Confidential
Private Placement Memorandum

InSitu Biologics, Inc.

200,000 Preferred Shares ("Shares") with Rights to Conversion
20,000 Shares at $4.80 per Share
30,000 Shares at $4.90 per Share
100,000 Shares at $5.00 per Share
30,000 Shares at $5.10 per Share
20,000 Shares at $5.20 per Share

$48,000-$52,000 Minimum Investment
Accredited Investors Only
BitCoin Accepted

This Confidential Private Placement Memorandum is confidential and private. InSitu Biologics, Inc. has not conducted any independent investigation, verification or audit of any information contained in this Offering Circular. InSitu Biologics, Inc. makes no representations or warranties, express or implied, regarding the accuracy or completeness of the information contained herein. "Management" herein refers to the officers and directors of the Company as individuals and as a group.

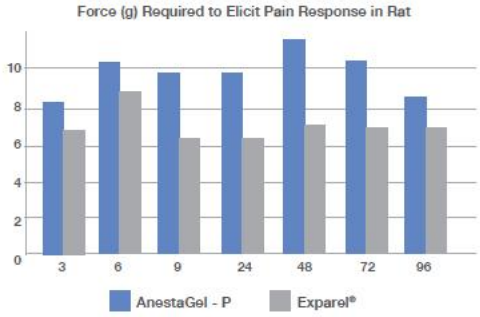
AnestaGel™

In Matrix™ BioHydrogel

AnestaGel is a novel approach to deliver sustained-release analgesics into target tissue using our proprietary Matrix BioHydrogel platform. Uniquely crosslinked, AnestaGel can provide a non-opioid option in perioperative applications.

In a pre-clinical feasibility study, our Matrix BioHydrogel platform was bound with 35 mg/mL sustained released particle Bupivicaine, creating an AnestaGel. The study results showed statistically significant, greater analgesic effect at 24 and 48 hours, as compared to Exparel®.

Pre-clinical Feasibility Study Results[1]



Initial data indicates increased efficacy over Exparel®

Based on these initial results we believe that AnestaGel, utilizing any of the 'caine' family of pharmaceuticals, is a breakthrough technology. Based on our market research, targeted development of high growth, high population segments could include:

- **SURGICAL SITE/PERIOPERATIVE**
- **PERIPHERAL NERVE BLOCK**
- **EPIDURAL**

[1] AnestaGel provides greater analgesia in a rat model of post-operative incisional pain with mechanical allydynia than Exparel® at 24 and 48 hours. In-house data. Study performed by independent laboratory.

AnestaGel and Matrix BioHydrogel are development stage products. They are not intended for any clinical use. The information provided on this brochure is for general information only.

Non-opiate Painkiller, AnestaGel, Found Superior In Preclinical Tests

NEWS PROVIDED BY
InSitu Biologics, LLC
Jan 25, 2017, 12:00 ET

ST. PAUL, Minn., Jan. 25, 2017 /PRNewswire/ -- InSitu Biologics, LLC ("InSitu" or "the Company"), an merging drug delivery company focusing on development of new and proprietary treatments using its Matrix™ BioHydrogel, today announced results from recent pre-clinical studies for their lead product, AnestaGel™. AnestaGel is a long-lasting and long-acting non-opiate painkiller, targeted for use in peri-operative regional pain management.

In a series of independent tests performed under GLP regulations, comparing operative site injections of AnestaGel and EXPAREL® from Pacira, Inc., AnestaGel was proven to last longer, and provide a greater analgesic effect than EXPAREL. In a separate test that determines the PharmacoKinetic(PK) effect for the painkiller bupivacaine, which is used in both AnestaGel and EXPAREL, bupivacaine was proven to be released from AnestaGel into the blood up to 96-120 hours after injection exceeding the presence of bupivacaine in the blood from both EXPAREL and straight bupivacaine injections.

"As we had hypothesized going in to these studies, we expected that AnestaGel would perform very well when compared to the non-opiate products available today," said Dr. Jake Hutchins, Director of the Regional Anesthesia Acute Pain and Ambulatory Surgery division at the University of Minnesota, and the Pre-Clinical Study Director for InSitu Biologics. James Segermark, CEO of InSitu added, "Early on we believed that AnestaGel could be tuned to act as a short-term reservoir, essentially a non-pulsatile organ, and that is what we have now verified and validated. We look forward to the next steps that will bring this predictable, very long-acting, non-opiate product to patients that face the prospect of post-surgical pain." The Company believes that AnestaGel could be used in three distinct markets for peri-operative pain management that represent nearly $31 billion in annual revenue in the US.

AnestaGel uses a novel approach to delivering sustained-released analgesics into the target tissue via the Matrix, which is a tunable, biocompatible, and pH neutral platform. This allows AnestaGel to provide target site-specific, non-migratory placement, a flexible and high dose drug-load reservoir capacity, and a tunable and predictable pharmacological effect.

About InSitu:

InSitu Biologics develops and manufactures implantable, timed release products composed of our proprietary tunable, bio-polymeric hydrogel, Matrix™. We are currently pursuing applications for delivery in soft and bone tissue(s). For more information, please contact James Segermark, CEO, at (651) 289-6444 or visit www.insitubiologics.com.

InSitu Biologics, LLC makes no representations or warranties, express or implied, regarding the accuracy or completeness of the information contained herein. Trademarks are the property of their respective owners.

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/non-opiate-painkiller-anestagel-found-superior-in-preclinical-tests-300396270.html

SOURCE InSitu Biologics, LLC

Related Links

http://www.insitubiologics.com

Executive Summary

What We Do

InSitu Biologics, LLC develops and manufactures implantable time release products composed of its proprietary tunable, bio-polymeric hydrogel, Matrix™ BioHydrogel. Implantable, tunable compounds similar to Matrix are gaining attention in biomedical applications targeting tissue and nerves, however, we are not aware of any that are even remotely similar to our three part, completely biocompatible, pH neutral, Matrix product.

InSitu is initially pursuing applications for soft and bone tissues. Our ability to encapsulate compounds with our medical device, and create biopolymers and mixtures used in regenerative applications, pain management for a wide and ever-growing range of treatments from osteoarthritis to ophthalmic procedures, presents enormous partnering opportunities for InSitu.

Procured through an exclusive license agreement via our manufacturing and advance development partner, the Matrix was invented and originally patented through the Cleveland Clinic Foundation. We have further developed, manufactured and completed testing and performed preliminary animal studies in several applications supporting conceptual clinical applications.

Upon completion of a battery of bench and per-clinical tests, we intend to partner with a leader in the Operative Pain Management product market to accelerate any further clinical studies prior to commercialization.

Technology Platform

All of the components in our tunable Matrix™ BioHydrogel are made in the body or can be metabolized by the body. Matrix is extremely hygroscopic as most of the weight is water (>90% aqueous buffer). Our ability to accurately tune the physical form and rate of absorption to the targeted length of use for a particular tissue is highly desirable for the patient, physician and all members in the patient care continuum. We believe that the end result of the Matrix being combined with the "caine" family of pharmaceuticals could result in a very safe, biocompatible and highly effective series of products.

Our technology is protected by numerous issued, allowed or pending patents, and multiple trademarks. Patents are issued worldwide, including the EU, Japan, and the U.S.

AnestaGel™ with Matrix™

BioHydrogel Non-Opioid Surgical Analgesic

Overview

We have developed our tunable Matrix™ BioHydrogel to deliver therapeutic molecules for new and existing indications. Our initial in-house effort is to partner with a leader in the Operative Pain Management field, bringing our Non-Opioid AnestaGel™ Product to market. Our Sustained Release, Tunable BioHydrogel, AnestaGel, consists of physical properties that allow us to create less viscous products to coat surfaces for migration to small spaces, and to create more viscous products that prevent migration from surgical site. We accomplish this by using hard particulates in soft matrix to enhance drug delivery time and continuous drug elution, and vary the substitution percentage to alter absorption rates.

Current Development Status

After characterizing the Matrix' ability to elute particles for 10 days, we have completed a series of pre-clinical tests tuning the Matrix to elute the pain drug bupivacaine, creating AnestaGel. **The Dosing Study**, yielding statistically significant results, were beyond the Company's expectation. AnestaGel carried 8 times more payload then Exparel and had full nerve block beyond 72 hours. **The GLP Study**, led by Dr. Jake Hutchins, a key advisor for Pacira and a PI for Exparel, was statistically proved to be superior to Exparel at every time point, and most critically, at 72 hours after implantation. Dr. Hutchins is very optimistic that the results with transfer to patients. **The PK Study** showed no toxicity, and far superior results at every time point when compared to Exparel and Bupivacaine. Multiple **Toxicity & Pathology Studies**, as long as 42 days post implant have been unremarkable. We are now preparing for clinical (human) studies.

Product Opportunity

We believe that AnestaGel, composed of our Matrix Technology and any of the "caine" family of pharmaceuticals, could be commercialized to have therapeutic application in many different surgical patient populations that suffer from pain. A few examples of those surgical markets include the following:

Soft Tissue Surgery	***Orthopedic Surgery***
Hernia	Hip
Cholecystectomy	Knee
Anal/Rectal	Spine
Hysterectomy	Fracture
Colon	Shoulder
Laparotomy/Laparoscopy	Foot & Ankle
Endocrine	

With additional development we believe that AnestaGel could be used for addressing chronic pain via epidural and direct long term placement.

Intellectual Property

Strong Patent Portfolio consisting of 22 issued, 3 published and numerous filed and pending patents. Our manufacturing and development Trade Secrets are aligned with our patent portfolio and maximize our core competencies across many medical platforms. Our patents relate to:

- Crosslinking technology and variations using multiple biopolymer backbones (proteins, polysacharides)
- Tunability of gel to create multiple physical forms
- Drug delivery in most applications
- Manufacturing Strengths
- Highly developed proprietary methods
- Rigorous quality control & documentation
- Numerous national government clearances; dock to stock shipping around the world

Biocompatibility Testing

We have completed ISO 10993 Safety & Toxicity

- Long-term Matrix implant data in cardiac & neurovascular tissue, various ligaments
- Passed all 14 stages of Safety & Toxicity Testing

Continued Product Development Support

Our goal is to bring the Technology to market through Partners recognized as a leader in its field. Accordingly, we are committed to enter into an agreement(s) that will allow us to support the Partner in our core competency of manufacturing high-end, medical grade biomaterials that meet the highest standards set by the United States Food and Drug Administration, the European Community and other international agencies.

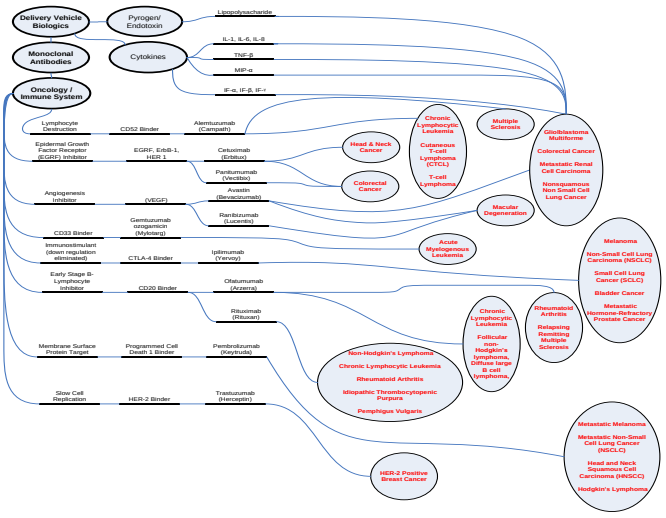
Our Process Development & Manufacturing Partner is publicly held, well financed and operates a robust $70m+ high margin business with numerous patents and trade secrets. We have unlimited Matrix / AnestaGel capacity due to the growing, expanding areas of other scalable products that we make.

Contact Information

James Segermark, CEO
Email: jim@insitubiologics.com
713 E. Minnehaha Avenue, Suite 212
St. Paul, MN 55106

Matrix™ BioHydrogel Technology Platform Highlights

In addition to creating the non-opioid AnestaGel, we believe that the Matrix can be used in a myriad of fields, providing sustained release for hundreds of known, and yet to be discovered molecules.



Develop a New Gold Standard Product

Based on our market research we believe that market specific development of AnestaGel applications could address untapped, rapid growth opportunities and large existing patient populations. Over the past 24 months, we have come to believe that AnestaGel has tremendous applications as it can be delivered in various forms and viscosities. We think a disruptive technology of this nature could have the traits required to develop a new Gold Standard for a medical procedure.

Rapid Growth

- ***Matrix provides a technical platform*** to develop a product that can be used to address the growing demographic of procedures performed in Ambulatory Surgery Centers (ASC's)

Acceptance and Interest

- ***Medical Community: Biomaterial injections*** in to synovial joints for temporary therapeutic treatment are routine therapy. Expanding the use of this class of materials has been contemplated for years, and until recent products became available, it was only a thought.

- ***Patients: Therapeutic patient driven choice*** is a requirement to become the new gold standard. Our AnestaGel technology is easily understood, and the obvious comparison of widespread interest and patient driven use of even potentially dangerous biomaterials in the pain management market is applicable to AnestaGel.

Experienced Management & Product Development Team

Our Team consists of seasoned medical device and pharmaceutical executives, combined with leading edge physicians. Our Combination Product development increases in value with the hundreds of years of experience that is brought to the table by this team and the resources that they access.

PRIVATE PLACEMENT MEMORANDUM
("Offering Circular" or "Private Placement Memorandum")
INSITU BIOLOGICS, INC.
A Delaware Corporation
$1,000,000
A Private Offering
of 200,000 Preferred Shares ("Preferred Shares" or "Shares")
20,000 Shares at $4.80 per Share
30,000 Shares at $4.90 per Share
100,000 Shares at $5.00 per Share
30,000 Shares at $5.10 per Share
20,000 Shares at $5.20 per Share
Minimum Purchase: $$48,000 - $52,000 (10,000 Preferred Shares)
FOR ACCREDITED INVESTORS ONLY

Insitu Biologics, Inc. (the "Company,") is a Delaware Corporation formed for the purpose of conducting Phase I Clinical Testing as discussed in this Offering Circular as well as for capital for a subsequent Regulation A+ offering. The Minimum Purchase amount of $48,000-$52,000, may be waived at the Company's election.

The Company was originally formed as a limited liability company in the state of Minnesota. In November of 2017, the Company converted to a Delaware corporation. InSitu Biologics, Inc. ("Company" or "InSitu") researches, develops, tests and manufactures implantable time release products composed of its proprietary tunable, bio-polymeric hydrogel, Matrix™ BioHydrogel. InSitu has developed AnestaGel™, a patented drug-delivery product based on technology originally created by scientists at the Cleveland Clinic and commercial partners. AnestaGel has been developed for the perioperative pain management market. AnestaGel has unique features including being completely biocompatible, pH neutral, site-specific placement and tunable.

Prospective purchasers should not regard the contents of this private placement memorandum or any other communication from the Company as a substitute for careful and independent tax and financial planning. Each potential investor is encouraged to consult with its own independent legal counsel, accountant and other professional with respect to the legal and tax aspects of this investment and with specific reference to his own tax situation, prior to subscribing for Preferred Shares.

The purchase of Preferred Shares by a qualified pension or profit-sharing plan, individual retirement account ("IRA"), Keogh plan or other qualified retirement plan involves special tax risks and other considerations that should be carefully considered. Income earned by qualified plans as a result of an investment in the Company may be subject to federal income taxes, even though such plans are otherwise tax exempt.

We will issue the Preferred Shares in book-entry form. Subject to certain limited exceptions, you will not receive a certificated security or a negotiable instrument that evidences your Preferred Shares. We will deliver written confirmations to purchasers of the Preferred Shares.

Preferred Shares being offered pursuant to this Offering Circular represent an investment in the convertible Preferred Shares ("Preferred Shares"). Purchasers of Preferred Shares will become Shareholders (the "Shareholders" or "Shareholder"). The Preferred Shares may be converted after the Company's Regulation A+ qualification into Class A Common Shares on a 1 to 1.1 basis. In other words, for every Preferred Share, a shareholder may convert to 1.1 of the Company's Class A Common Shares.

The Company is committed to raising a minimum of $100,000 prior to using funds ("Minimum Offering"). If the Minimum Offering requirement is not met within one year from the date of this Offering, the Offering will terminate and funds will be returned to subscribers. The maximum capital available through this Offering is One Million Dollars ($1,000,000). (See "USE OF PROCEEDS"). The Manager does not expect that any dividends will be paid in the near future and has no intention of declaring any dividends. THE USE OF FORECASTS IN THIS OFFERING IS PROHIBITED. ANY REPRESENTATIONS TO THE CONTRARY AND ANY PREDICTIONS, WRITTEN OR ORAL, AS TO THE AMOUNT OR CERTAINTY OF ANY PRESENT OR FUTURE CASH BENEFIT OR TAX CONSEQUENCE WHICH MAY FLOW FROM AN INVESTMENT IN THIS PROGRAM IS NOT PERMITTED.

AN INVESTMENT IN PREFERRED SHARES INVOLVES SIGNIFICANT RISKS, DESCRIBED IN DETAIL IN THIS OFFERING CIRCULAR. See "RISK FACTORS" beginning on page 36 for certain factors investors should consider before buying Preferred Shares. Significant risks include the following: (i) we have no operating history, no significant assets; and we will rely upon officers and directors to manage our business, specifically, James Segermark; (ii) our business strategy involves substantial risk; (iii) an investment in Preferred Shares is subject to substantial withdrawal restrictions and investors will have a limited ability to liquidate their investment in the Company; (iv) the transfer of Preferred Shares is restricted and no public market for Preferred Shares exists or is likely to develop; (v) the Management is entitled to various forms of compensation and is subject to certain conflicts of interest; and (vi) Shareholders will have no right to participate in the management of the Company. The Preferred Shares offered hereby should be purchased only by Investors who have no need for liquidity in their investment.

