncertainties described below together with all the of the other information in this Annual Report on Form 10-K, including our consolidated financial statements and related notes. If any of the following risks actually occur, our business, operating results and financial condition could be harmed and the value of our stock could go down. This means you could lose all or a part of your investment.

Risks related to our financial condition and capital requirements

We have a limited commercialization history and have incurred significant losses since our inception, and we anticipate that we will continue to incur substantial losses for the foreseeable future. We have generated limited commercial sales to date, which, together with our limited operating history, makes it difficult to evaluate our business and assess our future viability.

We are a developer of therapeutics and diagnostics with a limited commercialization history. Evaluating our performance, viability or future success will be more difficult than if we had a longer operating history or approved products for sale on the market. We continue to incur significant research and development and general and administrative expenses related to our operations. Investment in medical product development is highly speculative, because it entails substantial upfront capital expenditures and significant risk that any planned product will fail to demonstrate adequate accuracy or clinical utility. We have incurred significant operating losses in each year since our inception, and expect that we will not be profitable for an indefinite period of time. As of December 31, 2016, we had an accumulated deficit of $98.3 million.

We expect that our future financial results will depend primarily on our success in launching, selling and supporting our neonatology and other products. This will require us to be successful in a range of activities, including manufacturing, marketing and selling our neonatology products. We are only in the preliminary stages of some of these activities. We may not succeed in these activities and may never generate revenue that is sufficient to be profitable in the future. Even if we are profitable, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to achieve sustained profitability would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our planned products, market our current and planned products, or continue our operations.

We currently have generated limited product revenue and may never become profitable.

To date, we have not generated significant revenues from our products or Serenz, and have not generated sufficient revenues from licensing activities to achieve profitability. Our ability to generate significant revenue from product sales and achieve profitability will depend upon our ability, alone or with any future collaborators, to successfully commercialize products, including our neonatology products, Serenz, or any planned products that we may develop, in-license or acquire in the future. Our ability to generate revenue from product sales from planned products also depends on a number of additional factors, including our ability to:

- develop a commercial organization capable of sales, marketing and distribution of any products for which we obtain marketing approval in markets where we intend to commercialize independently;
- achieve market acceptance of our neonatology products and our other future products, if any;
- set a commercially viable price for our neonatology product and our other future products, if any;
- establish and maintain supply and manufacturing relationships with reliable third parties, and ensure adequate and legally compliant manufacturing to maintain that supply;

- obtain coverage and adequate reimbursement from third-party payors, including government and private payors;

- find suitable global and U.S. distribution partners for our neonatology products and distribution partners for Serenz in the E.U to help us market, sell and distribute our approved products in other markets;
- demonstrate the safety and effectiveness of Serenz to the satisfaction of FDA and obtain regulatory approval for Serenz;
- complete and submit applications to, and obtain regulatory approval from, foreign regulatory authorities;
- complete development activities, including any potential Phase 3 clinical trials of Serenz, successfully and on a timely basis;
- establish, maintain and protect our intellectual property rights and avoid third-party patent interference or patent infringement claims; and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with product development and commercialization, including that Serenz in the U.S. or any or our planned products may not advance through development, achieve the endpoints of applicable clinical trials or obtain approval, we are unable to predict the timing or amount of increased expenses, or when or if we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide, or are required by the FDA or foreign regulatory authorities, to perform studies or clinical trials in addition to those that we currently anticipate. Even if we are able to complete the development and regulatory process for Serenz in the U.S. or any planned products worldwide, we anticipate incurring significant costs associated with commercializing these products.

Even if we are able to generate significant revenue from the sale of our neonatology products, Serenz or any planned products that may be approved, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or shut down our operations.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or below our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into collaboration agreements with other companies that include development funding and significant upfront and milestone payments or royalties, which may become an important source of our revenue. Accordingly, our revenue may depend on development funding and the achievement of development and clinical milestones under any potential future collaboration and license agreements and sales of our products, if approved. These upfront and milestone payments may vary significantly from period to period, and any such variance could cause a significant fluctuation in our operating results from one period to the next. In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our Board of Directors, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly. Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the cost and risk of initiating sales and marketing activities;
- the timing and cost of, and level of investment in, research and development activities relating to our planned products, which will change from time to time;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the cost of manufacturing our Serenz and our neonatology products may vary depending on FDA and other regulatory requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we will or may incur to acquire or develop additional planned products and technologies;
- the design, timing and outcomes of clinical studies for Serenz in the U.S. and any planned products or competing planned products;

- changes in the competitive landscape of our industry, including consolidation among our competitors or potential partners;
- any delays in regulatory review or approval in the U.S., or, if applicable, globally, of Serenz or any of our planned products;
- the level of demand for our neonatology products, and for Serenz and any planned products, should they receive approval, in the U.S., or, if applicable, globally,which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our future products, if approved, and existing and potential future drugs that compete with our planned products;
- competition from existing and potential future offerings that compete with neonatology products, Serenz or any of our planned products;
- our ability to commercialize our neonatology products or any planned product inside and outside of the U.S., either independently or working with third parties;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic environment.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our Common Stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

We may need additional funds to support our operations, and such funding may not be available to us on acceptable terms, or at all, which would force us to delay, reduce or suspend our research and development programs and other operations or commercialization efforts. Raising additional capital may subject us to unfavorable terms, cause dilution to our existing stockholders, restrict our operations, or require us to relinquish rights to our planned products and technologies.

The commercialization of our products, as well as the completion of the development and the potential commercialization of planned products, will require substantial funds. As of December 31, 2016, we had approximately $2.7 million in cash and cash equivalents. Our future financing requirements will depend on many factors, some of which are beyond our control, including the following:

- the cost of activities and added personnel associated with the commercialization of our products, including marketing, manufacturing, and distribution;
- the cost to manufacture our products on a larger scale;
- the degree and rate of market acceptance of our products, and the revenue that we are able to collect as a result;
- our ability to set a commercially attractive price for our products, and our customers’ perception of the value relative to the prices we set;
- our ability to clarify the regulatory path in the U.S. for Serenz, and the potential requirement for additional pivotal clinical studies;

- the timing of, and costs involved in, seeking and obtaining approvals from the FDA and other regulatory authorities for Serenz and other planned products;
- our ability to obtain additional partners for Serenz in the E.U. on attractive economic terms, or engage in commercial sales of Serenz on our own or through distributors, or maintain existing distributors;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights and/or the loss of those rights;
- our ability to enter into distribution, collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements;
- the emergence of competing technologies or other adverse market developments;
- the costs of attracting, hiring and retaining qualified personnel;
- unforeseen developments during our clinical trials;
- unforeseen changes in healthcare reimbursement for any of our approved products;
- our ability to maintain commercial scale manufacturing capacity and capability with a commercially acceptable cost structure;
- unanticipated financial resources needed to respond to technological changes and increased competition;
- enactment of new legislation or administrative regulations;
- the application to our business of new regulatory interpretations;
- claims that might be brought in excess of our insurance coverage;
- the failure to comply with regulatory guidelines; and
- the uncertainty in industry demand.