THESE SECURITIES HAVE NOT BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), IN RELIANCE UPON THE EXEMPTION FROM REGISTRATION PROVIDED BY SECTION 4(2) OF THE ACT, RULE 506 OF REGULATION D OF THE GENERAL RULES AND REGULATIONS PROMULGATED THEREUNDER BY THE SECURITIES AND EXCHANGE COMMISSION. ACCORDINGLY, DISTRIBUTION OF THIS PRIVATE PLACEMENT MEMORANDUM IS LIMITED TO PERSONS WHO MEET CERTAIN MINIMUM FINANCIAL QUALIFICATIONS, AND THIS PRIVATE PLACEMENT MEMORANDUM DOES NOT CONSTITUTE AN OFFER TO SELL OR SOLICITATION OF AN OFFER TO BUY WITH RESPECT TO ANY PERSON WHO DOES NOT MEET SUCH FINANCIAL QUALIFICATIONS. THESE SECURITIES HAVE NOT BEEN APPROVED OR DISAPPROVED BY THE SECURITIES AND EXCHANGE COMMISSION, NOR HAS THE COMMISSION PASSED UPON OR ENDORSED THE MERITS OF THE OFFERING OR THE ACCURACY OR

ADEQUACY OF THIS PRIVATE PLACEMENT MEMORANDUM. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this Private Placement Memorandum is dated as of November 10, 2017

The Offering will terminate on May 1, 2018 or twenty-one (21) days prior to the qualification of our Regulation A+ offering, whichever is first, unless extended for an additional 180 days at the sole discretion of the Company (the "Offering Termination Date"). The Company's officers ("Management") reserve the right to terminate the Offering at any time. Any subscriptions that have been tendered to the Company and have not been accepted on or before the Offering Termination Date will be returned to subscribers and any subscription funds included therewith will be returned without interest thereon unless the Offering Termination Date is extended, or the Company elects, in its sole discretion, to accept such subscriptions.

Subscription funds received from purchasers of Preferred Shares will be admitted to the Company upon meeting the minimum requirement of $100,000. (See "PLAN OF DISTRIBUTION.")

SUBSCRIPTION INSTRUCTIONS

In order to subscribe for Preferred Shares, an investor who meets the investor suitability standards described herein should proceed as follows:

Read the entire Private Placement Memorandum and any supplements accompanying this private placement memorandum.

Have their status as an "Accredited Investor" verified by Manhattan Street Securities. Manhattan Street Securities may require verification by a Certified Public Accountant, licensed attorney, or Registered Investment Adviser. Such verification based on income may be done by reviewing copies of any Internal Revenue Service form that reports income, such as a Form W-2, Form 1099, Schedule K-1 or Form 1065, and a filed Form 1040. Such verification based on net worth may be done by reviewing specific types of documentation dated within the prior three months, such as bank statements and a credit report from at least one of the nationwide consumer reporting agencies, and obtaining a written representation from the investor.

Make funds payable to Prime Trust LLC as escrow agent for the Company and complete the Subscription Agreement any other verification documents via Manhattan Street Securities. If investing with the crytpocurrency know as BitCoin, the required amount of BitCoins will be calculated and immediately converted in to US Dollars (USD), and held in trust until the minimum escrow amount ($100,000) is reached. In the event a Subscription for a BitCoin Investor is rejected by Management, the refund will be made to the BitCoin Investor in USD. If investing with the crytpocurrency know as BitCoin, the required amount of BitCoins will be calculated and immediately converted in to US Dollars (USD), and held in trust until the minimum escrow amount ($100,000) is reached. In the event a Subscription for a BitCoin Investor is rejected by Management, the refund will be made to the BitCoin Investor in USD.

To purchase Shares, an Investor must meet certain eligibility and investor suitability standards, and must execute a Subscription Agreement and Accredited Investor Questionnaire and Verification in the form attached hereto. By executing the Subscription Agreement and Accredited Investor Questionnaire and Verification, an Investor makes certain representations and warranties, upon which the General Partner will rely in accepting subscriptions. By executing the Subscription Agreement and Accredited Investor Questionnaire and Verification and paying the total purchase price for our Preferred Shares subscribed for, each Investor agrees to be bound by all of their terms and attests that the Investor meets the minimum income and net worth standards as described herein. Subscriptions will be effective only upon our acceptance, and we reserve the right to reject any subscription in whole or in part. Subscriptions will be accepted or rejected within 30 days of receipt by us, and if rejected, all funds will be returned to subscribers without interest and without deduction for any expenses within 10 business days from the date the subscription is rejected. We are not permitted to accept a subscription for our Preferred Shares until at least 5 business days after the date you receive the final private placement memorandum. If accepted, all or a portion of each investor's subscription funds will be admitted into the Company and such subscribers will become Shareholders. During the period prior to admittance of investors as Shareholders, proceeds from the sale of shares are irrevocable, and will be held by the Company for the account of investors in a subscription account and invested in a money market or other liquid asset account. Generally, investors' funds will be transferred from the subscription account into the Company on a first-in, first-out basis; however, the Management reserves the right to admit non-ERISA plan investors before ERISA plan investors in order for the Company to remain exempt from the application of the plan asset regulations issued by the Department of Labor in 1986. Upon admission to the Company, subscription funds will be released to the Company and shares will be issued at the rate commensurate with the timing of the investment by the investor (see pricing on the Cover Page of this Offering). Interest earned on subscription funds while in the subscription account will not be distributed to subscribers.

By executing the subscription agreement, an investor unconditionally and irrevocably agrees to purchase the number of shares shown thereon on a "when issued basis." Accordingly, upon executing the subscription agreement, an investor is not yet an owner of Shares or a Shareholder. Shares will be issued when the investor is admitted to the Company. The General Partner anticipates that the delay between delivery of a subscription agreement and admission to the Company will be less than 90 days, during which time investors will not earn any interest. Subscription Agreements are non-cancelable and irrevocable and subscription funds are non-refundable for any reason, except with the consent of the Management. After having subscribed for at least 10,000 shares ($48,000-$52,000), an investor may at any time, and from time to time, subscribe to purchase additional units in the Company so long as the offering is open. Each investor is liable for the payment of the full purchase price of all units for which he has subscribed.

An approved trustee or custodian must process and forward to us subscriptions made through IRAs, Keogh plans and 401(k) plans. In the case of investments through IRAs, Keogh plans and 401(k) plans, we will send the confirmation and notice of our acceptance to the trustee.

[THE REMAINDER OF THIS PAGE INTENTIONALLY BLANK]

IMPORTANT INFORMATION ABOUT THIS PRIVATE PLACEMENT MEMORANDUM

Please carefully read the information in this private placement memorandum and any accompanying private placement memorandum supplements, which we refer to collectively as the private placement memorandum. You should rely only on the information contained in this private placement memorandum. We have not authorized anyone to provide you with different information. This private placement memorandum may only be used where it is legal to sell these securities. You should not assume that the information contained in this private placement memorandum is accurate as of any date later than the date hereof or such other dates as are stated herein or as of the respective dates of any documents or other information incorporated herein by reference.

Periodically, as we make material investments or have other material developments, we will provide a private placement memorandum supplement that may add, update or change information contained in this private placement memorandum. Any statement that we make in this private placement memorandum will be modified or superseded by any inconsistent statement made by us in a subsequent private placement memorandum supplement.

[THE REMAINDER OF THIS PAGE INTENTIONALLY BLANK]

TABLE OF CONTENTS

SUMMARY 7
DISCLOSURE AND DISCLAIMERS 9
INVESTOR SUITABILITY STANDARDS 12
BUSINESS DESCRIPTION 16
LEGAL 32
USE OF PROCEEDS TO COMPANY 33
RISK FACTORS 34
DIRECTORS, EXECUTIVE OFFICERS AND SIGNIFICANT EMPLOYEES 59
COMPENSATION OF DIRECTORS AND EXECUTIVE OFFICERS 63
CAPITALIZATION TABLE 66
INTEREST OF MANAGEMENT AND OTHERS IN CERTAIN RELATED-PARTY TRANSACTIONS AND AGREEMENTS 67
DESCRIPTION OF SECURITIES BEING SOLD 67
DISQUALIFYING EVENTS DISCLOSURE 71
ERISA CONSIDERATIONS 73

EXHIBITS

Appendix 1 – Proforma
Appendix 2 – References & Studies
Appendix 3 – Addendum
Appendix 4 – Articles of Incorporation and Amendments
Appendix 5 – Bylaws
Appendix 6 – Stockholder's Agreement
Appendix 7 – Subscription Agreement

SUMMARY

InSitu Biologics, Inc. ("Company" or "InSitu") researches, develops, tests and manufactures implantable time release products composed of its proprietary tunable, bio-polymeric hydrogel, Matrix™ BioHydrogel. InSitu has developed AnestaGel™, a patented drug-delivery product based on technology originally created by scientists at the Cleveland Clinicand commercial partners. AnestaGel has been developed for the perioperative pain management market. AnestaGel has unique features including being completely biocompatible, pH neutral, site-specific placement and tunable.

The Company has completed its product development and pre-clinical testing, bringing us to the next steps in our business: production of AnestaGel for human use, and the clinical (human) study of AnestaGel for people having certain surgeries.

Milestone Achievement

The Company has developed a culture of achievement and fiscal responsibility. The Company's only funding of $1.3 million concluded in June 2015. Since that time, the Company has completed the following major milestones:

- Integration of the drug bupivacaine in to the Matrix at the time of production.
- Elude the drug bupivacaine out of the Matrix up to 120 hours after delivery in tissue.
- Initial animal study revealed AnestaGel lasted up to 300% longer than Exparel (Pacira, Inc.) the industry leading post-operative pain treatment, using the same dose of the same drug, therefore testing the efficacy of the sustained-release delivery system.
- Initial toxicity study proved AnestaGel was non-toxic with drug present.
- Initial pathology study, 6 days post-implant, proved AnestaGel was readily metabolized by the body.
- Dosing (second) animal study proved that AnestaGel can safely and sustainably deliver up to 8x the amount of bupivacaine as Exparel over 72 hours; and yet that is only 25% of the maximum dose.
- Second toxicity study proved AnestaGel was non-toxic with drug present.
- Second pathology study, 7 days post-implant, proved AnestaGel was readily metabolized by the body.
- GLP (third) animal study, an independent study performed under the Good Lab Practices Act governed by FDA regulations, proved AnestaGel to be statistically superior in alleviating pain at every time point up to and through 72 hours when compared to Exparel. *This study was published after rigorous Peer Review*.
- Third toxicity study proved AnestaGel was non-toxic with drug present.
- Third pathology study, 42 days post-implantation, proved AnestaGel was readily metabolized by the body.
- PharmacoKinetic (PK) study was performed to measure the amount of drug being eluded from AnestaGel and Exparel. The study proved that AnestaGel eluded the same amount of the drug at 72 hours that Exparel did from 6-12 hours. AnestaGel eluded drug for96 to 120 hours, and in no instance did Exparel elude drug past 48 hours.
- Patent(s) filed based in part on knowledge and formula's captured from animal studies.

DISCLOSURE AND DISCLAIMERS

THIS PRIVATE PLACEMENT MEMORANDUM HAS BEEN PREPARED BY INSITU BIOLOGICS, INC. AND IS SUBMITTED SOLELY FOR THE PURPOSE OF EVALUATING THE INVESTMENT OFFERED HEREBY. NOTHING CONTAINED IN THIS PRIVATE PLACEMENT MEMORANDUM IS OR SHOULD BE RELIED UPON AS A GUARANTEE OR REPRESENTATION AS TO FUTURE EVENTS. MUCH OF THE INFORMATION CONTAINED HEREIN IS CONFIDENTIAL AND HAS NOT, AND WILL NOT BE PUBLICLY DISCLOSED. BY ACCEPTING THIS PRIVATE PLACEMENT MEMORANDUM, THE RECIPIENT AGREES NOT TO REPRODUCE THIS PRIVATE PLACEMENT MEMORANDUM, EITHER IN PART OR IN WHOLE, AND ITS USE IS PERMITTED ONLY BY THE PARTY IDENTIFIED ON THE COVER PAGE HEREOF FOR THE SOLE PURPOSE OF EVALUATING THE INVESTMENT OFFERED HEREBY. IF THE PARTY IDENTIFIED ON THE COVER PAGE HEREOF DECIDES NOT TO SUBSCRIBE FOR PREFERRED SHARES, THIS PRIVATE PLACEMENT MEMORANDUM MUST BE RETURNED TO INSITU BIOLOGICS, INC.

NO PERSON HAS BEEN AUTHORIZED TO GIVE ANY INFORMATION OR TO MAKE ANY REPRESENTATIONS OTHER THAN THOSE CONTAINED HEREIN AND, IF GIVEN OR MADE, SUCH INFORMATION OR REPRESENTATION(S) MUST NOT BE RELIED ON AS HAVING BEEN AUTHORIZED BY INSITU BIOLOGICS, INC. ANY PROSPECTIVE PURCHASER OF PREFERRED SHARES WHO RECEIVES ANY SUCH INFORMATION OR REPRESENTATIONS SHOULD CONTACT THE MANAGEMENT IMMEDIATELY TO CHECK ITS ACCURACY. INSITU BIOLOGICS, INC. WILL MAKE AVAILABLE TO PERSPECTIVE PURCHASERS, DURING THE OFFERING PERIOD, THE OPPORTUNITY TO ASK QUESTIONS AND RECEIVE ANSWERS FROM THE MANAGER OF THE MANAGEMENT OF INSITU BIOLOGICS, INC. CONCERNING ANY ASPECT OF THIS INVESTMENT AND TO OBTAIN ADDITIONAL INFORMATION CONCERNING THE BUSINESS OF INSITU BIOLOGICS, INC. NEITHER THE DELIVERY OF THIS PRIVATE PLACEMENT MEMORANDUM NOR ANY SALES HEREUNDER SHALL UNDER ANY CIRCUMSTANCES CREATE AN IMPLICATION THAT THERE HAS BEEN NO CHANGE IN THE AFFAIRS OF THE PARTNERSHIP SINCE THE DATE HEREOF.

THESE SECURITIES HAVE NOT BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION UNDER THE SECURITIES ACT OF 1933, AS (THE "**ACT**"), IN RELIANCE UPON THE EXEMPTION FROM REGISTRATION PROVIDED BY SECTION 4(2) OF THE ACT, RULE 506 OF REGULATION D PROMULGATED THEREUNDER AND SUCH OTHER EXEMPTIONS AS MAY BE AVAILABLE TO INSITU BIOLOGICS, INC. FURTHER, THE SECURITIES HAVE NOT BEEN QUALIFIED OR REGISTERED UNDER THE LAWS OF ANY STATE OR JURISDICTION. DISTRIBUTION OF THIS PRIVATE PLACEMENT MEMORANDUM IS LIMITED TO PERSONS WHO MEET CERTAIN MINIMUM FINANCIAL QUALIFICATIONS. THIS PRIVATE PLACEMENT MEMORANDUM DOES NOT CONSTITUTE AN OFFER TO SELL OR SOLICITATION OF AN OFFER TO BUY WITH RESPECT TO ANY PERSON WHOM DOES NOT MEET SUCH MINIMUM FINANCIAL QUALIFICATIONS.

PROJECTIONS ARE CONTAINED IN THIS PRIVATE PLACEMENT MEMORANDUM.

PROJECTIONS CAN BE INHERENTLY UNRELIABLE. (SEE "IV. RISK FACTORS AND CONFLICTS OF INTEREST.") ANY ASSUMPTIONS, PREDICTIONS OR PROMISES, WHETHER WRITTEN OR ORAL, WHICH DO NOT CONFORM TO THOSE IN THIS PRIVATE PLACEMENT MEMORANDUM SHOULD BE DISREGARDED AND THEIR USE IS A VIOLATION OF THE LAW.

NO PREFERRED SHARES MAY BE SOLD, ASSIGNED OR OTHERWISE TRANSFERRED UNLESS INSITU BIOLOGICS, INC. AND ITS LEGAL COUNSEL HAVE RECEIVED EVIDENCE SATISFACTORY TO BOTH THAT SUCH TRANSFER DOES NOT INVOLVE A TRANSACTION REQUIRING QUALIFICATION UNDER SAID STATE SECURITIES LAWS AND IS IN COMPLIANCE WITH SUCH LAW.

THIS MEMORANDUM IS NOT KNOWN TO CONTAIN AN UNTRUE STATEMENT OF A MATERIAL FACT, NOR TO OMIT MATERIAL FACTS WHICH IF OMITTED, WOULD MAKE THE STATEMENTS HEREIN MISLEADING. IT CONTAINS A FAIR SUMMARY OF THE MATERIAL TERMS OF DOCUMENTS PURPORTED TO BE SUMMARIZED HEREIN.

HOWEVER, THIS IS A SUMMARY ONLY AND DOES NOT PURPORT TO BE COMPLETE. ACCORDINGLY, REFERENCE SHOULD BE MADE TO THE SUBSCRIPTION AGREEMENT AND OTHER AGREEMENTS AND DOCUMENTS, COPIES OF WHICH ARE ATTACHED HERETO OR WILL BE SUPPLIED UPON REQUEST, FOR THE EXACT TERMS OF SUCH AGREEMENTS AND DOCUMENTS.