We do not have any material committed external source of funds or other support for our commercialization and development efforts. Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never achieve, we expect to finance future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. Additional financing may not be available to us when we need it or it may not be available on favorable terms. If we raise additional capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to Serenz, CoSense, or potential planned products, technologies, future revenue streams or research programs, or grant licenses on terms that may not be favorable to us. If we raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of, or suspend one or more of our clinical studies or research and development programs or our commercialization efforts.

The extent to which we utilize the 2017 Aspire Purchase Agreement (see Note 2) with Aspire Capital as a source of funding will depend on a number of factors, including the prevailing market price of our Common Stock, the volume of trading in our Common Stock and the extent to which we are able to secure funds from other sources. The number of shares that we may sell to Aspire Capital under the 2017 Aspire Purchase Agreement on any given day and during the term of the agreement is limited. Additionally, we and Aspire Capital may not effect any sales of shares of our Common Stock under the 2017 Aspire Purchase Agreement during the continuance of an event of default or on any trading day that the closing sale price of our Common Stock is less than $0.25 per share. Even if we are able to access the full $17.0 million under the Purchase Agreement, we will still need additional capital to fully implement our business, operating and development plans.

On October 12, 2015, we entered into the Securities Purchase Agreement, or the 2015 Sabby Purchase Agreement with funds managed by Sabby Management, LLC, or Sabby, to purchase up to $10 million of Series A Convertible Preferred Stock, or Preferred Stock, together with related Series D Warrants to purchase shares of our Common Stock, or the Series D Warrants. The sale of the Preferred Stock took place in two separate closings. On October 15, 2015,

the date of the first closing, we

received proceeds of approximately $4.1 million, net of $0.4 million in estimated expenses. On January 8, 2016, the date of the second closing, we received proceeds of approximately $5 million, net of $0.5 million in estimated expenses.

On July 5, 2016 and September 29, 2016, we issued $3,151,000 and $10,629,000 worth of shares of Series B Convertible Preferred Stock, respectively, which are convertible into 13,780,000 shares of our Common Stock, to funds affiliated with Sabby Management, LLC, or Sabby, pursuant to a Securities Purchase Agreement, or the 2016 Sabby Purchase Agreement, by and among us and Sabby.

In addition, at the first closing held on July 5, 2016 under the 2016 Sabby Purchase Agreement and the second closing held on September 29, 2016 under the 2016 Sabby Purchase Agreement, we repurchased $1,779,012 and $6,000,988, respectively, worth of Series A Convertible Preferred Stock held by Sabby.

Risks related to the development and commercialization of our products

Our success depends heavily on the successful commercialization of our CoSense device to aid in diagnosis of neonatal hemolysis and of our Serenz device to relieve the nasal symptoms of allergic rhinitis. If we are unable to sell sufficient numbers of our products, our revenues may be insufficient to achieve profitability.

With the exception of revenue generated from the sale of products acquired from NFI, we will derive substantially all of our revenues from sales of CoSense devices and consumables globally and our Serenz devices in the E.U. for the foreseeable future. If we cannot generate sufficient revenues from sales, we may be unable to finance our continuing operations.

We may not be successful in commercializing our approved products

Our efforts to launch CoSense into the neonatology marketplace and Serenz in the E.U. are subject to a variety of risks, any of which may prevent or limit sales of CoSense and Serenz. Furthermore, commercialization of products into the medical marketplace is subject to a variety of regulations regarding the manner in which potential customers may be engaged, the manner in which products may be lawfully advertised, and the claims that can be made for the benefits of the product, among other things. Our lack of experience with product launches may expose us to a higher than usual level of risk of non-compliance with these regulations, with consequences that may include fines or the removal of our approved products from the marketplace by regulatory authorities.

If we are unable to execute our sales and marketing strategy for our neonatology products and for Serenz, and are unable to gain acceptance in the market, we may be unable to generate sufficient revenue to sustain our business.

Although we believe that Serenz, our neonatology, and other planned products represent promising commercial opportunities, our products may never gain significant acceptance in the marketplace and therefore may never generate substantial revenue or profits for us. We will need to establish a market for Serenz in the E.U. and for our neonatology products globally and build these markets through physician education, awareness programs, and other marketing efforts. Gaining acceptance in medical communities depends on a variety of factors, including clinical data published or reported in reputable contexts and word-of-mouth between physicians. The process of publication in leading medical journals is subject to a peer review process and peer reviewers may not consider the results of our studies sufficiently novel or worthy of publication. Failure to have our studies published in peer-reviewed journals may limit the adoption of our products. Our ability to successfully market Serenz in the E.U., as well as products globally will depend on numerous factors, including:

- the outcomes of clinical utility studies of such products in collaboration with key thought leaders to demonstrate our products' value in informing important medical decisions such as treatment selection;
- the success of our distribution partners;
- whether healthcare providers believe such tests provide clinical utility;
- whether the medical community accepts that such tests are sufficiently sensitive and specific to be meaningful in patient care and treatment decisions; and
- whether hospital administrators, health insurers, government health programs and other payors will cover and pay for such tests and, if so, whether they will adequately reimburse us.

We are relying, or will rely, on third parties with whom we are directly engaged with, but who we do not control, to distribute and sell our products. If these distributors are not committed to our products or otherwise run into their own financial

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or other difficulties, it may result in failure to achieve widespread market acceptance of Serenz, and our neonatology and other products, and would materially harm our business, financial condition and results of operations.

If physicians decide not to order our neonatology products in significant numbers, we may be unable to generate sufficient revenue to sustain our business.

To generate demand for our neonatology and other planned products, we will need to educate physicians, neonatologists, pediatricians, and other health care professionals on the clinical utility, benefits and value of the tests we provide through published papers, presentations at scientific conferences, educational programs and one-on-one education sessions by members of our sales force. In addition, we will need support of hospital administrators that the clinical and economic utility of CoSense justifies payment for the device and consumables at adequate pricing levels. We need to hire additional commercial, scientific, technical and other personnel to support this process.

In addition, although treatment guidelines recommend ETCO testing, physicians are free to practice in accordance with their own judgment, and may not adopt ETCO testing to the extent recommended by the guidelines, or at all. While the current AAP guidelines recommend ETCO measurement be performed to assess the presence of hemolysis in neonates requiring phototherapy, neonates unresponsive to phototherapy or readmitted for phototherapy, and neonates with bilirubin levels approaching exchange transfusion levels. AAP guidelines are updated approximately every ten years, and since the current guidelines were published in 2004, these guidelines may change in the near term.

If we cannot convince medical practitioners to order and pay for our current test and our planned tests, and if we cannot convince institutions to pay for our current test and our planned tests, we will likely be unable to create demand in sufficient volume for us to achieve sustained profitability.

If Serenz or our neonatology or other planned products do not continue to perform as expected, our operating results, reputation and business will suffer.