PROSPECTIVE INVESTORS ARE NOT TO CONSTRUE THE CONTENTS OF THIS MEMORANDUM OR OF ANY PRIOR OR SUBSEQUENT COMMUNICATIONS FROM INSITU BIOLOGICS, INC. OR ANY OF ITS EMPLOYEES OR PARTNERS, AS INVESTMENT, LEGAL OR TAX ADVICE. EACH INVESTOR SHOULD CONSULT HIS/HER OWN COUNSEL, ACCOUNTANT AND OTHER PROFESSIONAL ADVISORS AS TO LEGAL, TAX AND OTHER RELATED MATTERS CONCERNING HIS/HER INVESTMENT.

THE OFFEREE, BY ACCEPTING DELIVERY OF THIS MEMORANDUM, AGREES TO PROMPTLY RETURN THIS MEMORANDUM, AND ANY OTHER DOCUMENTS OR INFORMATION FURNISHED BY INSITU BIOLOGICS, INC. IF THE OFFEREE DOES NOT PURCHASE ANY OF INSITU BIOLOGICS, INC. SHARES OFFERED HEREBY. IN MAKING AN INVESTMENT DECISION, INVESTORS MUST RELY ON THEIR OWN EXAMINATION OF THE ISSUER AND THE TERMS OF THE OFFERING, INCLUDING THE MERITS AND THE RISKS INVOLVED.

THIS MEMORANDUM INVOLVES A VERY HIGH DEGREE OF RISK, AND THE PURCHASE OF PREFERRED SHARES SHOULD ONLY BE CONSIDERED BY PERSONS WHO CAN AFFORD THE TOTAL LOSS OF THEIR INVESTMENT. (SEE "RISK FACTORS.")

[THE REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]

INVESTOR SUITABILITY STANDARDS

The Preferred Shares we are offering are suitable only as a long-term investment for persons of adequate financial means. It may be difficult for you to sell your Preferred Shares since we do not expect to have a public market for them. On a limited basis, you may be able to have Preferred Shares repurchased through our limited Preferred Shares repurchase program. You should not buy our Preferred Shares if you need to sell them immediately or if you will need to sell them quickly in the future.

Investors who wish to purchase these Preferred Shares as an "**Accredited**" investor must meet the following suitability standards as defined by SEC Rules 501; 17 CFR 230.501(a):

1. A natural person whose individual net worth or joint net worth with that person's spouse, at the time of the purchase of the Preferred Shares, exceeds $1,000,000, exclusive of primary residence; or
2. A natural person who had individual income in excess of $200,000 in each of the two most recent years or joint income with that person's spouse in excess of $300,000 in each of those years and has a reasonable expectation of reaching the same income level in the current year.
3. A retirement fund, such as an Individual Retirement Account (IRA) or Self Employed Person (SEP) Retirement Account must have all of the beneficial owners meet one of the above standards. The beneficial owners may be either natural persons or other entities as long as each meet the definition of accredited to be deemed an Accredited Investor.
4. A bank, insurance company, registered investment company, business development company, or small business investment company; or
5. An employee benefit plan, within the meaning of the Employee Retirement Income Security Act, if a bank, insurance company, or registered investment adviser makes the investment decisions, or if the plan has total assets in excess of One Million Dollars ($1,000,000); or
6. A charitable organization, corporation, or partnership with assets exceeding One Million Dollars ($1,000,000); or
7. A director, executive officer, Manager or general partner of the company selling the securities; or
8. A business in which all the equity owners are accredited investors; or
9. A trust with assets in excess of One Million Dollars ($1,000,000) that was not formed to acquire these Preferred Shares.

The Management intends on using general solicitation to market this Offering. Therefore, we are required to comply with Rule 506(c) in third party verification of the accredited investor status of any interested investor. Rule 506(c) sets forth a principles-based method of verification which requires an objective determination by the issuer (or those acting on its behalf) as to whether the steps taken are "**reasonable**" in the context of the particular facts and circumstances of each purchaser and transaction. Among the factors that an issuer should consider under this principles-based method are:

- the nature of the purchaser and the type of accredited investor that the purchaser claims to be;

- the amount and type of information that the issuer has about the purchaser; and
- the nature of the offering, such as the manner in which the purchaser was solicited to participate in the offering, and the terms of the offering, such as a minimum investment amount.

In addition to this flexible, principles-based method, Rule 506(c) includes a non-exclusive list of verification methods that issuers may use, but are not required to use, when seeking greater certainty that they satisfy the verification requirement with respect to natural person purchasers. This non-exclusive list of verification methods consists of:

- verification based on income, by reviewing copies of any Internal Revenue Service form that reports income, such as Form W-2, Form 1099, Schedule K-1 of Form 1065, and a filed Form 1040;
- verification on net worth, by reviewing specific types of documentation dated within the prior three months, such as bank statements, brokerage statements, certificates of deposit, tax assessments and a credit report from at least one of the nationwide consumer reporting agencies, and obtaining a written representation from the investor; and/or
- a written confirmation from a registered broker-dealer, an SEC-registered investment adviser, a licensed attorney or a certified public accountant stating that such person or entity has taken reasonable steps to verify that the purchaser is an accredited investor within the last three months and has determined that such purchaser is an accredited investor.

In addition, the Management must ascertain, based on a review of the information provided by you, that a prospective investor can bear the economic risks of an investment in the Company, and that the investment is appropriate for the investor's investment objectives, portfolio structure, and financial situation; and that the investor has the capacity to protect their own interests in connection with the investment and will make the final decision to invest in the Company. We will consider:

- Meet the minimum income and net worth standards;
- Can reasonably benefit from an investment in our Preferred Shares based on your overall investment objectives and portfolio structure;
- Are able to bear the economic risk of the investment based on your net worth and overall financial situation; and
- Have an apparent understanding of:
    - The fundamental risks of an investment in our Preferred Shares;
    - The risk that you may lose your entire investment;
    - The lack of liquidity of our Preferred Shares;
    - The restrictions on transferability of our Preferred Shares;
    - The background and qualifications of our Management; and
    - The tax, including ERISA, consequences of an investment in our Preferred Shares.

In consideration of these factors, we will take reasonable steps to verify that all purchasers of our Preferred Shares are accredited investors. We will objectively assess your eligibility in light of your particular facts and circumstances. We will use

one of the following methods to verify your accredited investor status if you are a natural person:

- **Income Verification** – Two most recent years of tax returns filed with the IRS (including, without limitation, Form W-2, Form 1099, Schedule K-1 of Form 1065 and a copy of a filed Form 1040) showing your income (extraneous information may be redacted), together with your written representation that you have a reasonable expectation of reaching the necessary income level during the current year;
- **Net Worth Verification** – Third party statements, such as personal financial statements prepared by your certified public accountant, bank statements, brokerage statements, certificates of deposit, tax assessments or appraisal reports, dated within the prior three months, identifying the value of your assets and liabilities (including a credit report form from at least one national agency dated within the last three months), together with your written representation that all of your liabilities necessary to determining your net worth have been disclosed; or
- **Third Party Verification** – A written confirmation from a registered broker-dealer, an SEC registered investment advisor, a licensed attorney or certified public accountant that such person has taken reasonable steps to verify and determine that, within the prior three months, the individual is an accredited investor.

The Management has the absolute right, in its sole discretion, to accept or reject any subscription offer submitted to them and shall incur no liability for rejection of any prospective investor.

Subscriptions Subject to Review and Acceptance by the Management

An investor who desires to invest in the Preferred Shares will complete the Subscription Agreement and other verification documents. This information will be reviewed by our third-party escrow agent, Manhattan Street Securities. The Management will review these documents to ensure that all investors have attested that they meet the suitability standards established by the Company set forth in "II. Investor Suitability Standards" hereto, and that the Agreement has been appropriately signed.

The Management will indicate acceptance of the Subscription in writing by returning fully executed copies of signature pages from the Subscription Agreement and Company Agreement showing the amount or number of Preferred Shares to be purchased in the Company once admitted. Prior to acceptance, the Management reserves the right to refuse a Subscription from any prospective investor at the Management's sole discretion.

ERISA Considerations

Please see our Section "ERISA CONSIDERATIONS"

Restrictions Imposed by the USA PATRIOT Act and Related Acts

Preferred Shares may not be offered, sold, transferred or delivered, directly or indirectly, to any "**Sanctioned Person**," a term which is defined for purposes of this Memorandum as any person who:

- is named on the list of "**specially designated nationals**" or "**blocked persons**" maintained by the U.S. Office of Foreign Assets Control ("**OFAC**") at http://www.treas.gov/offices/eotffc/ofac/sdn/index.html, or as otherwise published from time to time; and an agency of the government of a Sanctioned Country, (2) an organization controlled by a Sanctioned Country, or (3) a person resident in a Sanctioned Country, to the extent subject to a sanctions program administered by OFAC. A "**Sanctioned Country**" shall mean a country subject to a sanctions program identified on the list maintained by OFAC and available at the following location http://www.treas.gov/offices/eotffc/ofac/sanctions/index.html, or as otherwise published from time to time.

In addition, Preferred Shares may not be offered, sold, transferred or delivered, directly or indirectly, to any person who:

- has more than 15% of its assets in Sanctioned Countries; or
- derives more than 15% of its operating income from investments in, or transactions with Sanctioned Persons or Sanctioned Countries.

Representations with respect to the foregoing and certain other matters will be made by each investor in the Instructions to Investors and Subscription Booklet attached hereto. The Company will rely on the accuracy of each investor's representations set forth in the Instructions to Investors and Subscription Agreement and may require additional evidence that an investor satisfies the applicable standards at any time prior to the acceptance of an investor's subscription. An investor is not obligated to supply any information so requested by the Company, but the Company may reject a subscription from any investor who fails to supply any information so requested.

IF YOU DO NOT MEET THE REQUIREMENTS DESCRIBED ABOVE, DO NOT READ FURTHER. IN THE EVENT YOU DO NOT MEET SUCH REQUIREMENTS, THIS MEMORANDUM SHALL NOT CONSTITUTE AN OFFER TO SELL PREFERRED SHARES TO YOU.

Methods to Assure Adherence to Investor Suitability Standards

Investors who are interested in purchasing Preferred Shares will be required to complete an **Accredited Investor Questionnaire and Verification** and submit it to Manhattan Street Securities and the Management along with their **Subscription Agreement.**

[THE REMAINDER OF THIS PAGE INTENTIONALLY BLANK]

BUSINESS DESCRIPTION

InSitu Biologics™, LLC was formed in 2015. In November 2017, InSitu Biologics, LLC was converted into a Delaware Corporation under the name, Insitu Biologics, Inc. Insitu Biologics, Inc. ("Company" or "InSitu") researches, develops, tests and manufactures implantable time release products composed of its proprietary tunable, bio-polymeric hydrogel, Matrix™ BioHydrogel. InSitu has developed AnestaGel™, a patented drug-delivery product based on technology originally created by scientists at the Cleveland Clinic and commercial partners. AnestaGel has been developed for the perioperative pain management market. AnestaGel has unique features including being completely biocompatible, pH neutral, site-specific placement and tunable.

The Company has completed its product development and pre-clinical testing, bringing us to the next steps in our business: production of AnestaGel for human use, and the clinical (human) study of AnestaGel for people having certain surgeries.

Summary

AnestaGel represents a potentially transformational technology in the perioperative pain control market. Its tunable, programmable nature, and the ability to modify its form factor to meet the need of nearly every surgery has not been contemplated for a targeted pain molecule.

- Matrix BioHydrogel is a tunable, biocompatible, and pH neutral platform. It allows AnestaGel to provide target site-specific, non-migratory placement, a flexible and high dose drug-load reservoir capacity, and tunable and a predictable pharmacological effect.
- The characteristics of Matrix BioHydrogel permit AnestaGel to be manufactured in a variety of form factors, allowing the product to be designed on an application-specific basis and to suit physician and hospital preference.
- InSitu's MULTIPLE preclinical feasibility studies suggest that AnestaGel may deliver faster and longer lasting pain relief than *EXPAREL*.
- InSitu's process development and manufacturing partner is a public company that operates a premier manufacturing facility and has developed numerous patents and trade secrets. InSitu has an unlimited AnestaGel capacity due to the unique manufacturing capability with this partner.

AnestaGel's financial opportunity is as potentially disruptive as the technology. AnestaGel represents the chance for a company to quickly take a leading position in the pain market, with the opportunity for product line extensions and new ancillary products to surround the AnestaGel franchise.

The company strongly believes that the significant investment and development history for AnestaGel and its Matrix BioHydrogel substantially mitigates the risk of final development and commercialization. InSitu believes AnestaGel is a unique, novel product for pain control that is safe, efficacious, and can be manufactured, in quantity, by the Company's world class manufacturing partner.

AnestaGel

AnestaGel is an exciting and novel approach to deliver sustained-released analgesics into the target tissue. The AnestaGel product uses InSitu's proprietary Matrix BioHydrogel platform, which is based on a patent portfolio and proof of concept for a biocompatible hydrogel created by the Cleveland Clinic Foundation (CCF) beginning in the early 2000's.

All of the components of Matrix BioHydrogel are made in the body or can be metabolized by the body. InSitu's ability to accurately tune the physical form and rate of absorption to the targeted length of use for a particular tissue is highly desirable. InSitu believes that AnestaGel, composed of the Company's Matrix BioHydrogel technology and any of the "caine" family of pharmaceuticals, could be commercialized to have therapeutic application in many different surgical patient populations that suffer from pain.

AnestaGel offers a new and transformational approach to perioperative pain management that is opioid-sparing, tunable, biocompatible, target site-specific, and flexible. Based on the Company's testing to date, AnestaGel may offer a superior solution for operative pain management, and potentially provide faster acting and longer lasting pain relief than *EXPAREL*® from Pacira Pharmaceuticals, Inc.

"When I first experienced AnestaGel, it is exactly what I have been looking for to help patients with pain management, in both the office and surgical setting. This product has the potential to change the way we care for patients in the future. I was even more excited to know that AnestaGel can be applied in a variety of methods, offering the versatility to be used in almost every patient."

Dr. Ryan Nunley, Orthopedic Surgeon

Washington University School of Medicine in St. Louis

The Company believes that AnestaGel can be used in three distinct markets for perioperative pain management:

- Surgical Site / Perioperative: There are an estimated 90 million surgical procedures in the US, resulting in $10B of drugs / devices being sold in the US.

- Peripheral Nerve Block: This occurs in the majority of surgical procedures, and is a product market that is estimated to grow to $20B by the year 2025
- Epidural: There are an estimated 2.5M procedures in the US and a product market estimated at $1B

Sources: U.S. Department of Health & Human Services; Pacira Pharmaceuticals; National Center for Biotechnology Information (NCBI)

Unique Characteristics and Advantages

AnestaGel has the following characteristics and advantages:

- Matrix BioHydrogel is a tunable, biocompatible, and pH neutral platform. It allows AnestaGel to provide target site-specific, non-migratory placement, a flexible and high dose drug-load reservoir capacity, and tunable and a predictable pharmacological effect.
- The characteristics of Matrix BioHydrogel permit AnestaGel to be manufactured in a variety of form factors, allowing the product to be designed on an application-specific basis and to suit physician and hospital preference.
- InSitu's preclinical GLP and feasibility studies suggests that AnestaGel may deliver faster and longer lasting pain relief than *EXPAREL*.
- InSitu's process development and manufacturing partner is a public company that operates a premier manufacturing facility and has developed numerous patents and trade secrets. InSitu has an unlimited AnestaGel capacity due to the unique manufacturing capability with this partner.

> *"If AnestaGel performs clinically like it does in the pre-clinical studies, we are looking at a massive change in the way we manage regional pain."*
>
> *Dr. Jacob Hutchins, Anesthesiologist Medical Director, University of Minnesota Acute Pain Service*

Gold Standard Product

AnestaGel applications can address untapped, rapid growth opportunities and large existing patient populations, based on InSitu's market research. InSitu believes that AnestaGel has tremendous applications because it can be delivered in various forms and viscosities and may be long lasting for perioperative applications. The Company believes a technology of this nature could develop a new Gold Standard for perioperative pain management.

Rapid Growth Opportunities

- AnestaGel provides the unique product materials to potentially dominate the non-opioid perioperative pain management market and compete very effectively with *EXPAREL*. AnestaGel can provide the foundation for multiple pain or site specific

pain agents. There is tremendous demand for non-opioid alternatives for perioperative pain management.
- AnestaGel provides a technical platform to develop products that can be used for multiple procedures performed in Ambulatory Surgery Centers (ASC's).

Acceptance and Interest
- Medical Community: Biomaterial injections into synovial joints for temporary therapeutic treatments are currently considered routine therapy. Expanding the use of this class of materials has been contemplated for years. *EXPAREL* has penetrated this market despite the drawbacks of the product.
- Patients: Therapeutic patient driven choice is expected to become an increasingly important factor. AnestaGel technology is easily understood and a natural biomaterial. The growing patient awareness and interest in potentially dangerous biomaterials in the pain management market will potentially promote the acceptance and use of AnestaGel in the future.

History

The patent portfolio and proof of concept for a biocompatible hydrogel were created by the Cleveland Clinic Foundation ("CCF") in the early 2000's.

Since then, extensive time, talent and money has been devoted to the development and research and unique technology behind AnestaGel. Cleveland Clinic, commercial partners and InSitu together have patented and validated the technology and applications of AnestaGel. InSitu Biologic founders, James Segermark ("Jim") and William Taylor ("Bill"), became involved with the CCF technology, in 2007 and 2006 respectively, using a form of the hydrogel for bulking applications.