Our success depends on the market’s confidence that Serenz in the E.U., and our neonatology and other planned products worldwide can provide reliable, high-quality diagnostic results or treatments. With respect to our neonatology and other diagnostic products, we believe that our customers are likely to be particularly sensitive to test defects and errors, and prior products made by other companies for the same diagnostic purpose have failed in the marketplace, in part as a result of poor diagnostic accuracy. As a result, the failure of our neonatology and other planned products to perform as expected would significantly impair our reputation and the clinical usefulness of such tests. Reduced sales might result, and we may also be subject to legal claims arising from any defects or errors.

If we cannot compete successfully with other diagnostic modalities, we may be unable to increase or sustain our revenues or achieve and sustain profitability.

Our principal competition for CoSense comes from mainstream diagnostic methods, used by physicians for many years, which focus on invasive blood tests such as the Coombs test, blood counts and serum bilirubin. In addition, transcutaneous monitors of bilirubin also create a competitive threat. It may be difficult to change the methods or behavior of neonatologists and pediatricians to incorporate CoSense in their practices in conjunction with, or instead of, blood tests.

In addition, several larger companies have extensive sales presence in the neonatology area and could potentially develop non-invasive diagnostic tests that compete with our neonatology or other planned products. These include General Electric Healthcare, Fischer & Paykel, Philips, Draeger, Covidien, Masimo, Natus Medical, and CAS Medical. Some of our present and potential competitors have widespread brand recognition and substantially greater financial and technical resources and development, production and marketing capabilities than we do. Others may develop lower-priced tests that payors and physicians could view as functionally equivalent to our current or planned tests, which could force us to lower the list price of our tests. This would impact our operating margins and our ability to achieve and maintain profitability. If we cannot compete successfully against current or future competitors, we may be unable to increase or create market acceptance and sales of our current or planned tests, which could prevent us from increasing or sustaining our revenues or achieving or sustaining profitability.

We expect to continue to incur significant expenses to develop and market additional diagnostic tests, which could make it difficult for us to achieve and sustain profitability.

In recent years, we have incurred significant costs in connection with the development of CoSense. For the three and twelve months ended December 31, 2016, our research and development expenses were $1 million and $5.2 million,

respectively. We expect our expenses to increase for the foreseeable future, as we conduct studies of CoSense and continue to develop our planned products, including tests for hydrogen nitric oxide and other analytes. We will also incur significant expenses to establish a sales and marketing infrastructure, and to drive adoption of and reimbursement for our products. As a result, we need to generate significant revenues in order to achieve sustained profitability.

Serenz may not be approved for sale in the U.S., or in any territory outside of the E.U.

Neither we nor any future collaboration partner can commercialize Serenz in the U.S. without first obtaining regulatory approval for the product from the FDA. In the E.U., we previously obtained CE Mark certification, clearing the device for commercial sale. We recently reactivated the CE Mark certification for Serenz. We commenced pilot sales of Serenz to pharmacies in the E.U. in the second quarter of 2016 to gather commercial feedback in preparation of a full launch of Serenz in 2017.

The approval route for Serenz in the U.S. may be through a device approval or a drug-device combination approval. If it is a device approval pathway, it may be either via the PMA process, a de novo510(k) pathway, or traditional 510(k). Additional randomized, controlled clinical trials and other development work may be necessary to obtain approval. The approval process may take several years to complete, and approval may never be obtained. Before obtaining regulatory approvals for the commercial sale of Serenz for treatment of AR, we must demonstrate with substantial evidence, gathered in preclinical and well-controlled clinical studies, that the planned product is safe and effective for use for that target indication. We may not conduct such a trial or may not successfully enroll or complete any such trial. Serenz may not achieve the required primary endpoint in the clinical trial, and Serenz may not receive regulatory approval. We must also demonstrate that the manufacturing facilities, processes and controls are adequate. Additionally, the FDA may determine that Serenz should be regulated as a combination product or as a drug, and in that case, the approval process would be further lengthened.

Moreover, obtaining regulatory approval for marketing of Serenz in one country does not ensure we will be able to obtain regulatory approval in other countries, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries.

Even if we or any future collaboration partners were to successfully obtain a regulatory approval for Serenz, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for Serenz in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient revenue to justify commercial launch. Also, any regulatory approval of Serenz, once obtained, may be withdrawn. Even if we obtain regulatory approval for Serenz in additional countries, the commercial success of the product will depend on a number of factors, including the following:

- establishment of commercially viable pricing, and obtaining approval for adequate reimbursement from third-party and government payors;
- our ability, or that of third-party manufacturers that we may retain, to manufacture quantities of Serenz using commercially viable processes at a scale sufficient to meet anticipated demand and reduce our cost of manufacturing, and that are compliant with cGMP regulations;
- our success in educating physicians and patients about the benefits, administration and use of Serenz;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;
- acceptance of Serenz as safe and effective by patients, caregivers and the medical community; and
- a continued acceptable safety profile of Serenz following approval.

Many of these factors are beyond our control. If we are unable to successfully commercialize Serenz, or unable to obtain a partner to commercialize it, we may not be able to earn any revenues related to Serenz. This would result in an adverse effect on our business, financial condition, results of operations and growth prospects.

One or more countries in the E.U. may reassess the Class 2a designation and determine that Serenz be regulated in a different manner.

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Serenz has CE Mark certification in the E.U. based on it being treated as a Class 2a medical device in constituent E.U. countries. One or more countries in the E.U. may reassess the Class 2a designation and determine that Serenz be regulated differently and if this occurs, controlled clinical trials and other development work may be necessary to maintain regulatory clearances in any such jurisdictions. We may be required to demonstrate with substantial evidence, gathered in preclinical and well-controlled clinical studies, that Serenz is safe and effective for use. We may not be able to conduct such a trial or may not successfully enroll or complete any such trial. Serenz may not achieve the required primary endpoint in the clinical trial As a result, the regulatory process in any such jurisdictions may take several years to complete, and requisite clearances may never be obtained.

The regulatory approval process is expensive, time consuming and uncertain, and may prevent us or our partners from obtaining approval for the commercialization of Serenz or our other development candidates. Approval of Serenz in the U.S. or other territories may require that we, or a partner, conduct additional randomized, controlled clinical trials. The regulatory pathway for approval of Serenz in the U.S. has not been determined. However, there is a significant risk that the FDA will require us to file for approval via the PMA pathway for devices, or may classify Serenz as a drug-device combination that must be approved via the NDA pathway typically used for drug products. In either of these cases, the FDA may require that additional randomized, controlled clinical trials be conducted before an application for approval can be filed. These are typically expensive and time consuming, and require substantial commitment of financial and personnel resources from the sponsoring company. These trials also entail significant risk, and the data that results may not be sufficient to support approval by the FDA or other regulatory bodies. Furthermore, regulatory approval of either a PMA or an NDA is not guaranteed, and the filing and approval process itself is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and expense exerted, failure may occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical studies. The FDA can delay, limit, or deny approval of a future product for many reasons, including but not limited to:

- a future product may not be deemed to be safe and effective;
- FDA officials may not find the data from clinical and preclinical studies sufficient;
- the FDA may not approve our or our third-party manufacturer’s processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

If Serenz, or our future products, fail to demonstrate safety and effectiveness in further clinical studies that may be required, or do not gain regulatory approval, our business and results of operations will be materially and adversely harmed.

The mechanism of action of Serenz has not been fully determined or validated

The exact mechanism of action(s) of Serenz is unknown. Therapeutics are increasingly focused on target-driven development, and an understanding of a future product’s mechanism of action is typically believed to make development less risky. The FDA may view this as increasing the potential risks, and diminishing the potential benefits, of Serenz. In addition, potential partners may view this as a limitation of the program, and it may be more challenging for us to obtain a partnership on favorable terms as a result.

Because the results of preclinical testing and earlier clinical trials, and the results to date in various clinical trials, are not necessarily predictive of future results, Serenz may not have favorable results in later clinical trials or receive regulatory approval.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate adequate data to demonstrate the effectiveness and safety of an investigational product. A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience, have suffered significant setbacks in clinical trials, even after seeing promising results in earlier clinical trials. Despite the results to date in the various clinical studies performed with Serenz, we do not know whether pivotal clinical trials, if the FDA requires they be conducted, will demonstrate adequate effectiveness and safety to result in regulatory approval to market Serenz. Even if we, or a future partner, believe that the data is adequate to support an application for regulatory approval to market our planned products, the FDA or other applicable foreign regulatory authorities may not agree and may require additional clinical trials. If these subsequent clinical trials do not produce favorable results, regulatory approval for Serenz may not be achieved.

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There can be no assurance that Serenz will not exhibit new or increased safety risks in subsequent clinical trials. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many other companies that have believed their planned products performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain regulatory approval for the marketing of their products.

Delays in the enrollment of patients in any of our clinical studies could increase development costs and delay completion of the study.

We or any future collaboration partner may not be able to initiate or continue clinical studies for Serenz if we are unable to locate and enroll a sufficient number of eligible patients to participate in these studies as required by the FDA or other regulatory authorities. Even if a sufficient number of patients can be enrolled in clinical trials, if the pace of enrollment is slower than we expect, the development costs for our planned products may increase and the completion of our studies may be delayed, or the studies could become too expensive to complete.

If clinical studies of Serenz or any of our planned products fail to demonstrate safety and effectiveness to the satisfaction of the FDA or similar regulatory authorities outside the U.S. or do not otherwise produce positive results, we may incur additional costs, experience delays in completing or ultimately fail in completing the development and commercialization of Serenz or our planned products.

Before obtaining regulatory approval for the sale of any planned product we must conduct extensive clinical studies to demonstrate the safety and effectiveness of our planned products in humans. Clinical studies are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. A failure of one or more of our clinical studies could occur at any stage of testing.

Numerous unforeseen events during, or as a result of, clinical studies could occur, which would delay or prevent our ability to receive regulatory approval or commercialize Serenz or any of our planned products, including the following:

- clinical studies may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical studies or abandon product development programs;
- the number of patients required for clinical studies may be larger than we anticipate, enrollment in these clinical studies may be insufficient or slower than we anticipate or patients may drop out of these clinical studies at a higher rate than we anticipate;
- the cost of clinical studies or the manufacturing of our planned products may be greater than we anticipate;
- third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical studies of our planned products for various reasons, including a finding that our planned products have unanticipated serious side effects or other unexpected characteristics or that the patients are being exposed to unacceptable health risks;
- regulators may not approve our proposed clinical development plans;
- regulators or IRBs may not authorize us or our investigators to commence a clinical study or conduct a clinical study at a prospective study site;
- regulators or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements; and
- the supply or quality of our planned products or other materials necessary to conduct clinical studies of our planned products may be insufficient or inadequate.

If we or any future collaboration partners are required to conduct additional clinical trials or other testing of Serenz or any planned products beyond those that we contemplate, if those clinical studies or other testing cannot be successfully completed, if the results of these studies or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our planned products;

- not obtain marketing approval at all;
- obtain approval for indications that are not as broad as intended;
- have the product removed from the market after obtaining marketing approval;
- be subject to additional post-marketing testing requirements; or
- be subject to restrictions on how the product is distributed or used.

Our product development costs will also increase if we experience delays in testing or approvals. We do not know whether any clinical studies will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical study delays also could shorten any periods during which we may have the exclusive right to commercialize our planned products or allow our competitors to bring products to market before we do, which would impair our ability to commercialize our planned products and harm our business and results of operations.

Even if subsequent clinical trials demonstrate acceptable safety and effectiveness of Serenz for the relief of nasal symptoms related to AR, the FDA or similar regulatory authorities outside the U.S. may not approve Serenz for marketing or may approve it with restrictions on the label, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

It is possible that the FDA or similar regulatory authorities may not consider the results of the clinical trials to be sufficient for approval of Serenz for this indication. In general, the FDA suggests that sponsors complete two adequate and well-controlled clinical studies to demonstrate effectiveness because a conclusion based on two persuasive studies will be more compelling than a conclusion based on a single study. The FDA may nonetheless require that we may conduct additional clinical studies, possibly using a different clinical study design.

Moreover, even if the FDA or other regulatory authorities approve Serenz, the approval may include additional restrictions on the label that could make Serenz less attractive to physicians and patients compared to other products that may be approved for broader indications, which could limit potential sales of Serenz.

If we fail to obtain FDA or other regulatory approval of Serenz, or if the approval is narrower than what we seek, it could impair our ability to realize value from Serenz, and therefore may have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Even if Serenz or any planned products receive regulatory approval, these products may fail to achieve the degree of market acceptance by physicians, patients, caregivers, healthcare payors and others in the medical community necessary for commercial success.

If Serenz or any planned products receive regulatory approval from the FDA or other regulatory agencies in jurisdictions in which they are not currently approved, they may nonetheless fail to gain sufficient market acceptance by physicians, hospital administrators, patients, healthcare payors and others in the medical community. The degree of market acceptance of our planned products, if approved for commercial sale, will depend on a number of factors, including the following:

- the prevalence and severity of any side effects;
- their effectiveness and potential advantages compared to alternative treatments;
- the price we charge for our planned products;
- the willingness of physicians to change their current treatment practices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength or effectiveness of marketing and distribution support or partners; and
- the availability of third-party coverage or reimbursement.

For example, a number of companies offer therapies for treatment of AR patients based on a daily regimen, and physicians, patients or their families may not be willing to change their current treatment practices in favor of Serenz even if it is able to offer additional efficacy or more attractive product attributes. If Serenz or any planned products, if approved, do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable on a sustained basis or at all.