Taylor and Segermark completed their work developed numerous hydrogels for various medical applications. In early 2014, after completing elution studies, they formed InSitu Biologics to begin making and testing AnestaGel. InSitu procured an exclusive, royalty free, milestone based license. InSitu has since transitioned the biohydrogel bulking agent to a far more sophisticated, implantable delivery vehicle for the newly created bio-absorbable subcutaneous regional pain control market.

"EXPAREL ushered in a new era for patient care in pain management. Based on what I have seen and read, I believe that AnestaGel will make pain control even better for the patient, easier and predictive for the physician, and more widely used in both the office and surgical settings."

Dr. Ryan Nunley

Washington University School of Medicine in St. Louis

The Market

Operative Pain Management

Operative pain management is a vast market that remains dominated by opioids. It is an area that hospitals, doctors and patients continue to find inadequate, despite inroads of new options.

According to The New Guidelines Released for Postoperative Pain Management, by Dr. Laurie Barclay and Pauline Anderson, acute postoperative pain is common, occurring in more than 80% of patients, with approximately 75% of these having moderate, severe, or extreme pain. Postoperative pain relief is inadequate in more than half of patients, which can negatively affect quality of life, function, and functional recovery, as well as increasing the risks for postsurgical complications and persistent postsurgical pain.

Numerous studies and research reinforces the fact that postoperative pain relief remains inadequate and there is a major need for non-opioid alternatives. A sample of the research findings are presented below:

- 73% of inpatient and 57% of outpatient surgeries have moderate to extreme pain postoperatively, despite opioid use by nearly 90% of patients. Pain continues to be undermanaged, according to, Habib AS, Miller research by Gan TJ TE, White W, Apfelbaum JL. Results from a US national survey, Curr Med Res Opin. 2014
- Experiencing postoperative pain was the most common concern (59%) of patients. Almost 25% of patients who received pain medications experienced adverse effects.
- In the United States, more than 73 million surgeries are performed annually, and up to 75% of patients experience pain after surgery. Managing patient pain after surgery often remains top of mind for hospitals despite inroads in new technology, therapies, and processes that have helped lower pain experiences, according to Elizabeth A Reid, Content Manager, Guidepoint; a leading global research services firm.
- ***There are about 46 million inpatient and 53 million outpatient surgeries performed in the United States each year that require drugs for post-operative pain, and over half of these patients still experience***

inadequate pain relief, according to a report by Cara Therapeutics on the acute pain market.

- Acute postoperative pain is a serious problem for many patients. Nearly 50% of postoperative patients have moderate pain, and more than one-third suffer severe pain. There are serious consequences to unrelieved pain, both physically and psychologically, according to PAINWeek.
- Inadequately managed and undertreated postoperative pain remains a major clinical, economic and social challenge. The current standard of care for the treatment of post-operative pain relies heavily on the use of opioids supplemented by other classes of pain medications, the combination of which is known as multi-modal pain therapy.
- Given the negative side effects and costs associated with opioid use in particular, there is increasing focus from hospitals, payors and regulators on treatments that reduce opioid use in the treatment of postoperative pain
- Stronger, Longer, and Opioid-sparing Postoperative Pain Management Approaches Are Urgently Needed
- Untapped Opportunity: Long-acting Anesthetics Currently Make Up Only 5% of the Postoperative Pain Relief Market
- According to Post-Surgical Pain Management TRACKER data from January 2015, "opioids were the most-used treatments, with oral and IV/PCA opioids used in the majority of cases. But early feedback from the TRACKER's panel demonstrates a broad range of post-surgical pain management regimens, with various user preferences. Data shows that while opioids are leading the pack, local anesthetic infiltration and nerve blocks are popular and gaining market share. Guidepoint's Post-Surgical Pain Management TRACKER also tracks the usage of *EXPAREL*, a single-dose, non-opioid, long-acting local anesthetic currently indicated for injection into tissues at the site of surgery, and finds that usage is lower than short-acting local anesthetics although the drug has been used in many cases and is growing share in its largest segment of use, the orthopedic setting."
- With more than 12 months of treatment data collected, Guidepoint's Post-Surgical Pain Management TRACKER shows a slow and steady trend of physicians exploring and moving to newer non-opioid therapies, such as *EXPAREL*,and pumps.
- Although 2015 saw a slight decline in opioid treatment share, TRACKER data finds that opioids are still used by the majority (90-95 percent) of post-operative arthroplasty patients.

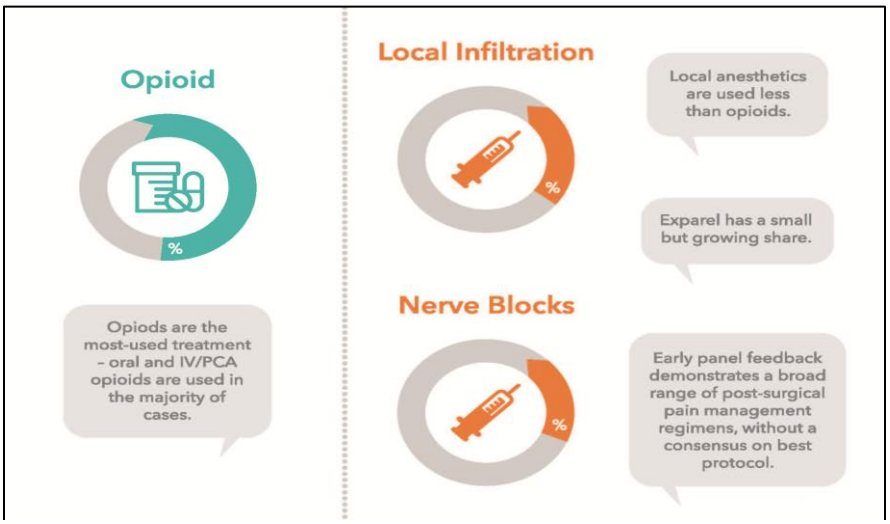
"As a high volume surgeon I use EXPAREL all of the time; but as a user, we know its performance varies from patient to patient. When I saw the work that was being done on Matrix BioHydrogel, I had to get involved. AnestaGel is the product I wanted from the start. That's why I am a shareholder."

Dr. Stefano Sinicropi, Spine Surgeon
President, Midwest Spine and Brain Institute

The Opioid Challenge

"Annually, more than 70 million postsurgical patients receive opioids, and research shows one in 15 will go on to long-term use, indicating that the surgical setting has become an inadvertent gateway to the overall societal epidemic....the best way for hospitals to take immediate action is to implement strategies to minimize preventable opioid exposure," according to Dr. Scott Sigman, orthopedic surgeon and team physician for the U.S. Ski Jump Team."States Move to Control How Painkillers Are Prescribed." New York Times, March 2016.

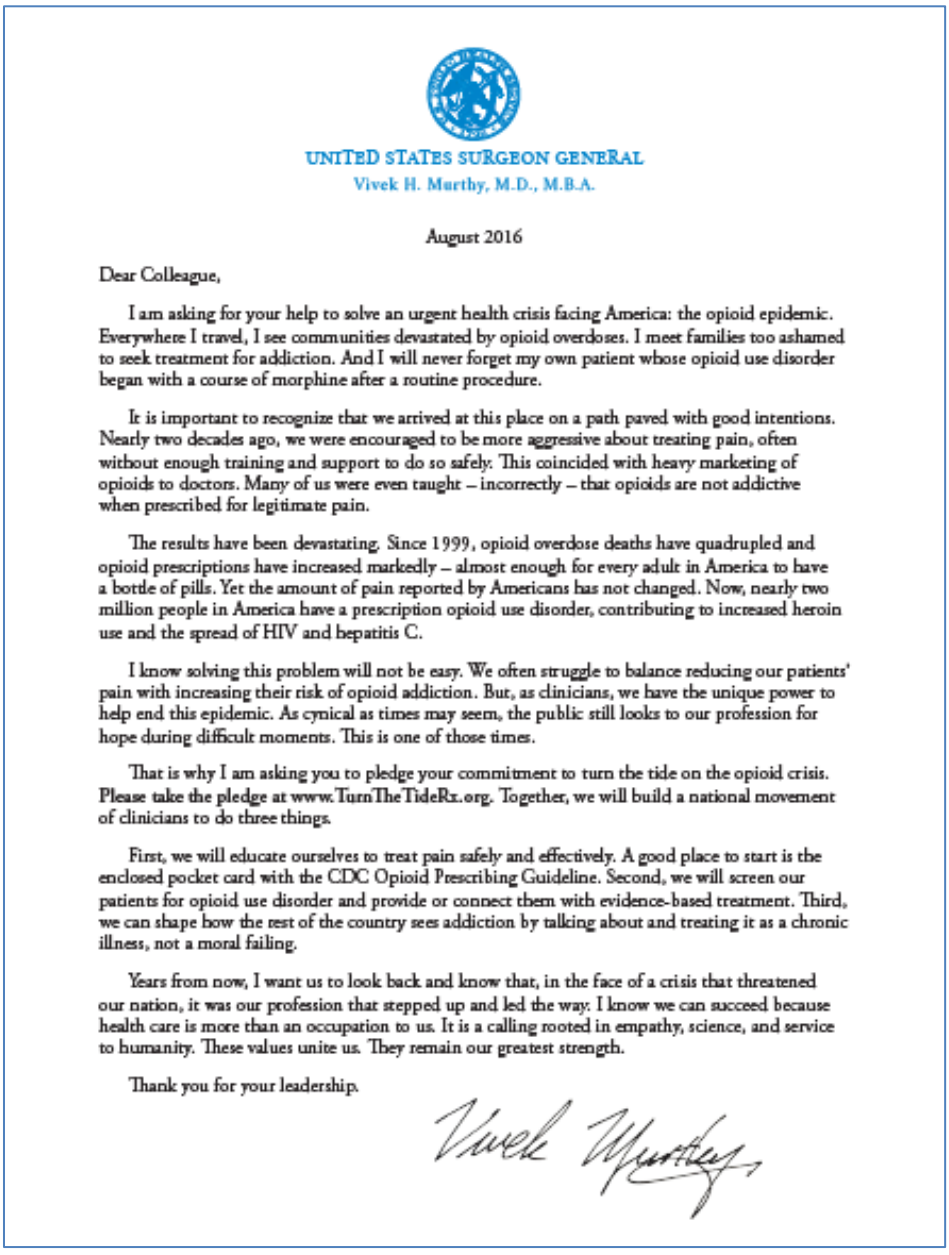
"Opioids present several potential problems, including side effects such as nausea and vomiting, post-operative ileus, respiratory depression, urinary retention, constipation and the potential for long-term dependence," according to a report by Frost & Sullivan in 2014, *Every Patient's Pain is Personal.* Although opioids prove to be an effective treatment for pain management, the drawbacks include the increased risk of fall-related injuries and potential abuse and addiction. As a result, many doctors are turning to emerging alternatives, including new formulations of local anesthetics and elastomeric pumps. *EXPAREL* has detailed its commitment to "providing patients with long-acting, non-opioid analgesic options". Halyard continues to conduct studies on how its products reduce opioid consumption. Future adoption of these therapies could impact usage of other modalities, according to Guidepost. In the U. S. there is a 55% increase in length of hospital stay due to opioid related AEs; according to Kessler ER, Shah M, Gruschkus SK, Raju A. Pharmacotherapy, 2013. Given the negative side effects and costs associated with opioid use, there is increasing focus from hospitals, payors and regulators on treatments that reduce opioid use in the treatment of postoperative pain.



Addressing the Opioid Epidemic Continues to Gain Attention

The issues associated with opioid addiction continue to garner major focus, which heightens the attention and importance of the development of safer, more effective products for pain management. Following the lead of the National Institutes of Health (NIH), the United States Surgeon General weighed in on this topic in a letter sent to all physicians in August 2016. While much of the focus is on patients in chronic pain, the need for a more effective, longer-lasting product for post-operative

pain management is critical, and represents a significant positive behind the early commercial acceptance and success of EXPAREL, despite its shortcomings, and in the development of superior alternatives such as AnestaGel.



UNITED STATES SURGEON GENERAL
Vivek H. Murthy, M.D., M.B.A.

August 2016

Dear Colleague,

I am asking for your help to solve an urgent health crisis facing America: the opioid epidemic. Everywhere I travel, I see communities devastated by opioid overdoses. I meet families too ashamed to seek treatment for addiction. And I will never forget my own patient whose opioid use disorder began with a course of morphine after a routine procedure.

It is important to recognize that we arrived at this place on a path paved with good intentions. Nearly two decades ago, we were encouraged to be more aggressive about treating pain, often without enough training and support to do so safely. This coincided with heavy marketing of opioids to doctors. Many of us were even taught – incorrectly – that opioids are not addictive when prescribed for legitimate pain.

The results have been devastating. Since 1999, opioid overdose deaths have quadrupled and opioid prescriptions have increased markedly – almost enough for every adult in America to have a bottle of pills. Yet the amount of pain reported by Americans has not changed. Now, nearly two million people in America have a prescription opioid use disorder, contributing to increased heroin use and the spread of HIV and hepatitis C.

I know solving this problem will not be easy. We often struggle to balance reducing our patients' pain with increasing their risk of opioid addiction. But, as clinicians, we have the unique power to help end this epidemic. As cynical as times may seem, the public still looks to our profession for hope during difficult moments. This is one of those times.

That is why I am asking you to pledge your commitment to turn the tide on the opioid crisis. Please take the pledge at www.TurnTheTideRx.org. Together, we will build a national movement of clinicians to do three things.

First, we will educate ourselves to treat pain safely and effectively. A good place to start is the enclosed pocket card with the CDC Opioid Prescribing Guideline. Second, we will screen our patients for opioid use disorder and provide or connect them with evidence-based treatment. Third, we can shape how the rest of the country sees addiction by talking about and treating it as a chronic illness, not a moral failing.

Years from now, I want us to look back and know that, in the face of a crisis that threatened our nation, it was our profession that stepped up and led the way. I know we can succeed because health care is more than an occupation to us. It is a calling rooted in empathy, science, and service to humanity. These values unite us. They remain our greatest strength.

Thank you for your leadership.

Vivek Murthy

Competition

EXPAREL (bupivacaine liposome injectable suspension) by Pacira Pharmaceuticals, Inc. is a direct competitor to the AnestaGel product. Currently EXPAREL dominates the market for non-opioid products used for postsurgical pain control. EXPAREL is a non-opioid local analgesic indicated for administration into the surgical site to produce postsurgical analgesia. EXPAREL combines bupivacaine with the DepoFoam® drug delivery platform to provide postsurgical pain control with a single intraoperative infiltration. EXPAREL's revenues exceeded $230 million in 2015.

EXPAREL has certain limitations including:

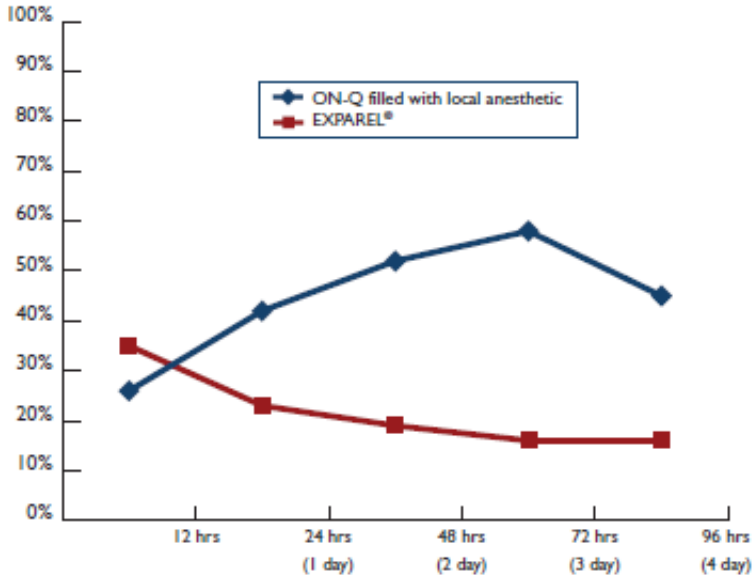
- EXPAREL is not tunable and can be migratory to the site and can be unpredictable
- EXPAREL has limited drug-load capacity
- EXPAREL is not manufactured in a variety of form factors to allow flexibility with physician preferences
- **EXPAREL provides inferior pain control over the full length of the post-operative period** as compared to pain pumps, such as the ON-Q Pain Relief System from I-Flow.

The Company believes that AnestaGel has unique characteristics that overcome these limitations. AnestaGel is tunable, can be manufactured in a variety of form factors, and can provide immediate and longer lasting pain control.