We currently have limited sales and distribution personnel, and limited marketing capabilities. If we are unable to develop a sales and marketing and distribution capability on our own or through collaborations or other marketing partners, we will not be successful in commercializing our neonatology products, Serenz, or other planned products.

We are currently building a sales and marketing infrastructure and have no experience in the sale, marketing or distribution of diagnostic or therapeutic products. To achieve commercial success for any approved product, we must either develop a sales and marketing infrastructure or outsource these functions to third parties.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming, and could delay any product launch. If the commercial launch of a planned product for which we recruit a sales force and establish marketing capabilities is delayed, or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

We also may not be successful entering into arrangements with third parties to sell and market our planned products or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively and could damage our reputation. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our planned products.

We may attempt to form partnerships in the future with respect to Serenz or other future products, but we may not be able to do so, which may cause us to alter our development and commercialization plans, and may cause us to terminate the Serenz program.

We may form strategic alliances, create joint ventures or collaborations, or enter into licensing agreements with third parties that we believe will more effectively provide resources to develop and commercialize our programs. For example, we currently intend to identify one or more new partners or distributors for the commercialization of Serenz. We may also attempt to find one or more strategic partners for the development or commercialization of one or more of our other future products.

We face significant competition in seeking appropriate strategic partners, and the negotiation process to secure favorable terms is time-consuming and complex. In addition, the termination of our license agreement for Serenz with our former partner, may negatively impact the perception of Serenz held by other potential partners for the program. We may not be successful in our efforts to establish such a strategic partnership for any future products and programs on terms that are acceptable to us, or at all.

Any delays in identifying suitable collaborators and entering into agreements to develop or commercialize our future products could negatively impact the development or commercialization of our future products, particularly in geographic regions like the E.U., where we do not currently have development and commercialization infrastructure. Absent a partner or collaborator, we would need to undertake development or commercialization activities at our own expense. If we elect to fund and undertake development and commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to do so, we may not be able to develop our future products or bring them to market, and our business may be materially and adversely affected.

Serenz or our planned products may cause serious adverse side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial desirability of an approved label or result in significant negative consequences following any marketing approval.

The risk of failure of clinical development is high. It is impossible to predict when or if this or any planned products will prove safe enough to receive regulatory approval. Undesirable side effects caused by Serenz or any of our planned products could cause us or regulatory authorities to interrupt, delay or halt clinical trials or could result in a

more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authority. Additionally, if Serenz or

any of our planned products receives additional marketing approvals, and we or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result, including:

- we may be forced to recall such product and suspend the marketing of such product;
- regulatory authorities may withdraw their approvals of such product;
- regulatory authorities may require additional warnings on the label that could diminish the usage or otherwise limit the commercial success of such products;
- the FDA or other regulatory bodies may issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;
- the FDA may require the establishment or modification of Risk Evaluation Mitigation Strategies or a comparable foreign regulatory authority may require the establishment or modification of a similar strategy that may, for instance, restrict distribution of our products and impose burdensome implementation requirements on us;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to subjects or patients;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular planned product, if approved.

We face competition, which may result in others discovering, developing or commercializing products before we do, or more successfully than we do.

Alternatives exist for our products and we will likely face competition with respect to any planned products that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies, medical device companies, and biotechnology companies worldwide. There are several large pharmaceutical and biotechnology companies that currently market and sell AR therapies to our target patient group. These companies may reduce prices for their competing drugs in an effort to gain or retain market share, and undermine the value proposition that Serenz or our neonatology products might otherwise be able to offer to payors. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Many of these competitors are attempting to develop therapeutics for our target indications.

Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified technical and management personnel, establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to maintain our existing partners in commercializing our neonatology products, Serenz, or any planned products, they may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.

The regulations that govern marketing approvals, pricing and reimbursement for new products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more planned products, even if our planned products obtain regulatory approval.

Our ability to commercialize our products successfully also will depend in part on the extent to which reimbursement for these products and related treatments becomes available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with products administered under the supervision of a physician. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any planned product that we successfully develop.

In the U.S., while we expect payments for CoSense to be part of a DRG (also known as a bundled payment) we may have to obtain reimbursement for it from payors directly. There may be significant delays in obtaining reimbursement for CoSense, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the U.S. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies.

Our inability to promptly obtain coverage and profitable payment rates from both government funded and private payors for new products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition. In some foreign countries, including major markets in the E.U. and Japan, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take nine to twelve months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. Our business could be materially harmed if reimbursement of CoSense, if any, is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the sale of Serenz, our neonatology products and any planned products in human clinical studies. The marketing, sale and use of Serenz, our neonatology products and our planned products could lead to the filing of product liability claims against us if someone alleges that our tests failed to perform as designed. We may also be subject to liability for a misunderstanding of, or inappropriate reliance upon, the information we provide. If we cannot successfully defend ourselves against claims that our neonatology products or our planned products caused injuries, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any planned products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of patients from clinical studies or cancellation of studies;
- significant costs to defend the related litigation and distraction to our management team;
- substantial monetary awards to patients;
- loss of revenue; and

- the inability to commercialize any products that we may develop.

We currently hold $8.0 million in product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

The loss of key members of our executive management team could adversely affect our business.

Our success in implementing our business strategy depends largely on the skills, experience and performance of key members of our executive management team and others in key management positions, including Dr. Anish Bhatnagar, our Chief Executive Officer, David D. O'Toole, our Senior Vice President, Chief Financial Officer, Anthony Wondka, our Senior Vice President of Research and Development, Otho Boone, our Vice President and General Manager of Neonatology, and Kristen Yen, our Vice President of Clinical & Regulatory. The collective efforts of each of these persons, and others working with them as a team, are critical to us as we continue to develop our technologies, tests and research and development and sales programs. As a result of the difficulty in locating qualified new management, the loss or incapacity of existing members of our executive management team could adversely affect our operations. If we were to lose one or more of these key employees, we could experience difficulties in finding qualified successors, competing effectively, developing our technologies and implementing our business strategy. Our Chief Executive Officer, Chief Financial Officer, Vice President & General Manager of Neonatology, Vice President of Clinical & Regulatory, and Senior Vice President of Research and Development all have employment agreements; however, the existence of an employment agreement does not guarantee retention of members of our executive management team and we may not be able to retain those individuals for the duration of or beyond the end of their respective terms. We have secured a $1,000,000 "key person" life insurance policy on our Chief Executive Officer, Dr. Anish Bhatnagar, but do not otherwise maintain "key person" life insurance on any of our employees.

The loss of a key employee, the failure of a key employee to perform in his or her current position or our inability to attract and retain skilled employees could result in our inability to continue to grow our business or to implement our business strategy.

In addition, we rely on collaborators, consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our collaborators, consultants and advisors are generally employed by employers other than us and may have commitments under agreements with other entities that may limit their availability to us.

There is a scarcity of experienced professionals in our industry. If we are not able to retain and recruit personnel with the requisite technical skills, we may be unable to successfully execute our business strategy.

The specialized nature of our industry results in an inherent scarcity of experienced personnel in the field. Our future success depends upon our ability to attract and retain highly skilled personnel, including scientific, technical, commercial, business, regulatory and administrative personnel, necessary to support our anticipated growth, develop our business and perform certain contractual obligations. Given the scarcity of professionals with the scientific knowledge that we require and the competition for qualified personnel among biotechnology and medical device businesses, we may not succeed in attracting or retaining the personnel we require to continue and grow our operations.

We may encounter manufacturing problems or delays that could result in lost revenue. Additionally, we currently rely on third-party suppliers for critical materials needed to manufacture our Serenz devices, CoSense monitors and consumables, other neonatology products, as well as our planned products. Any problems experienced by these suppliers could result in a delay or interruption of their supply to us, and as a result, we may face delays in the commercialization of our neonatology products or the development and commercialization of planned products.

We perform final assembly of CoSense monitors and consumables at our facility in Redwood City, CA. We believe that we currently have adequate manufacturing capacity. If demand for our current products and our planned products increases significantly, we will need to either expand our manufacturing capabilities or outsource to other manufacturers. We currently have limited experience in commercial-scale manufacturing of our planned products, and we currently rely upon third-party contract manufacturing organizations to manufacture and supply components for our products. The manufacture of these products in compliance with the FDA's regulations requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of medical device products often encounter difficulties in production, including difficulties

with production costs and yields, quality control, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced FDA requirements, other federal and state regulatory requirements, and foreign regulations.

We currently purchase components for our products under purchase orders and do not have long-term contracts with most of the suppliers of these materials. If suppliers were to delay or stop producing our components, or if the prices they charge us were to increase significantly, or if they elected not to sell to us, we would need to identify other suppliers. We could experience delays in manufacturing the instruments or consumables while finding another acceptable supplier, which could impact our results of operations. The changes could also result in increased costs associated with qualifying the new materials or reagents and in increased operating costs. Further, any prolonged disruption in a supplier's operations could have a significant negative impact on our ability to manufacture and deliver products in a timely manner. Some of the components used in our products are currently sole-sourced, and substitutes for these components might not be able to be obtained easily or may require substantial design or manufacturing modifications. Any significant problem experienced by one of our sole source suppliers may result in a delay or interruption in the supply of components to us because the number of third-party manufacturers with the necessary manufacturing and regulatory expertise and facilities is limited. Any delay or interruption would likely lead to a delay or interruption in our manufacturing operations. The inclusion of substitute components must meet our product specifications and could require us to qualify the new supplier with the appropriate government regulatory authorities. It could be expensive and take a significant amount of time to arrange for alternative suppliers, which could have a material adverse effect on our business. New manufacturers of any planned product would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing the product. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third-party intellectual property rights could result in a significant interruption of supply and could require the new manufacturer to bear significant additional costs that may be passed on to us.

We currently contract manufacture Serenz in China with a sole-source third party out-sourced manufacturing supplier. We do not have any backup manufacturing capability. If our sole-source supplier is harmed or rendered inoperable by natural or man-made disasters, including fire, earthquake, flooding and power outages, our supply of Serenz will be interrupted. Also there can be no guarantee that we can maintain a commercial relationship with this supplier on acceptable economic terms.

We may acquire other businesses or form joint ventures or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt or cause us to incur significant expense.

As part of our business strategy, we may pursue acquisitions or licenses of assets or acquisitions of businesses, including the merger of Essentialis pursuant to Merger Agreement entered into on December 22, 2016. We completed the merger with Essentialis, Inc. on March 7, 2017, and concurrently with the closing of the Merger, completed financing transaction with total aggregate proceeds of approximately $10 million from current stockholder and new investors (see Note 14). We also may pursue strategic alliances and joint ventures that leverage our core technology and industry experience to expand our product offerings or sales and distribution resources. Our company has limited experience with acquiring other companies, acquiring or licensing assets or forming strategic alliances and joint ventures. We may not be able to find suitable partners or acquisition candidates, and we may not be able to complete such transactions on favorable terms, if at all. If we make any acquisitions, we may not be able to integrate these acquisitions successfully into our existing business, and we could assume unknown or contingent liabilities. Any future acquisitions also could result in significant write-offs or the incurrence of debt and contingent liabilities, any of which could have a material adverse effect on our financial condition, results of operations and cash flows. Integration of an acquired company also may disrupt ongoing operations and require management resources that would otherwise focus on developing our existing business. We may experience losses related to investments in other companies, which could have a material negative effect on our results of operations.

We may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the anticipated benefits of any acquisition, license, strategic alliance or joint venture. To finance such a transaction we may choose to issue shares of our Common Stock as consideration, which would dilute the ownership of our stockholders. If the price of our Common Stock is low or volatile, we may not be able to acquire other companies or fund a joint venture project using our stock as consideration. Alternatively, it may be necessary for us to

raise additional funds for acquisitions through public or private financings. Additional funds may not be available on terms that are favorable to us, or at all.

International expansion of our business will expose us to business, regulatory, political, operational, financial and economic risks associated with doing business outside of the U.S.

We have distribution partners for CoSense in China, India, Canada, Turkey, Denmark, Qatar and Saudi Arabia. We recently launched pilot sales of Serenz in the U.K. and Ireland. Our business strategy contemplates international expansion, including partnering with medical device distributors, and introducing our neonatology products and other planned products outside the U.S. Doing business internationally involves a number of risks, including:

- multiple, conflicting and changing laws and regulations such as tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;
- potential failure by us or our distributors to obtain regulatory approvals for the sale or use of our current products and our planned future products in various countries;
- difficulties in managing foreign operations;
- complexities associated with managing government payor systems, multiple payor-reimbursement regimes or self-pay systems;
- logistics and regulations associated with shipping products, including infrastructure conditions and transportation delays;
- limits on our ability to penetrate international markets if our distributors do not execute successfully;
- financial risks, such as longer payment cycles, difficulty enforcing contracts and collecting accounts receivable, and exposure to foreign currency exchange rate fluctuations;
- reduced protection for intellectual property rights, or lack of them in certain jurisdictions, forcing more reliance on our trade secrets, if available;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions; and
- failure to comply with the Foreign Corrupt Practices Act, including its books and records provisions and its anti-bribery provisions, by maintaining accurate information and control over sales activities and distributors' activities.

Any of these risks, if encountered, could significantly harm our future international expansion and operations and, consequently, have a material adverse effect on our financial condition, results of operations and cash flows.

Intrusions into our computer systems could result in compromise of confidential information.

The accuracy of CoSense depends, in part, on the function of software run by the microprocessors embedded in the device. This software is proprietary to us. While we have made efforts to test the software extensively, it is potentially subject to malfunction. It may be vulnerable to physical break-ins, hackers, improper employee or contractor access, computer viruses, programming errors, or similar problems. Any of these might result in confidential medical, business or other information of other persons or of ourselves being revealed to unauthorized persons.