Pain pumps remain a primary and effective weapon against post-operative pain, et they continue to lose market share. "Based on Frost & Sullivan's own market research, pain pumps such as the On-Q® Pain Relief System from I-Flow® (subsidiary of Halyard), provide significant advantages over Pacira Pharmaceutical's EXPAREL for post-operative pain relief. Clinicians surveyed reported that the adoption of EXPAREL was rapid in 2013, but the aggregate clinical perspective is that ON-Q pumps deliver superior pain control over the full length of the post-operative period, and at a lower cost when looked at across the entire recovery period," according to the Frost & Sullivan 2014 White Paper, *Every Patient's Pain is Personal*

> *"Can you imagine putting a time-release pain agent in a pump, then stopping that pump and pulling its catheter after 24 hours because you just delivered another 72 hours of regional, non-opioid pain relief – without a pump? With the versatility of AnestaGel, this could happen for us."*
>
> *Dr. Ryan Nunley*
>
> *Washington University School of Medicine in St. Louis*

Which Pain Management Approach Provides Better Pain Relief at Specific Time Points (Anesthesiologists' Clinical Perspective)



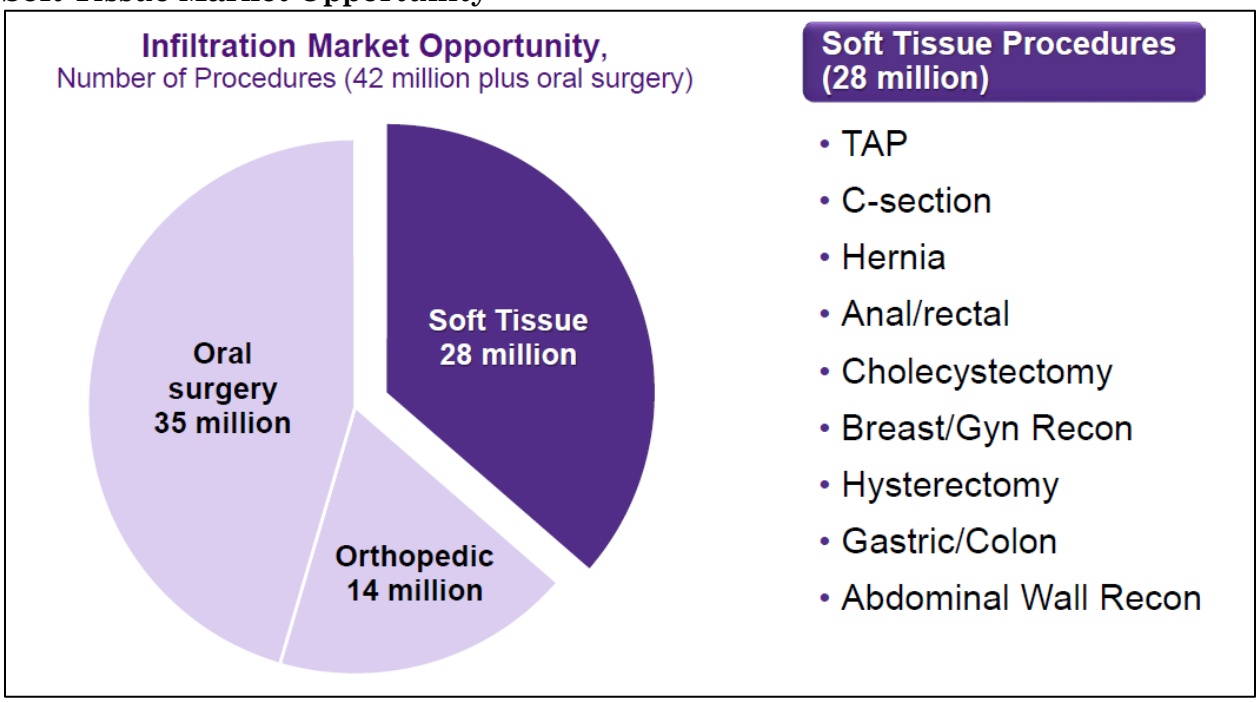
Source: Frost & Sullivan

Unlike the claim of up to 72 hours of pain control marketed by Pacira, anesthesiologist respondents stated that when EXPAREL was used without any adjunctive medications, it provided, on average, only 25 hours of pain relief in their clinical experience. Yet, according to Frost & Sullivan's research, clinicians expect that almost half of major surgery patients will have severely disabling pain beyond 25 hours.

EXPAREL's own clinical data is focused on bunionectomy and hemorrhoidectomy cases, where the clinicians surveyed reported that pain is lower in comparison to major surgery at that 25-hour threshold. Frost & Sullivan's research found that 85% of applications of the drug reported in this survey were neither of those two surgeries.

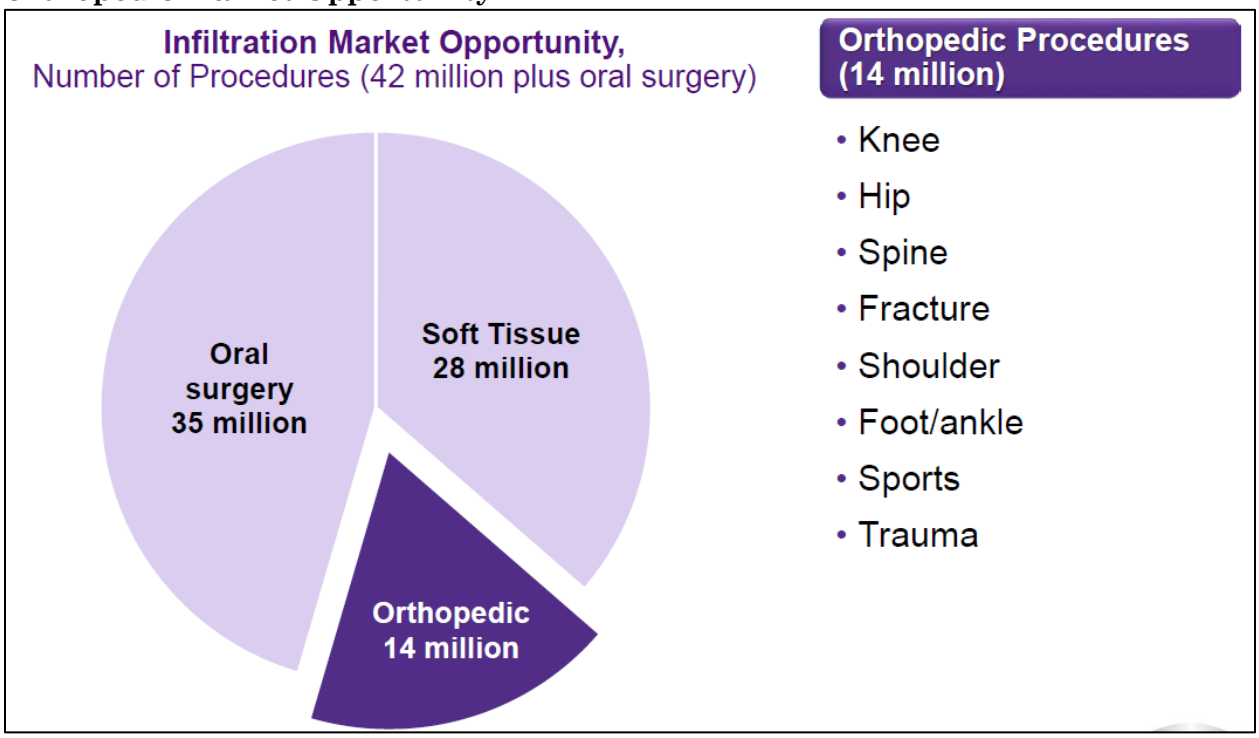
Relying on EXPAREL as a primary method of post-operative pain relief for major surgical cases runs the risk of under-treating pain later in the critical recovery period. The duration of actual pain relief the two products provide is a significant difference between the products. EXPAREL's claims to provide "up to 72 hours of pain control" are not supported by clinical perspective of participants surveyed or in independent research. The FDA's medical review for EXPAREL reported; "In the clinical trials described in the medical review, the duration of EXPAREL's analgesic effect appears to be no more than 24 hours and not longer than that of encapsulated bupivacaine HCl,"Buvanendran A, Fiala J, Patel KA, Golden AD, Moric M, Kroin JS. The incidence and severity of postoperative pain following inpatient surgery. Pain Med. 2015;16(12):2277–2283.

Soft Tissue Market Opportunity



Source: Pacira Pharmaceuticals Corporate Presentation

Orthopedic Market Opportunity



Source: Pacira Pharmaceuticals Corporate Presentation

There are a number of companies that are in various stages of development with new options for post-operative, non-opioid pain management, including (but not limited to) the following:

- Xaracoll – developing a collagen matrix with bupivacaine for postoperative pain management
- Regeneron Pharmaceuticals developing Fasinumab
- Innocoll, with its bupivicaine collagen sponge
- Heron Therapeutics and its HTX-011 product, a mix of bupivacaine and meloxicam for post-operative pain.

Intellectual Property & Patent Portfolio

The materials and AnestaGel applications are supported by a strong patent portfolio consisting of over 20 issued patents (primarily the Calabro patents through The Cleveland Clinic Foundation), and numerous published, pending, and filed and patents. InSitu's manufacturing and development Trade Secrets are aligned with the patent portfolio and maximize InSitu's core competencies across many medical platforms. In general terms, patents 6,982,298, 7,465,766 and 8,207,262 are foundation patents. These explain the chemistry of the hydrogel and introduce basic applications for the hydrogel. Patents 8,138,265, 8,080,260 and 8,410,180 are application specific, but will become foundational patents in the future as InSitu expands IP to include tissue engineering, delivery of hydrogel, and materials/cells to target sites and ways to manipulate the formulation specifically. The Company's existing patents primarily relate to:

- Crosslinking technology and variations using multiple biopolymer backbones
- Tunability of gel to create multiple physical forms
- Drug delivery in numerous applications
- Manufacturing Capabilities
- Significantly developed, proprietary methods

"Every aspect of AnestaGel intrigues me. It seems so simple, but to have the ability to deliver a PH neutral, bio-absorbable, bio-compatible carrier loaded with long-acting pain medications, have it stay where it's placed regardless of movement, deliver anesthesia for days, and is superior to any other product on the market.....this is a medical breakthrough and a definite GAME CHANGER."

Dr. Ryan Nunley
Washington University School of Medicine in St. Louis

U. S. PATENTS

Title	Inventors	Country	Date Filed	Date Issued	Status	Focus	Description
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Richard A. Gross, Aniq B.Darr	United States	1/8/2004	1/3/2006	Issued as U.S. Pat. No. 6,982,298 on 1/3/2006; 3rd maintenance fee due 7/3/2017	Broad macromolecular network generally; T-HA hydrogels	Primary foundation patent. Important for describing the chemistry and possible biopolymers that may be crosslinked using the same technology. Introduces concept of living cells and tissue encapsulated within the hydrogel. It also introduces concept of using bioactive compounds within the hydrogel that will elicit a response for the cells within the hydrogel and surrounding the hydrogel.
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	United States	7/7/2005	12/16/2008	Issued as U.S. Pat. No. 7,465,766 on 12/16/2008; 3rd maintenance fee due 6/16/2020	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material	Foundation 2 patent. Describing the original chemistry but also claiming tissue augmentation applications and other potential clinical applications. For example vocal cord augmentation, mitral valve prolapse, dermal augmentation, vitreal replacement, coatings on non-biological devices, etc. Where previous patent focused on chemicstry, cartilage and tissue matrix, this patent provides applications for many areas utilizing the hydrogel material.
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Richard A. Gross, Aniq B.Darr	United States	8/5/2005	5/6/2008	Issued as U.S. Pat. No. 7,368,502 on 5/6/2008; 3rd maintenance fee due 11/06/2019	Methods of making macromolecular networks and hydrogels (Divisional of US1)	Methods and Manufacturing Patent. Focused on freeze thaw approach to creating 3D structures using the gel. For example, and ear. Less important, but does introduce the concept of creating 3D structures and target specific geometries that can be seeded with tissues, bioactive compunds, etc.
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	United States	9/15/2008	6/26/2012	Issued as U.S. Pat. No. 8,207,262 on 6/26/2012; 2nd maintenance fee due 12/26/2019	Broader synthetic macromolecular network/ hydrogel claims;	Expanded foundational claims related to chemistry. Blocks others from side stepping original patent claims using similar but not the same chemistry. Introduces use of photofrin as a crosslinking material and UV light. Advantage of use of light could open applications where the material is injected into tartge tissues, shaped or filled completely into voids, then crosslinked externally using light or UV light.
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Aniq B. Darr, Richard A. Gross	United States	1/29/2009	3/20/2012	Issued as U.S. Pat. No. 8,138,265 on 3/20/2012; 2nd maintenance fee due 9/20/2019	Method of making hydrogel in situ	Methods and Manufacturing patent. Important concept of insitu crosslinking. Expands on examples of how to crosslink the material insitu. There are advantages to injecting a non-crosslinked material in the target tissue, manipulating the liquid or adding/subtracting material from a target site and then cross linking insitu when the desired augmentation or placement has been achieved.
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, Keiji Kamohara	United States	1/29/2009	9/20/2011	Issued as U.S. Pat. No. 8,021,350 on 9/20/2011; 2nd maintenance fee due 3/20/2019	Method of treating regurgitation of cardiac valves	Clkinical Application Specific patent. Treatment of mitral valve regurgitation using tissue augmentation via injected hydrogels. Although application specific, introduces concept of augmenting tissue by injection within walls of tissues to modify shape and thereby alter function of the tissue. Can be extropolated to cardiovascular tissue, gastrointestinal tissue, muscle contraction efficiency, etc.
Hydroxyphenyl Cross-Linked Macromolecular Network and	Peter A. Zahos, Anthony Calabro, Aniq B. Darr, Richard A. Gross	United States	2/27/2009	3/20/2012	Issued as U.S. Pat. No. 8,137,688 on 3/20/2012; 2nd	Synthetic nucleus pulposus	Clincal application specific patent. Focused on augmenting the spinal pulposa and introducing viable cells and bioactive compounds into the hydrogel. Autologous cell collection, separation and implantation.
Molecular Enhancement of Extracellular Matrix and Methods of Use	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony Calabro	United States	2/13/2009	12/20/2011	Issued as U.S. Pat. No. 8,080,260 on 12/20/2011; 2nd maintenance fee due 6/20/2019	Enhancement of ECM using Calabro material (fascia lata); Patch for tissue (e.g. tendon) repair	impregnating an extracellular matrix with the hydrogel to ellicit desired healing response and promote healing of tissues. Important in that it introduces the concept of introducing ECM and other similar materials (synthetic ECM) within the hydrogel. Critical step for future tissue engineering applications.
Compositions and Methods to Treat Urinary Incontinence	Anthony Calabro, Aniq B. Darr, Firouz Daneshgari	United States	4/30/2009	4/2/2013	Issued as U.S. Pat. No. 8,410,180 on 4/2/2013; 1st maintenance fee due 10/2/2016	Methods of treating SUI using hydroxyphenyl-substituted collagen network	focused on method to promote tissue regeneration (possible scar tissue) in a deisred location to augment and support neighboring tissue structures. In this case it is treating SUI by causing the body to reconfigure the protein based hydrogel into supportive tissue that will hold the urethra up and maintain geometry and prevent leakage due to deformed urethra. Important in that it introduces the concept of the body remoldeling a protein based hydrogel. In comgination with ECM, HA based hydrogel, concept of tensegrity and geometric pockets to promote desired tissue engineering response.

INTERNATIONAL PATENTS

Title	Inventors	Country	Date Filed	Focus
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Richard A. Gross, Aniq B.Darr	Czech Republic	7/8/2005	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Richard A. Gross, Aniq B.Darr	Europe	1/9/2004	Synthetic macromolecular network generally; Methods of making and hydrogel so-made
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	Europe	7/8/2005	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	France	7/8/2005	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	Germany	7/8/2005	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	United Kingdom	7/8/2005	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	Hong Kong	9/3/2007	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material (Extension from EP1)
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	Italy	7/8/2005	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material
Hydroxyphenyl Cross-Linked Macromolecular Network and Applications Thereof	Anthony Calabro, Lee Akst, Daniel Alam, James Chan, Aniq B. Darr, Kiyotaka Fukamachi, Richard A. Gross, David Haynes, Keiji Kamohara, Daniel P. Knott, Hilel Lewis, Alex Melamud, Anthony Miniaci, Marshall Strome	Sweden	7/8/2005	Synthetic, implantable tissue matrix; Specific synthetic tissues made of that material
Molecular Enhancement of Extracellular Matrix and Methods of Use	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony Calabro	Europe	2/13/2009	Enhancement of ECM using Calabro material (fascia lata); Patch for tissue (e.g. tendon) repair
Molecular Enhancement of Extracellular Matrix and Methods of Use	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony Calabro	Germany	2/13/2009	Enhancement of ECM using Calabro material (fascia lata); Patch for tissue (e.g. tendon) repair
Molecular Enhancement of Extracellular Matrix and Methods of Use	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony Calabro	Spain	2/13/2009	Enhancement of ECM using Calabro material (fascia lata); Patch for tissue (e.g. tendon) repair
Molecular Enhancement of Extracellular Matrix and Methods of Use	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony Calabro	France	2/13/2009	Enhancement of ECM using Calabro material (fascia lata); Patch for tissue (e.g. tendon) repair
Molecular Enhancement of Extracellular Matrix and Methods of Use	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony Calabro	United Kingdom	2/13/2009	Enhancement of ECM using Calabro material (fascia lata); Patch for tissue (e.g. tendon) repair
Molecular Enhancement of Extracellular Matrix and Methods of Use	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony Calabro	Italy	2/13/2009	Enhancement of ECM using Calabro material (fascia lata); Patch for tissue (e.g. tendon) repair
Molecular Enhancement of Extracellular	Kathleen Anne Derwin, Joseph Patrick Iannotti, LiKang Chin, Anthony	WIPO	2/13/2009	
Compositions and Methods to Treat Urinary Incontinence	Anthony Calabro, Aniq B. Darr, Firouz Daneshgari	WIPO	4/30/2009	

InSitu has also begun filing its own patent applications. The Company's focus applies specifically to drug delivery, and expands on applications and introduces concepts for tissue engineering, drug elution, different types of depots (drug any type of material that can hold an excess of drug material.

Other areas of IP focus on tuning the hydrogel to target a desired elution rate of a delivered drug or bioactive molecule. The IP describes the types of depots, or drug reservoirs, which could work with the formulation, the binding matrix that holds the depots in place during the elution process, and ways to tune the reservoirs (and matrix) to work with multiple types of drug molecules and bioactive molecules of various size and molecular weight. Finally, the Company's IP strategy contemplates all of the different formulations and configurations that can be delivered through a variety of placement devices.

Overview of Clinical Data & Process

GLP ANIMAL STUDY& PHARMOKINETIC (PK) STUDIES

InSitu completed its GLP animal study in Q1 2017. The study was designed to evaluate and compare the effects of AnestaGel and EXPAREL on mechanical allodynia in a post-operative pain model in rats. The study was designed for statistical superiority, with 30 rats per arm. Testing took place at NAMSA in Brooklyn Park, Minnesota.

In a series of independent tests performed under GLP regulations, comparing operative site injections of AnestaGel and EXPAREL® from Pacira, Inc., AnestaGel was proven to last longer, and provide a greater analgesic effect than EXPAREL. In a separate test that determines the PharmacoKinetic(PK) effect for the painkiller bupivacaine, which is used in both AnestaGel and EXPAREL, bupivacaine was proven to be released from AnestaGel into the blood as long as 96-120 hours after injection exceeding the presence of bupivacaine in the blood from both EXPAREL and straight bupivacaine injections.

DOSING STUDY

InSitu completed dosing studies in Q3 2016 to maximize pain relief and mitigate toxicity. AnestaGel has an unlimited capacity to carry bupivicaine, while liposomes are limited in carrying its drug dose. InSitu's Matrix BioHydrogel crosslinks with the bupivicaine in the pH neutral solution. The liposome formation, on the other hand, is sensitive to production conditions, limiting the bupivicaine solubility in the formation phase of production. Ultimately, the more bupivicaine present in the depot/reservoir, the longer the elution will occur, and the higher the elution rate. The new AnestaGel formulation is designed to maximize elution rate and duration in a safe manner that does not exceed the maximum daily dose of Bupivacaine.

During the company's dosing study, three different formulations were tested using standard nerve block techniques. Three animals were tested for each formulation, and immediately after recovering from the block procedure all rats were observed to have motor block in the tested limb and no toxicity

At 72 hours post-procedure, rats in two of the three formulas had regained use of the affected limb. Rats in the other formulation had started to recover use of the affected limb, but did not recover full motor function until 84 hours or more.

The formulations, which dispensed up to eight times (8x) the amount of bupivicaine as compared to EXPAREL, clearly demonstrated pain relief without toxic effect.

InSitu believes they may have the ability to load even more bupivacaine without toxicity, should the company's eventual commercialization partner desire a form of product that provides more than five (5) days of region pain relief. InSitu expects that it will be able to determine this based on the blood serum levels observed in the company's upcoming GLP testing.

Feasibility Study

InSitu Biologics initiated a preclinical feasibility study on AnestaGel in early 2016, comparing its AnestaGel-P™ formulation in a post-operative incisional pain rat model versus a positive control, EXPAREL from Pacira. AnestaGel-P is a tunable bio-hydrogel, offering customizable concentrations of local anesthetics with consistent elution mechanics of superior duration. Liposomal delivery systems are not crosslinked. Low viscosity exposes greater surface area relative to volume, accelerating degradation, with resultant less consistent elution mechanics.

AnestaGel-P provided superior analgesic effectiveness 24 and 48 hours post administration of the hydrogel compared toEXPAREL Liposome suspended solution. Histology results demonstrate the AnestaGel-P test article was still present at conclusion of the study, but the EXPAREL was not present in tissue samples. Delivery vehicle migration away from the injection

site will reduce analgesic drug delivery to the surgical site as it will carry the drug material within it as it migrates away.

Matrix BioHydrogel engineered AnestaGel-P exceeded EXPAREL in efficacy in a pre-clinical study, due to AnestaGel's customized tunable unique crosslinking. It performed as well as EXPAREL< 24hrs and exceeded EXPAREL analgesic effectiveness at 24 and 48 hours. AnestaGel-P also remained present in the injection location while EXPAREL was no longer present at the end of the study. Due to its consistency, AnestaGel-P will not migrate from the injection site.

Due to its crosslinked reservoir design, AnestaGel-P was able to carry more bupivacaine and demonstrated the ability to supply pain relief superior to EXPAREL up to 72 hours. AnestaGel-P is designed to quickly release drug from the binding matrix short term and then continuously supply the drug to the injection site by elution from the dense hydrogel particle reservoirs. EXPAREL is dependent upon the continuous degradation of the liposomes and is dosed at a lower concentration.The physical properties of a homogeneous, densely crosslinked molecular structure facilitates superior elution mechanics. Demonstrating non-Newtonian fluid properties, the viscosity of AnestaGel-P increases with resistance, retarding migration from the targeted site of placement. EXPAREL, in contrast, possesses classical low viscosity fluid mechanics, freely migrating through the interstitial space away from the target tissue, diminishing efficacy. Liposome technology relies on the chance meeting of it being metabolized in a timely manner. AnestaGel is over 90%

water, just like the body, leaving nothing to chance; it delivers the relief as the Matrix opens up.

Safety & Toxicity

The Matrix Biohydrogel product has also successfully completed ISO 10993 Safety & Toxicity testing, passing all 14 stages of safety and toxicity tests.

LEGAL

There are no pending legal issues relating to the Company.

USE OF PROCEEDS TO COMPANY

The Use of Proceeds is an estimate based on the Company's current business plan. A portion of the proceeds from this Offering may ultimately be used to compensate or otherwise make payments to officers or directors of the Company. The officers and directors of the Company may be paid salaries and receive benefits that are commensurate with similar companies, and a portion of the proceeds may be used to pay these ongoing business expenses.

The Company reserves the right to change the use of proceeds set out herein based on the needs of the ongoing business of the Company and the discretion of the Company's management. The Company may reallocate the estimated use of proceeds among the various categories or for other uses if management deems such a reallocation to be appropriate. Until sufficient funds are raised by the Company to sufficiently fund research activities, management may utilize some or all of the funds from this Offering for further capital raising efforts, rather than as set out in this Use of Proceeds section of the Offering Circular.

The Company has attempted to identify, in context, certain of the factors it currently believes may cause actual future experience and results to differ from its current expectations. The differences may be caused by a variety of factors, including but not limited to adverse economic conditions, lack of market acceptance, reduction of consumer demand, unexpected costs and operating deficits, lower sales and revenues than forecast, default on leases or other indebtedness, loss of suppliers, loss of supply, loss of distribution and service contracts, price increases for capital, supplies and materials, inadequate capital, inability to raise capital or financing, failure to obtain customers, loss of customers and failure to obtain new customers, the risk of litigation and administrative proceedings involving the Company or its employees, loss of government licenses and permits or failure to obtain them, higher than anticipated labor costs, the possible acquisition of new businesses or products that result in operating losses or that do not perform as anticipated, resulting in unanticipated losses, the possible fluctuation and volatility of the Company's operating results and financial condition, adverse publicity and news coverage, inability to carry out marketing and sales plans, loss of key executives, changes in interest rates, inflationary factors, and other specific risks that may be referred to in this Offering Circular or in other reports issued by us or by third-party publishers.

The Matrix BioHydrogel platform and AnestaGel have established technological credibility through its extensive patents, preclinical testing, and long-term development work. InSitu's long term goal is to bring the AnestaGel product to the global market with a Strategic Marketing Partner(s). The market partner strategy is very common in the pharmaceutical marketplace, as the infrastructure, overhead, and barriers to entry dilute the focus and crush the financial well-being of small, product development based companies such as ours. By identifying the Strategic Marketing Partner at an early stage, the companies can deliver a final product, or family of products, in a form factor or variety of form factors over time, that specifically suit the Strategic Marketing Partner's preference. The Company believes AnestaGel represents a significant opportunity for a platform technology,

with numerous product-line extensions, and the potential for new, ancillary products such as delivery devices.

The short-term goal for InSitu is to complete extensive Phase I Clinical Testing and prepare for rapid Phase 2, and Phase 3 Clinical Study completion. To achieve the next phase of the Plan, an additional minimum of five million dollars is required. With these monies, the Company expects to complete the following:

- Complete repeat dose, one-month duration subcutaneous toxicology studies, in two species.
- Regulatory filings / consultant fees for New Drug Application
- Complete production of AnestaGel for Phase 1 human use.
- Product and Process Development, filling, and packaging, sterility testing
- Clinical Study Phase I: Evaluate the Onset of Action for AnestaGel Following Local Infiltration in Healthy Volunteers
    - 132 healthy volunteer patients randomized to AnestaGel , Exparel or a Placebo after creation of pain.
    - Core lab analysis, lab fees, patient enrollment, product, clinical and regulatory oversight.
- General and Administration obligations

Detailed financial information can be found in Appendix One: Financial Pro Forma.

RISK FACTORS

In addition to the other information in this Memorandum, a number of factors may affect our business and prospects. These factors include but are not limited to the following, which you should consider carefully in evaluating our business and prospects. If any of the following risks actually occur, our business, financial condition, results of operations and growth prospects may be materially and adversely affected.

Risks Related to Our Business

New chemical entities derived from our Matrix BioHydrogel Program, which is in the early stages of development, may require more time and resources for development, testing and regulatory clearance, and may not result in viable commercial products.

Our Matrix BioHydrogel Program is in the early stages of development, involves a novel therapeutic approach and new chemical entities, requires significant further research and development and regulatory approvals and is subject to the risks of failure inherent in the development of products based on innovative approaches. New chemical entities derived from our Matrix BioHydrogel Program are molecules that have not previously been approved and marketed as therapeutics, unlike product candidates in our Drug Delivery Programs, in which we apply our formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which we aim to improve in some manner through a new formulation. As a result, the product candidates from our

Matrix BioHydrogel Program may face greater risk of unanticipated safety issues or other side-effects, or may not demonstrate efficacy. Further, the regulatory pathway for our new chemical entities may be more demanding than that for product candidates under our Drug Delivery Programs, for which we may be able to leverage existing data under Section 505(b)(2) of the Act to reduce development risk, time and cost.

Also, because our Matrix BioHydrogel Program is in early stages, we have not defined with precision those indications we wish to pursue initially, each of which may have unique challenges. If the first indications pursued do not show positive results, the credibility of any product candidate from this program may be tarnished, even if the molecule might be effective for other indications. Our decisions regarding which indications to pursue may cause us to fail to capitalize on indications that could have given rise to viable commercial products and profitable market opportunities.

New chemical entities derived from our Matrix BioHydrogel Program, which is in the early stages of development, may require more time and resources for development, testing and regulatory clearnace, and may not result in viable commercial products

Our Matrix BioHydrogel Program is in the early stages of development, involves a novel therapeutic approach and new chemical entities, requires significant further research and development and regulatory approvals and is subject to the risks of failure inherent in the development of products based on innovative approaches. New chemical entities derived from our Matrix BioHydrogel Program are molecules that have not previously been approved and marketed as therapeutics, unlike product candidates in our Drug Delivery Programs, in which we apply our formulation expertise and technologies largely to active pharmaceutical ingredients whose safety and efficacy have previously been established but which we aim to improve in some manner through a new formulation. As a result, the product candidates from our Matrix BioHydrogel Program may face greater risk of unanticipated safety issues or other side-effects, or may not demonstrate efficacy. Further, the regulatory pathway for our new chemical entities may be more demanding than that for product candidates under our Drug Delivery Programs, for which we may be able to leverage existing data under Section 505(b)(2) of the Act to reduce development risk, time and cost.

Also, because our Matrix BioHydrogel Program is in early stages, we have not defined with precision those indications we wish to pursue initially, each of which may have unique challenges. If the first indications pursued do not show positive results, the credibility of any product candidate from this program may be tarnished, even if the molecule might be effective for other indications. Our decisions regarding which indications to pursue may cause us to fail to capitalize on indications that could have given rise to viable commercial products and profitable market opportunities.

Early indications of activity from GLP Pre-clinical (animal) studies of AnestaGel may not predict the results of clinical (human) trials

There can be no assurance that clinical studies will demonstrate the safety or efficacy of AnestaGel in a statistically significant manner. The failure of AnestaGel to show efficacy in Phase 2 or Phase 3 clinical trials would significantly harm our business.

Clinical trial safety results, including for AnestaGel, may not be confirmed

While some clinical trials of our product candidates may show indications of safety and efficacy, there can be no assurance that these results will be confirmed in subsequent clinical trials or provide a sufficient basis for regulatory approval. In addition, side effects observed in clinical trials, or other side effects that appear in later clinical trials, may adversely affect our or our collaborators' ability to obtain regulatory approval or market our product candidates. For example, the reduction in pain intensity on movement of AnestaGel compared to bupivacaine HCl in previous trials may not be repeated in the ongoing AnestaGe trials. There can be no assurance that the additional clinical trial that could be conducted for AnestaGel will be sufficient to obtain FDA approval, and any additional trials would entail added expense and further delay or may preclude product approval, harming our business, prospects and financial condition.

Regulatory action or failure to obtain product approvals could delay or limit development and commercialization of our product candidates and result in failure to achieve anticipated revenues

The manufacture and marketing of our pharmaceutical product candidates and our research and development activities are subject to extensive regulation for safety, efficacy and quality by numerous government authorities in the United States and abroad. We or our third-party collaborators must obtain clearance or approval from applicable regulatory authorities before we or they, as applicable, can perform clinical trials, market or sell our products in development in the United States or abroad. Clinical trials, manufacturing and marketing of products are subject to the rigorous testing and approval process of the FDA and equivalent foreign regulatory authorities. In particular, the FDA rigorously focuses on the safety of drug products at every stage of drug development and commercialization from initial clinical trials to regulatory approval and beyond, and the interpretation of data that may pertain to safety can be subject to the interpretation of individual reviewers within the FDA. These rigorous and potentially evolving standards, that often differ by therapeutic area, may delay and increase the expenses of our development efforts. The FDA or other foreign regulatory agency may, at any time, halt our and our collaborators' development and commercialization activities due to safety concerns, in which case our business will be harmed. In addition, the FDA or other foreign regulatory agency may refuse or delay approval of our or our collaborators' drug candidates for failure to collect sufficient clinical or animal safety data, and require us or our collaborators to conduct additional clinical or animal safety studies which may cause lengthy delays and increased costs to our programs.

The Federal Food, Drug and Cosmetic Act and other federal, state and foreign statutes and regulations govern and influence the testing, manufacture, labeling, advertising, distribution and promotion of drugs and medical devices. These laws and regulations are complex and subject to change. Furthermore, these laws and regulations may be subject to varying interpretations, and we may not be able to

predict how an applicable regulatory body or agency may choose to interpret or apply any law or regulation to our pharmaceutical product candidates. As a result, clinical trials and regulatory approval can take a number of years to accomplish and require the expenditure of substantial resources. We or our third-party collaborators, as applicable, may encounter delays or rejections based upon administrative action or interpretations of current rules and regulations. We or our third-party collaborators, as applicable, may not be able to timely reach agreement with the FDA on our clinical trials or on the required clinical or animal data we or they must collect to continue with our clinical trials or eventually commercialize our product candidates.

We or our third-party collaborators, as applicable, may also encounter delays or rejections based upon additional government regulation from future legislation, administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. We or our third-party collaborators, as applicable, may encounter similar delays in foreign countries. Sales of our pharmaceutical product candidates outside the United States are subject to foreign regulatory standards that vary from country to country.

The time required to obtain approvals from foreign countries may be shorter or longer than that required for FDA approval, and requirements for foreign licensing may differ from FDA requirements. We or our third-party collaborators, as applicable, may be unable to obtain requisite approvals from the FDA and foreign regulatory authorities, and even if obtained, such approvals may not be on a timely basis, or they may not cover the clinical uses that we specify. If we or our third-party collaborators, as applicable, fail to obtain timely clearance or approval for our development products, we or they will not be able to market and sell our pharmaceutical product candidates, which will limit our ability to generate revenue.

We may depend to a large extent on third-party collaborators, and we have limited or no control over the development, sales, distribution and disclosure for our pharmaceutical product candidates which are the subject of third-party collaborative or license agreements

Our performance may depend to a large extent on the ability of third-party collaborators to successfully develop and obtain approvals for our pharmaceutical product candidates. We hope to enter into agreements with many companies under which we grant such third parties the right to develop, apply for regulatory approval for, market, promote or distribute AnestGel and certain other Matrix BioHydrogel based product candidates, subject to payments to us in the form of product royalties and other payments. We have limited or no control over the expertise or resources that any collaborator may devote to the development, clinical trial strategy, regulatory approval, marketing or sale of these product candidates, or the timing of their activities. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreement with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. Enforcing any of these agreements in the event of a breach by the other party could require the expenditure of significant resources and consume a significant amount of management time and attention. Our collaborators may also conduct their activities in a manner that is different from the manner we would have chosen, had we been developing such product candidates ourselves. Further, our collaborators may elect not to develop or commercialize product candidates arising

out of our collaborative arrangements or not devote sufficient resources to the development, clinical trials, regulatory approval, manufacture, marketing or sale of these product candidates. If any of these events occur, we may not recognize revenue from the commercialization of our product candidates based on such collaborations. In addition, these third parties may have similar or competitive products to the ones which are the subject of their collaborations with us, or relationships with our competitors, which may reduce their interest in developing or selling our product candidates. We may not be able to control public disclosures made by some of our third-party collaborators, which could negatively impact our stock price.

Cancellation of collaborations regarding our product candidates may impact our revenues and adversely affect potential economic benefits

Third-party collaboration agreements typically allow the third party to terminate the agreement (or a specific program within an agreement) by providing notice.