The CoSense monitor also stores test results, a feature which assists medical professionals in interfacing the device with electronic medical records systems. There are a number of state, federal and international laws protecting the privacy and security of health information and personal data. As part of the American Recovery and Reinvestment Act 2009, or ARRA, Congress amended the privacy and security provisions of the HIPAA. HIPAA imposes limitations on the use and disclosure of an individual's healthcare information by healthcare providers, healthcare clearinghouses, and health insurance plans, collectively referred to as covered entities. The HIPAA amendments also impose compliance obligations and corresponding penalties for non-compliance on individuals and entities that provide services to healthcare providers and other covered entities, collectively referred to as business associates. ARRA also made significant increases in the penalties for improper use or disclosure of an individual's health information under HIPAA and extended enforcement authority to state attorneys general. The amendments also create notification requirements for individuals whose health information has been inappropriately accessed or disclosed: notification requirements to federal regulators and in some cases, notification to local and national media. Notification is not required under HIPAA if the health information that is improperly used or disclosed is deemed secured in accordance with encryption or other standards developed by HHS. Most states have laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA. Many state laws impose significant data security requirements, such as encryption or mandatory contractual terms to ensure ongoing protection of personal information. Activities outside of the U.S. implicate local and national data protection standards, impose additional compliance requirements and generate additional risks of enforcement for non-compliance. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws, to protect against security breaches and hackers or to alleviate problems caused by such breaches.

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Risks related to the operation of our business

Any future distribution or commercialization agreements we may enter into for our neonatology products, Serenz, or any other planned product, may place the development of these products outside our control, may require us to relinquish important rights, or may otherwise be on terms unfavorable to us.

We may enter into additional distribution or commercialization agreements with third parties with respect to our neonatology products, to Serenz, or with respect to planned products, for commercialization in or outside the U.S. Our likely collaborators for any distribution, marketing, licensing or other collaboration arrangements include large and mid-size medical device and diagnostic companies, regional and national medical device and diagnostic companies, and distribution or group purchasing organizations. We will have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our products. Our ability to generate revenue from these arrangements will depend in part on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our products are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to any such collaborations;
- collaborators may not pursue development and commercialization of our products, or may elect not to continue or renew efforts based on clinical study results, changes in their strategic focus for a variety of reasons, potentially including the acquisition of competitive products, availability of funding, and mergers or acquisitions that divert resources or create competing priorities;
- collaborators may delay clinical studies, provide insufficient funding for a clinical study program, stop a clinical study, abandon a product, repeat or conduct new clinical studies or require a new engineering iterations of a product for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our products or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable products; and
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

Any termination or disruption of collaborations could result in delays in the development of products, increases in our costs to develop the products or the termination of development of a product.

We expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2016, we had 26 employees and 3 full-time or part-time consultants. Over the next several years, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of engineering, product development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively

manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Future growth would impose significant added responsibilities on members of management, including:

- managing our clinical trials effectively, which we anticipate being conducted at numerous clinical sites;
- identifying, recruiting, maintaining, motivating and integrating additional employees with the expertise and experience we will require;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;
- managing additional relationships with various strategic partners, suppliers and other third parties;
- improving our managerial, development, operational and finance reporting systems and procedures; and
- expanding our facilities.

Our failure to accomplish any of these tasks could prevent us from successfully growing. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Because we intend to commercialize our products outside the U.S., we will be subject to additional risks.

A variety of risks associated with international operations could materially adversely affect our business, including:

- different regulatory requirements for device approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires

We rely on third parties to conduct certain components of our clinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such studies.

We rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to perform various functions for our clinical trials. Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. We remain responsible for ensuring that each of our clinical studies is conducted in accordance with the general investigational plan and protocols for the study. Moreover, the FDA requires us to comply with regulations and with standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical studies to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of patients in clinical studies are protected. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical studies in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our planned products and will not be able to, or may be delayed in our efforts to, successfully commercialize our planned products.

If we use biological and hazardous materials in a manner that causes injury, we could be liable for damages.

Our manufacturing processes currently require the controlled use of potentially harmful chemicals. We cannot eliminate the risk of accidental contamination or injury to employees or third parties from the use, storage, handling or disposal of these materials. In the event of contamination or injury, we could be held liable for any resulting damages, and any liability could exceed our resources or any applicable insurance coverage we may have. Additionally, we are subject to, on an ongoing basis, federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. These are particularly stringent in California, where our manufacturing facility and several suppliers are located. The cost of compliance with these laws and regulations may become significant and could have a material adverse effect on our financial condition, results of operations and cash flows. In the event of an accident or if we otherwise fail to comply with applicable regulations, we could lose our permits or approvals or be held liable for damages or penalized with fines.

Risks related to intellectual property

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

Patent litigation is prevalent in the medical device and diagnostic sectors. Our commercial success depends upon our ability and the ability of our distributors, contract manufacturers, and suppliers to manufacture, market, and sell our planned products, and to use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights or intellectual property of third parties. We may become party to, or be threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology. Third parties may assert infringement claims against us based on existing or future intellectual property rights. If we are found to infringe a third-party's intellectual property rights, we could be required to obtain a license from such third-party to continue developing and marketing our products and technology. We may also elect to enter into such a license in order to settle pending or threatened litigation. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us, and could require us to pay significant royalties and other fees.

We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our planned products or force us to cease some of our business operations, which could materially harm our business. Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. These and other claims that we have misappropriated the confidential information or trade secrets of third parties can have a similar negative impact on our business to the infringement claims discussed above.

Even if we are successful in defending against intellectual property claims, litigation or other legal proceedings relating to such claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our Common Stock. Such litigation or proceedings could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of litigation or other intellectual property related proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we fail to comply with our obligations in our intellectual property agreements, we could lose intellectual property rights that are important to our business.

We are a party to intellectual property arrangements and expect that our future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, any licensor may have the right to terminate such agreements, in which event we may not be able to develop and market any product that is covered by such agreements.

The risks described elsewhere pertaining to our intellectual property rights also apply to any intellectual property rights that we may license, and any failure by us or any future licensor to obtain, maintain, defend and enforce these rights could have a material adverse effect on our business.

Our ability to successfully commercialize our technology and products may be materially adversely affected if we are unable to obtain and maintain effective intellectual property rights for our technologies and planned products, or if the scope of the intellectual property protection is not sufficiently broad.

Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the U.S. and in other countries with respect to our proprietary technology and products.

The patent position of medical device and diagnostic companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unresolved. In recent years patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability and commercial value of the patent rights we rely on are highly uncertain. Pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of the patents we rely on or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we or were the first to file for patent protection of such inventions.

Even if the patent applications we rely on issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and the patents we rely on may be challenged in the courts or patent offices in the U.S. and abroad. Such challenges may result in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new planned products, patents protecting such products might expire before or shortly after such products are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage.

We may become involved in legal proceedings to protect or enforce our intellectual property rights, which could be expensive, time-consuming, or unsuccessful.