Our revenues may depend on collaboration agreements with other companies. These agreements may subject us to obligations which must be fulfilled and also make our revenues dependent on the performance of such third parties. If we are unable to meet our obligations or manage our relationships with our collaborators under these agreements or enter into additional collaboration agreements or if our existing collaborations are terminated, our revenues may decrease. Acquisitions of our collaborators can be disruptive

Our revenues may be based to a significant extent on collaborative arrangements with third parties, pursuant to which we receive payments based on our performance of research and development activities set forth in these agreements. We may not be able to fulfill our obligations or attain milestones set forth in any specific agreement, which could cause our revenues to fluctuate or be less than anticipated and may expose us to liability for contractual breach. In addition, these agreements may require us to devote significant time and resources to communicating with and managing our relationships with such collaborators and resolving possible issues of contractual interpretation which may detract from time our management would otherwise devote to managing our operations. Such agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property under collaborations. Such disputes can delay or prevent the development of potential new product candidates, or can lead to lengthy, expensive litigation or arbitration. From time to time, our licensees may be the subject of an acquisition by another company. Such transactions can lead to turnover of program staff, a review of development programs and strategies by the acquirer, and other events that can disrupt a program, resulting in program delays or discontinuations.

If any of our collaborative agreements were to be terminated or delayed, our anticipated revenues may be reduced or not materialize, and our products in development related to those agreements may not be commercialized.

Our cash flows are likely to differ from our reported revenues

Our revenues will likely differ from our cash flows from revenue-generating activities. Upfront payments received upon execution of collaborative agreements are recorded as deferred revenue and generally recognized on a straight-line basis over

the period of our continuing involvement with the third-party collaborator pursuant to the applicable agreement.

Our revenues may also depend on milestone payments based on achievements by our third-party collaborators. Failure of such collaborators to attain such milestones would result in our not receiving additional revenues

In addition to payments based on our performance of research and development activities, our revenues may also depend on the attainment of milestones set forth in our collaboration agreements. Such milestones are typically related to development activities or sales accomplishments. While our involvement is necessary to the achievement of development-based milestones, the performance of our third-party collaborators is also required to achieve those milestones. Under our third-party collaborative agreements, our third party collaborators will take the lead in commercialization activities and we are typically not involved in the achievement of sales-based milestones. Therefore, we are even more dependent upon the performance of our third-party collaborators in achieving sales-based milestones. To the extent we and our third-party collaborators do not achieve such development-based milestones or our third-party collaborators do not achieve sales-based milestones, we will not receive the associated revenues, which could harm our financial condition and may cause us to defer or cut-back development activities or forego the exploitation of opportunities in certain geographic territories, any of which could have a material adverse effect on our business.

Our business strategy includes the entry into additional collaborative agreements. We may not be able to enter into additional collaborative agreements or may not be able to negotiate commercially acceptable terms for these agreements

Our current business strategy includes the entry into additional collaborative agreements for the development and commercialization of our pharmaceutical product candidates. The negotiation and consummation of these types of agreements typically involve simultaneous discussions with multiple potential collaborators and require significant time and resources from our officers, business development, legal, and research and development staff. In addition, in attracting the attention of pharmaceutical and biotechnology company collaborators, we compete with numerous other third parties with product opportunities as well the collaborators' own internal product opportunities. We may not be able to consummate additional collaborative agreements, or we may not be able to negotiate commercially acceptable terms for these agreements. If we do not consummate additional collaborative agreements, we may have to consume money more rapidly on our product development efforts, defer development activities or forego the exploitation of certain geographic territories, any of which could have a material adverse effect on our business.

We will require and may have difficulty raising needed capital in the future

Our business currently does not generate sufficient revenues to meet our capital requirements and we do not expect that it will do so in the near future. We have expended and will continue to expend substantial funds to complete the research, development and clinical testing of our pharmaceutical product candidates. We will require additional funds for these purposes, to establish additional clinical- and commercial-scale manufacturing arrangements and facilities, and to provide for the marketing and distribution of our product candidates. Additional funds may not be

available on acceptable terms, if at all. If adequate funds are unavailable from operations or additional sources of financing, we may have to delay, reduce the scope of or eliminate one or more of our research or development programs which would materially harm our business, financial condition and results of operations.

We believe that our cash, cash equivalents and investments, will be adequate to satisfy our capital needs for at least the next 12 months. However, our actual capital requirements will depend on many factors, including:

- regulatory actions with respect to our product candidates;
- continued progress and cost of our research and development programs;
- the continuation of our collaborative agreements that provide financial funding for our activities;
- success in entering into collaboration agreements and meeting milestones under such agreements;
- progress with preclinical studies and clinical trials;
- the time and costs involved in obtaining regulatory clearance;
- costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- costs of developing sales, marketing and distribution channels and our ability and that of our collaborators to sell our pharmaceutical product candidates;
- costs involved in establishing manufacturing capabilities for clinical and commercial quantities of our product candidates;
- competing technological and market developments;
- market acceptance of our product candidates;
- costs for recruiting and retaining employees and consultants; and
- unexpected legal, accounting and other costs and liabilities related to our business.

We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding. We may seek to raise any necessary additional funds through equity or debt financings, convertible debt financings, collaborative arrangements with corporate collaborators or other sources, which may be dilutive to existing stockholders and may cause the price of our common stock to decline. In addition, in the event that additional funds are obtained through arrangements with collaborators or other sources, we may have to relinquish rights to some of our technologies or pharmaceutical product candidates that we would otherwise seek to develop or commercialize ourselves. If adequate funds are not available, we may be required to significantly reduce or refocus our product development efforts, resulting in delays in generating future product revenue.

We and any third-party collaborators may not be able to manufacture sufficient quantities of our pharmaceutical product candidates and components to support the clinical and commercial requirements of our collaborators and ourselves at an acceptable cost or in compliance with applicable government regulations, and we have limited manufacturing experience

We or any third-party collaborators to whom we have assigned such responsibility must manufacture our pharmaceutical product candidates and components in clinical and commercial quantities, either directly or through third parties, in compliance with regulatory requirements and at an acceptable cost. The manufacturing processes associated with our product candidates are complex. We have not yet completed development of the manufacturing process for any product candidates or components, including AnestaGel and our other Matrix BioHydrogel-based drug candidates. If we and our third-party collaborators, where relevant, fail to timely complete the development of the manufacturing process for our product candidates, we and our third-party collaborators, where relevant, will not be able to timely produce product for clinical trials and commercialization of our product candidates. We have also committed to manufacture and supply product candidates or components under a number of our collaborative agreements with third-party companies. We have limited experience manufacturing pharmaceutical products, and we may not be able to timely accomplish these tasks. If we and our third-party collaborators, where relevant, fail to develop manufacturing processes to permit us to manufacture a product candidate or component at an acceptable cost, then we and our third-party collaborators may not be able to commercialize that product candidate or we may be in breach of our supply obligations to our third-party collaborators.

Our manufacturing partner in Chaska, Minnesota is a multi-disciplinary site that we contract with to manufacture our products, including AnestGel and our other Matrix BioHydrogel based candidates. If we experience delays or technical difficulties in scaling up the manufacturing of our product candidates, it could result in delays or added cost in our development programs. We have not manufactured commercial quantities of any of our product candidates. In the future, we intend to develop additional manufacturing capabilities for our product candidates and components to meet our demands and those of our third-party collaborators by contracting with third-party manufacturers.

If we and our third-party collaborators, where relevant, are unable to manufacture our pharmaceutical product candidates or components in a timely manner or at an acceptable cost, quality or performance level, and are unable to attain and maintain compliance with applicable regulations, the clinical trials and the commercial sale of our product candidates and those of our third-party collaborators could be delayed. Additionally, we may need to alter our facility design or manufacturing processes, install additional equipment or do additional construction or testing in order to meet regulatory requirements, optimize the production process, increase efficiencies or production capacity or for other reasons, which may result in additional cost to us or delay production of product needed for the clinical trials and commercial launch of our product candidates and those of our third-party collaborators.

If we or our third-party collaborators cannot manufacture our pharmaceutical product candidates or components in time to meet the clinical or commercial

requirements of our collaborators or ourselves or at an acceptable cost, our operating results will be harmed.

Failure to comply with ongoing governmental regulations for our pharmaceutical product candidates could materially harm our business in the future

Marketing or promoting a drug is subject to very strict controls. Furthermore, clearance or approval may entail ongoing requirements for post-marketing studies. The manufacture and marketing of drugs are subject to continuing FDA and foreign regulatory review and requirements that we update our regulatory filings. Later discovery of previously unknown problems with a product, manufacturer or facility, or our failure to update regulatory files, may result in restrictions, including withdrawal of the product from the market. Any of the following or other similar events, if they were to occur, could delay or preclude us from further developing, marketing or realizing full commercial use of our product candidates, which in turn would materially harm our business, financial condition and results of operations:

- failure to obtain or maintain requisite governmental approvals;

- failure to obtain approvals for clinically intended uses of our pharmaceutical product candidates under development; or

- FDA required product withdrawals or warnings arising from identification of serious and unanticipated adverse side effects in our product candidates.

Manufacturers of drugs must comply with the applicable FDA good manufacturing practice regulations, which include production design controls, testing, quality control and quality assurance requirements as well as the corresponding maintenance of records and documentation. Compliance with current good manufacturing practices regulations is difficult and costly. Manufacturing facilities are subject to ongoing periodic inspection by the FDA and corresponding state agencies, including unannounced inspections, and must be licensed before they can be used for the commercial manufacture of our development products. We and/or our present or future suppliers and distributors may be unable to comply with the applicable good manufacturing practice regulations and other FDA regulatory requirements. We have not been subject to a good manufacturing regulation inspection by the FDA relating to our product candidates. If we, our third-party collaborators or our respective suppliers do not achieve compliance for our product candidates we or they manufacture, the FDA may refuse or withdraw marketing clearance or require product recall, which may cause interruptions or delays in the manufacture and sale of our product candidates.

We have a history of operating losses, expect to continue to have losses in the future and may never achieve or maintain profitability

We have incurred operating losses since our inception in 2014 and, as of October 1, 2017, had an accumulated deficit of approximately $1.3 million. We expect to continue to incur significant operating losses over the next several years as we continue to incur significant costs for research and development, clinical trials, manufacturing, sales, and general and administrative functions. Our ability to achieve profitability depends upon our ability, alone or with others, to successfully complete the development of our proposed product candidates, obtain the required

regulatory clearances, and manufacture and market our proposed product candidates. Development of pharmaceutical product candidates is costly and requires significant investment. In addition, we may choose to license from third parties either additional drug delivery platform technology or rights to particular drugs or other appropriate technology for use in our product candidates. The license fees for these technologies or rights would increase the costs of our product candidates.

We do not anticipate meaningful revenues to derive from the commercialization and marketing of our product candidates in development in the near future, and therefore do not expect to generate sufficient revenues to cover expenses or achieve profitability in the near future.

We may develop our own sales force and commercial group to market future products but we have limited sales and marketing experience with respect to pharmaceuticals and may not be able to do so effectively

We may choose to develop our own sales force and commercial group to market products that we may develop in the future. Developing a sales force and commercial group will require substantial expenditures and the hiring of qualified personnel. We have limited sales and marketing experience, and may not be able to effectively recruit, train or retain sales personnel. If we are not able to put in place an appropriate sales force and commercial group for AnestaGel, we may not be able to effectively launch the product. We may not be able to effectively sell our product candidates, if approved, and our failure to do so could limit or materially harm our business.

We and our third-party collaborators may not sell our product candidates effectively

We and any third-party collaborators compete with many other companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts and those of our third-party collaborators may be unable to compete successfully against these other companies. We and our third-party collaborators, if relevant, may be unable to establish a sufficient sales and marketing organization on a timely basis, if at all. We and our third-party collaborators, if relevant, may be unable to engage qualified distributors. Even if engaged, these distributors may:

- fail to satisfy financial or contractual obligations to us;
- fail to adequately market our product candidates;
- cease operations with little or no notice to us;
- offer, design, manufacture or promote competing product lines;
- fail to maintain adequate inventory and thereby restrict use of our product candidates; or
- build up inventory in excess of demand thereby limiting future purchases of our product candidates resulting in significant quarter-to-quarter variability in our sales.

The failure of us or any third-party collaborators to effectively develop, gain regulatory approval for, sell, manufacture and market our product candidates will hurt our business, prospects and financial results.

We will rely heavily on third parties to support development, clinical testing and manufacturing of our product candidates

We will rely on third-party contract research organizations, consultants, service providers and suppliers to provide critical services to support development, clinical testing, and manufacturing of our product candidates. For example, we currently depend on third-party vendors to manage and monitor our clinical trials and to perform critical manufacturing steps for our product candidates. These third parties may not execute their responsibilities and tasks competently in compliance with applicable laws and regulations or in a timely fashion. We rely on third-parties to manufacture or perform manufacturing steps relating to our product candidates or components. We anticipate that we will continue to rely on these and other third-party contractors to support development, clinical testing, and manufacturing of our product candidates. Failure of these contractors to provide the required services in a competent or timely manner or on reasonable commercial terms could materially delay the development and approval of our development products, increase our expenses and materially harm our business, financial condition and results of operations.

Key components of our product candidates are provided by limited numbers of suppliers, and supply shortages or loss of these suppliers could result in interruptions in supply or increased costs

Certain components and drug substances used in our product candidates, including AnestaGel, and our other Matrix BioHydrogel-based drug candidates, are currently purchased from a single or a limited number of outside sources. The reliance on a sole or limited number of suppliers could result in:

- delays associated with redesigning a pharmaceutical product candidate due to a failure to obtain a single source component;
- an inability to obtain an adequate supply of required components; and
- reduced control over pricing, quality and delivery time.

We have supply agreements in place for certain components of our pharmaceutical product candidates, but do not have in place long term supply agreements with respect to all of the components of any of our product candidates. Therefore the supply of a particular component could be terminated at any time without penalty to the supplier. In addition, we may not be able to procure required components or drugs from third-party suppliers at a quantity, quality and cost acceptable to us. Any interruption in the supply of single source components could cause us to seek alternative sources of supply or manufacture these components internally. Furthermore, in some cases, we are relying on our third-party collaborators to procure supply of necessary components. If the supply of any components for our product candidates is interrupted, components from alternative suppliers may not be available in sufficient volumes or at acceptable quality levels

within required timeframes, if at all, to meet our needs or those of our third-party collaborators. This could delay our ability to complete clinical trials and obtain approval for commercialization and marketing of our product candidates, causing us to lose sales, incur additional costs, delay new product introductions and could harm our reputation.

If we are unable to adequately protect, maintain or enforce our intellectual property rights or secure rights to third-party patents, we may lose valuable assets, experience reduced market share or incur costly litigation to protect our rights or our third-party collaborators may choose to terminate their agreements with us

Our ability to commercially exploit our products will depend significantly on our ability to obtain and maintain patents, maintain trade secret protection and operate without infringing the proprietary rights of others.

As of October 1, 2017, we have licensed over 20 unexpired issued U.S. patents and over 23 unexpired issued foreign patents (which include granted European patent rights that have been validated in various EU member states). In addition, we have a pending U.S. patent application and over numerous foreign applications pending in Europe, Australia, Japan, Canada and other countries.

There can be no assurance that the pending patent applications will be granted. The granted claims in the U.S. include both composition of matter and method of treatment claims. There can be no assurance that the pending patent applications will be granted.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, our patent applications or those that are licensed to us may not issue into patents, and any issued patents may not provide protection against competitive technologies or may be held invalid if challenged. Our competitors may also independently develop products similar to ours or design around or otherwise circumvent patents issued to us or licensed by us. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as U.S. law.

The patent laws of the U.S. have recently undergone changes through court decisions which may have significant impact on us and our industry. Decisions of the U.S. Supreme Court and other courts with respect to the standards of patentability, enforceability, availability of injunctive relief and damages may make it more difficult for us to procure, maintain and enforce patents. In addition, the America Invents Act was signed into law in September 2011, which among other changes to the U.S. patent laws, changes patent priority from "first to invent" to "first to file," implements a post-grant opposition system for patents and provides a prior user defense to infringement. These judicial and legislative changes have introduced significant uncertainty in the patent law landscape and may potentially negatively impact our ability to procure, maintain and enforce patents to provide exclusivity for our products.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our

employees, consultants, advisors and collaborators to execute appropriate confidentiality and assignment-of-inventions agreements with us. These agreements typically provide that all materials and confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual's relationship with us will be our exclusive property. These agreements may be breached, and in some instances, we may not have an appropriate remedy available for breach of the agreements. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer our information and techniques, or otherwise gain access to our proprietary technology.

We may be unable to meaningfully protect our rights in trade secrets, technical know-how and other non-patented technology. We may have to resort to litigation to protect our intellectual property rights, or to determine their scope, validity or enforceability. In addition, interference, derivation, post-grant oppositions, and similar proceedings may be necessary to determine rights to inventions in our patents and patent applications. Enforcing or defending our proprietary rights is expensive, could cause diversion of our resources and may be unsuccessful. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technology to develop or sell competing products.

Our future collaboration agreements may depend on our intellectual property

We expect to be party to collaborative agreements with pharmaceutical companies. Potential third-party collaborators may have entered into these agreements based on the exclusivity that our intellectual property rights confer on the products being developed. The loss or diminution of our intellectual property rights could result in a decision by our third-party collaborators to terminate their agreements with us. In addition, these agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property and data under collaborations. Such disputes can lead to lengthy, expensive litigation or arbitration requiring us to devote management time and resources to such dispute which we would otherwise spend on our business. To the extent that our agreements call for future royalties to be paid conditional on our having patents covering the royalty-bearing subject matter, the decision by the Supreme Court in the case of *MedImmune v. Genentech* could encourage our licensees to challenge the validity of our patents and thereby seek to avoid future royalty obligations without losing the benefit of their license. Should they be successful in such a challenge, our ability to collect future royalties could be substantially diminished.