Competitors may infringe or otherwise violate the patents we rely on, or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. In addition, in an infringement proceeding, a court may decide that a patent we are asserting is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that the patents we are asserting do not cover the technology in question. An adverse result in any litigation proceeding could put one or more patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Interference or derivation proceedings provoked by third parties or brought by the U.S. Patent and Trademark Office, or USPTO, or any foreign patent authority may be necessary to determine the priority of inventions or other matters of inventorship with respect to patents and patent applications. We may become involved in proceedings, including oppositions, interferences, derivation proceedings inter partes reviews, patent nullification proceedings, or re-examinations, challenging our patent rights or the patent rights of others, and the outcome of any such proceedings

are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, important patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Our business also could be harmed if a prevailing party does not offer us a license on commercially reasonable terms, if any license is offered at all. Litigation or other proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

We may also become involved in disputes with others regarding the ownership of intellectual property rights. If we are unable to resolve these disputes, we could lose valuable intellectual property rights.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical or management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our Common Stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected, harming our business and competitive position.

In addition to our patented technology and products, we rely upon confidential proprietary information, including trade secrets, unpatented know-how, technology and other proprietary information, to develop and maintain our competitive position. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in the market. We seek to protect our confidential proprietary information, in part, by confidentiality agreements with our employees and our collaborators and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. These agreements are designed to protect our proprietary information, however, we cannot be certain that our trade secrets and other confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets, or that technology relevant to our business will not be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees, consultants or collaborators that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could be disclosed, misappropriated or otherwise become known or be independently discovered by our competitors. In addition, intellectual property laws in foreign countries may not protect trade secrets and confidential information to the same extent as the laws of the U.S. If we are unable to prevent disclosure of the intellectual property related to our technologies to third parties, we may not be able to establish or maintain a competitive advantage in our market, which would harm our ability to protect our rights and have a material adverse effect on our business.

We may not be able to protect or enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on all of our planned products throughout the world would be prohibitively expensive to us. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as in the U.S. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

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Others may be able to make products that are similar to our neonatology products or other planned products, but that are not covered by claims in our patents;

- The original filers of our patents that we developed or purchased might not have been the first to make the inventions covered by the claims contained in such patents;

- We might not have been the first to file patent applications covering an invention;
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- Pending patent applications may not lead to issued patents;
- Issued patents may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- We may not develop or in-license additional proprietary technologies that are patentable; and
- The patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to be paid by us to the USPTO and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents or applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to use our technologies and this circumstance would have a material adverse effect on our business

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

In March 2013, under the America Invents Act, or AIA, the U.S. moved to a first-to-file system and made certain other changes to its patent laws. The effects of these changes are currently unclear as the USPTO must still implement various regulations, the courts have yet to address these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. Accordingly, it is not yet clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents, all of which could have a material adverse effect on our business and financial condition.

If we do not obtain a patent term extension in the U.S. under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for our planned products, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our products, if any, one or more of the U.S. patents covering any such approved product(s) or the use thereof may be eligible for up to five years of patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product. Patent term extension also may be available in certain foreign countries upon regulatory approval of our planned products. Nevertheless, we may not be granted patent term extension either in the U.S. or in any foreign country because of, for example, our failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than requested, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be

reduced, possibly materially.

Risks related to government regulation

The regulatory approval process is expensive, time consuming and uncertain, and may prevent us from obtaining approvals for the commercialization of Serenz or our planned products.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of medical devices are subject to extensive regulation by the FDA in the U.S. and other regulatory authorities in other countries, which regulations differ from country to country. We are not permitted to market our planned products in the U.S. until we received the requisite approval or clearance from the FDA. We have not submitted an application or received marketing approval for Serenz or any planned products. Obtaining PMA or 510(k) clearance for a medical device from the FDA can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable U.S. and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions, including the following:

- warning letters;
- civil or criminal penalties and fines;
- injunctions;
- suspension or withdrawal of regulatory approval;
- suspension of any ongoing clinical studies;
- voluntary or mandatory product recalls and publicity requirements;
- refusal to accept or approve applications for marketing approval of new drugs or biologics or supplements to approved applications filed by us;
- restrictions on operations, including costly new manufacturing requirements; or
- seizure or detention of our products or import bans.

Prior to receiving approval to commercialize any of our planned products in the U.S. or abroad, we may be required to demonstrate with substantial evidence from well-controlled clinical studies, and to the satisfaction of the FDA and other regulatory authorities abroad, that such planned products are safe and effective for their intended uses. Results from preclinical studies and clinical studies can be interpreted in different ways. Even if we believe the preclinical or clinical data for our planned products are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering any of our planned products to humans may produce undesirable side effects, which could interrupt, delay or cause suspension of clinical studies of our planned products and result in the FDA or other regulatory authorities denying approval of our planned products for any or all targeted indications.

Regulatory approval from the FDA is not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and expense exerted, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical studies, or perform additional preclinical studies and clinical studies. The number of preclinical studies and clinical studies that will be required for FDA approval varies depending on the planned product, the disease or condition that the planned product is designed to address and the regulations applicable to any particular planned product. The FDA can delay, limit or deny approval of a planned product for many reasons, including, but not limited to, the following:

- a planned product may not be deemed safe or effective;
- FDA officials may not find the data from preclinical studies and clinical studies sufficient;
- the FDA might not approve our or our third-party manufacturer’s processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

If Serenz or any planned products fail to demonstrate safety and effectiveness in clinical studies or do not gain regulatory approval, our business and results of operations will be materially and adversely harmed.

Even if we receive regulatory approval for a planned product, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and subject us to penalties if we fail to comply with applicable regulatory requirements.

Once regulatory approval has been obtained, the approved product and its manufacturer are subject to continual review by the FDA or non-U.S. regulatory authorities. Our regulatory approval for CoSense, as well as any additional regulatory approval that we receive for Serenz or for any planned products may be subject to limitations on the indicated uses for which the product may be marketed. Future approvals may contain requirements for potentially costly post-marketing follow-up studies to monitor the safety and effectiveness of the approved product. In addition, we are subject to extensive and ongoing regulatory requirements by the FDA and other regulatory authorities with regard to the labeling, packaging, adverse event reporting, storage, advertising, promotion and recordkeeping for our products. In addition, we are required to comply with cGMP regulations regarding the manufacture of Serenz, which include requirements related to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Further, regulatory authorities must approve these manufacturing facilities before they can be used to manufacture drug products, and these facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a third party discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturer or us, including requiring withdrawal of the product from the market or suspension of manufacturing.

Failure to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our products internationally.

We intend to seek a distribution and marketing partner for our neonatology products outside the U.S. and may market planned products in international markets. We have obtained a CE Mark certification for CoSense and Serenz and it is therefore authorized for sale in the E.U.; however, in order to market our planned products in Asia, Latin America and other foreign jurisdictions, we must obtain separate regulatory approvals