We may be sued by third parties claiming that our product candidates infringe on their intellectual property rights, particularly because there is substantial uncertainty about the validity and breadth of medical patents

We or our potential collaborators may be exposed to future litigation by third parties based on claims that our product candidates or activities infringe the intellectual property rights of others or that we or our collaborators have misappropriated the trade secrets of others. This risk is exacerbated by the fact that the validity and breadth of claims covered in medical technology patents and the breadth and scope of trade secret protection involve complex legal and factual

questions for which important legal principles are unresolved. Any litigation or claims against us or our collaborators, whether or not valid, could result in substantial costs, could place a significant strain on our financial resources and could harm our reputation. We also may not have sufficient funds to litigate against parties with substantially greater resources. In addition, pursuant to our collaborative agreements, we have provided our collaborators with the right, under specified circumstances, to defend against any claims of infringement of the third party intellectual property rights, and such collaborators may not defend against such claims adequately or in the manner that we would do ourselves. Intellectual property litigation or claims could force us or our collaborators to do one or more of the following, any of which could harm our business or financial results:

- cease selling, incorporating or using any of our pharmaceutical product candidates that incorporate the challenged intellectual property, which would adversely affect our revenue;

- obtain a license from the holder of the infringed intellectual property right, which license may be costly or may not be available on reasonable terms, if at all; or

- redesign our product candidates, which would be costly and time-consuming.

Technologies and businesses which we acquire or license may be difficult to integrate, disrupt our business, dilute stockholder value or divert management attention

We may acquire technologies, products or businesses to broaden the scope of our existing and planned product lines and technologies. Future acquisitions expose us to:

- increased costs associated with the acquisition and operation of the new businesses or technologies and the management of geographically dispersed operations;
- the risks associated with the assimilation of new technologies, operations, sites and personnel;
- the diversion of resources from our existing business and technologies;
- the inability to generate revenues to offset associated acquisition costs;
- the requirement to maintain uniform standards, controls, and procedures; and
- the impairment of relationships with employees and customers or third-party collaborators as a result of any integration of new management personnel.

Acquisitions may also result in the issuance of dilutive equity securities, the incurrence or assumption of debt or additional expenses associated with the amortization of acquired intangible assets or potential businesses. Acquisitions may not generate any additional revenue or provide any benefit to our business.

Some of our pharmaceutical product candidates contain controlled substances, the making, use, sale, importation and distribution of which are subject to regulation by state, federal and foreign law enforcement and other regulatory agencies

Some of our product candidates currently under development contain, and our products in the future may contain, controlled substances which are subject to state, federal and foreign laws and regulations regarding their manufacture, use, sale, importation and distribution. For our product candidates containing controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation and distribution of controlled substances. These regulations are extensive and include regulations governing manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, record keeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of drug candidates including controlled substances. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. In addition, because of their restrictive nature, these regulations could limit our commercialization of our product candidates containing controlled substances. In particular, among other things, there is a risk that these regulations may interfere with the supply of the drugs used in our clinical trials, and in the future, our ability to produce and distribute our products in the volume needed to meet commercial demand.

Write-offs related to the impairment of long-lived assets, inventories and other non-cash charges, as well as stock-based compensation expenses may adversely impact or delay our profitability

We may incur significant non-cash charges related to impairment write-downs of our long-lived assets, including goodwill and other intangible assets. We will continue to incur non-cash charges related to amortization of other intangible assets. We are required to perform periodic impairment reviews of our goodwill at least annually. However, there can be no assurance that upon completion of subsequent reviews a material impairment charge will not be recorded. If future periodic reviews determine that our assets are impaired and a write-down is required, it will adversely impact or delay our profitability.

The valuation of inventory requires us to estimate the value of inventory that may become expired prior to use. We may be required to expense previously capitalized inventory costs upon a change in our judgment, due to, among other potential factors, a denial or delay of approval of a product by the necessary regulatory bodies, changes in product development timelines, or other information that suggests that the inventory will not be saleable.

Global credit and financial market conditions could negatively impact the value of our current portfolio of cash equivalents, short-term investments or long-term investments and our ability to meet our financing objectives

Our cash and cash equivalents will be maintained in highly liquid investments with remaining maturities of 90 days or less at the time of purchase. Our short-term investments could consist primarily of readily marketable debt securities with original maturities of greater than 90 days from the date of purchase but remaining maturities of less than one year from the balance sheet date. Our long-term investments could consist primarily of readily marketable debt securities with maturities in one year or beyond from the balance sheet date. While, as of the date of this filing, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents, short-term investments or long-term investments, no assurance can be given that deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents, short-term investments or long-term investments or our ability to meet our financing objectives.

We depend upon key personnel who may terminate their employment with us at any time, and we may need to hire additional qualified personnel

Our success will depend to a significant degree upon the continued services of key management, technical and scientific personnel. In addition, our success will depend on our ability to attract and retain other highly skilled personnel, particularly as we develop and expand our Epigenomic Regulator Program. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all. Our management and other employees may voluntarily terminate their employment with us at any time. The loss of the services of key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to product development or approval, loss of sales and diversion of management resources.

We may not successfully manage our company through varying business cycles

Our success will depend on properly sizing our company through growth and contraction cycles caused in part by changing business conditions, which places a significant strain on our management and on our administrative, operational and financial resources. To manage through such cycles, we must expand or contract our facilities, our operational, financial and management systems and our personnel. If we were unable to manage growth and contractions effectively our business would be harmed.

Our business involves environmental risks and risks related to handling regulated substances

In connection with our research and development activities and our manufacture of materials and pharmaceutical product candidates, we are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Although we believe that we have complied with the applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the use, generation and disposal of hazardous materials, including but not limited to certain

hazardous chemicals, solvents, agents and biohazardous materials. The extent of our use, generation and disposal of such substances has increased substantially since we started manufacturing and selling biodegradable polymers. Although we believe that our safety procedures for storing, handling and disposing of such materials comply with the standards prescribed by state and federal regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. We currently contract with third parties to dispose of these substances generated by us, and we rely on these third parties to properly dispose of these substances in compliance with applicable laws and regulations. If these third parties do not properly dispose of these substances in compliance with applicable laws and regulations, we may be subject to legal action by governmental agencies or private parties for improper disposal of these substances. The costs of defending such actions and the potential liability resulting from such actions are often very large. In the event we are subject to such legal action or we otherwise fail to comply with applicable laws and regulations governing the use, generation and disposal of hazardous materials and chemicals, we could be held liable for any damages that result, and any such liability could exceed our resources.

We currently have debt. Compliance with repayment obligations and other covenants may be difficult, and failure by us to fulfill our obligations under the applicable loan agreements may cause the repayment obligations to accelerate.

From July through October 2014, we entered into a Convertible Loan Agreement (the "Loan Agreement") with five individuals. The principal loan amounts total $300,000 and accrue interest at a rate of 10% annually. The Notes are not secured, and have a 10-year term from the date of funding. The Noteholders have the option of conversion or a preferred repayment upon the sale or license of AnestaGel to a third party. The loan and interest, or any part thereof can be converted in to shares. There is no prepayment fee. The Loan Agreement may prove a burden to the Company as they become due.

Risks Related To Our Industry

The market for our pharmaceutical product candidates is rapidly changing and competitive, and new products or technologies developed by others could impair our ability to grow our business and remain competitive

The pharmaceutical industry is subject to rapid and substantial technological change. Developments by others may render our product candidates under development or technologies noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition in the industry from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase.

We may face competition from other companies in numerous industries including pharmaceuticals, medical devices and drug delivery. Our Matrix BioHydrogel based products, including AnestaGel, if cleared by the FDA and other governing bodies, will compete with currently marketed oral opioids, transdermal opioids, local anesthetic patches, anti-psychotics, stimulants, implantable and external infusion pumps which can be used for infusion of opioids and local anesthetics. Products of these types are marketed by Purdue Pharma, AbbVie, Janssen, Medtronic, Endo, AstraZeneca, Pernix

Therapeutics, Tricumed, Halyard Health, Cumberland Pharmaceuticals, Pacira, Acorda Therapeutics, Mallinckrodt, Shire, Johnson & Johnson, Eli Lilly, Pfizer, Novartis and others. Purdue Pharma, Sandoz, Actavis, Collegium Pharmaceutical, Pfizer, Elite Pharmaceuticals, Intellipharmaceutics, Egalet, Teva Pharmaceuticals and others have also announced regulatory approval or development plans for abuse deterrent opioid products. Numerous companies are applying significant resources and expertise to the problems of drug delivery and several of these are focusing or may focus on delivery of drugs to the intended site of action, including Alkermes, Pacira, Immune Pharmaceuticals, Innocoll, Nektar, Kimberly-Clark, Acorda Therapeutics, Flamel, Alexza, Mallinckrodt, Hospira, Pfizer, Cumberland Pharmaceuticals, Egalet, Acura, Elite Pharmaceuticals, Phosphagenics, Intellipharmaceutics, Collegium Pharmaceutical, Heron Therapeutics and others. Some of these competitors may be addressing the same therapeutic areas or indications as we are. Our current and potential competitors may succeed in obtaining patent protection or commercializing products before us. Many of these entities have significantly greater research and development capabilities than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors' financial, marketing, manufacturing and other resources.

We are engaged in the development of novel therapeutic technologies. Our resources are limited and we may experience technical challenges inherent in such novel technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these products may have an entirely different approach or means of accomplishing similar therapeutic effects than our product candidates. Our competitors may develop products that are safer, more effective or less costly than our product candidates and, therefore, present a serious competitive threat to our product offerings.

The widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our product candidates even if commercialized. Chronic and post-operative pain are currently being treated by oral medication, transdermal drug delivery systems, such as drug patches, injectable products and implantable drug delivery devices which will be competitive with our product candidates. These treatments are widely accepted in the medical community and have a long history of use. The established use of these competitive products may limit the potential for our product candidates to receive widespread acceptance if commercialized.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and

relationships through which we would market, sell and distribute our products. As a pharmaceutical company, even though we do not and may not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. These regulations include:

- the Federal Healthcare Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid, and which will constrain our marketing practices and the marketing practices of our licensees, educational programs, pricing policies, and relationships with healthcare providers or other entities;

- the federal physician self-referral prohibition, commonly known as the Stark Law, which prohibits physicians from referring Medicare or Medicaid patients to providers of "designated health services" with whom the physician or a member of the physician's immediate family has an ownership interest or compensation arrangement, unless a statutory or regulatory exception applies;

- federal false claims laws that prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other government reimbursement programs that are false or fraudulent, and which may expose entities that provide coding and billing advice to customers to potential criminal and civil penalties, including through civil whistleblower or qui tam actions, and including as a result of claims presented in violation of the Federal Healthcare Anti-Kickback Statute, the Stark Law or other healthcare-related laws, including laws enforced by the FDA;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services, and which as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- federal physician sunshine requirements under the Affordable Care Act, which requires manufacturers of drugs, devices, biologics and medical supplies to report annually to HHS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations;

- the Federal Food, Drug, and Cosmetic Act, which, among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing

drug products for off-label use and regulates the distribution of drug samples; and

- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payors, including private insurers, state laws requiring pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and which may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state and foreign laws governing the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws such as HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

In the United States, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future revenue and profitability and the future revenue and profitability of our collaborators or potential collaborators. Federal and state lawmakers regularly propose and, at times, enact legislation that results in significant changes to the healthcare system, some of which is intended to contain or reduce the costs of medical products and services. For example, in March 2010, the President signed one of the most significant healthcare reform measures in decades, the Affordable Care Act. It contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which impact existing government healthcare programs and will result in the development of new programs. The Affordable Care Act, among other things:

- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs";

- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;

- requires collection of rebates for drugs paid by Medicaid managed care organizations;

- addresses new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extension products;

- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and

- mandates a further shift in the burden of Medicaid payments to the states.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, automatic reductions to several government programs were enacted during "sequestration." These reductions included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or the ATRA, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additional state and federal healthcare reform measures may be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates once approved or additional pricing pressures.

We could be exposed to significant product liability claims which could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage

The testing, manufacture, marketing and sale of our product candidates involve an inherent risk that product liability claims will be asserted against us. Although we are insured against such risks up to an annual aggregate limit in connection with clinical trials and commercial sales of our product candidates, our present product liability insurance may be inadequate and may not fully cover the costs of any claim or any ultimate damages we might be required to pay. Product liability claims or other claims related to our product candidates, regardless of their outcome, could require us to spend significant time and money in litigation or to pay significant damages. Any successful product liability claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable or reasonable terms. In addition, product liability coverage may cease to be available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our product

candidates. A product liability claim could also significantly harm our reputation and delay market acceptance of our product candidates.

Acceptance of our pharmaceutical product candidates in the marketplace is uncertain, and failure to achieve market acceptance will delay our ability to generate or grow revenues

Our future financial performance will depend upon the successful introduction and customer acceptance of our products in research and development, including AnestaGel and other Matrix BioHydrogel-based candidates. Even if approved for marketing, our product candidates may not achieve market acceptance. The degree of market acceptance will depend upon a number of factors, including:

the receipt of regulatory clearance of marketing claims for the uses that we are developing;

the establishment and demonstration in the medical community of the safety and clinical efficacy of our products and their potential advantages over existing therapeutic products, including oral medication, transdermal drug delivery products such as drug patches, injectable therapeutics, or external or implantable drug delivery products; and

pricing and reimbursement policies of government and third-party payors such as insurance companies, health maintenance organizations, hospital formularies and other health plan administrators.

Physicians, patients, payors or the medical community in general may be unwilling to accept, utilize or recommend any of our products. If we are unable to obtain regulatory approval, commercialize and market our future products when planned and achieve market acceptance, we will not achieve anticipated revenues.

If users of our products are unable to obtain adequate reimbursement from third-party payors, or if new restrictive legislation is adopted, market acceptance of our products may be limited and we may not achieve anticipated revenues

The continuing efforts of government and insurance companies, health maintenance organizations and other payors of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and third-party collaborators and the availability of capital. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, recent federal and state government initiatives have been directed at lowering the total cost of health care, and the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such proposals could materially harm our business, financial condition and results of operations.

The successful commercialization of our product candidates will depend in part on the extent to which appropriate reimbursement levels for the cost of our product candidates and related treatment are obtained by governmental authorities, private

health insurers and other organizations, such as HMOs. Third-party payors often limit payments or reimbursement for medical products and services. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may limit reimbursement or payment for our products. The cost containment measures that health care payors and providers are instituting and the effect of any health care reform could materially harm our ability to operate profitably.

If we or our third-party collaborators are unable to train physicians to use our pharmaceutical product candidates to treat patients' diseases or medical conditions, we may incur delays in market acceptance of our products

Broad use of our product candidates will require extensive training of numerous physicians on the proper and safe use of our product candidates. The time required to begin and complete training of physicians could delay introduction of our products and adversely affect market acceptance of our products. We or third parties selling our product candidates may be unable to rapidly train physicians in numbers sufficient to generate adequate demand for our product candidates. Any delay in training would materially delay the demand for our product candidates and harm our business and financial results. In addition, we may expend significant funds towards such training before any orders are placed for our products, which would increase our expenses and harm our financial results.

Potential new accounting pronouncements and legislative actions are likely to impact our future financial position or results of operations

Future changes in financial accounting standards may cause adverse, unexpected fluctuations in the timing of the recognition of revenues or expenses and may affect our financial position or results of operations. New pronouncements and varying interpretations of pronouncements have occurred with frequency and may occur in the future and we may make changes in our accounting policies in the future. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new SEC regulations, PCAOB pronouncements and NASDAQ rules, are creating uncertainty for companies such as ours and insurance, accounting and auditing costs are high as a result of this uncertainty and other factors. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

Our operating history makes evaluating our stock difficult

Our quarterly and annual results of operations have historically fluctuated and we expect will continue to fluctuate for the foreseeable future. We believe that period-to-period comparisons of our operating results should not be relied upon as predictive of future performance. Our prospects must be considered in light of the risks,

expenses and difficulties encountered by companies with no approved pharmaceutical products, particularly companies in new and rapidly evolving markets such as pharmaceuticals, drug delivery and biotechnology. To address these risks, we must, among other things, obtain regulatory approval for and commercialize our product candidates, which may not occur. We may not be successful in addressing these risks and difficulties. We may require additional funds to complete the development of our product candidates and to fund operating losses to be incurred in the next several years.

Investors may experience substantial dilution of their investment

Investors may experience dilution of their investment if we raise capital through the sale of additional equity securities or convertible debt securities or grant additional stock options to employees and consultants.

The price of our common stock may be volatile

The stock markets in general, and the markets for pharmaceutical stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock.

Price declines in our common stock could result from general market and economic conditions and a variety of other factors, including:

failure of third-party collaborators to work with the Company;

adverse results or delays in our clinical and non-clinical trials AnestGel or our other Matrix BioHydrogel-based product candidates;

announcements of FDA non-approval of our product candidates, or delays in the FDA or other foreign regulatory agency review process;

adverse actions taken by regulatory agencies or law enforcement agencies with respect to our product candidates, clinical trials, manufacturing processes or sales and marketing activities, or those of our third party collaborators;

announcements of technological innovations, patents, product approvals or new products by our competitors;

regulatory, judicial and patent developments in the United States and foreign countries;

any lawsuit involving us or our product candidates including intellectual property infringement or product liability suits;

announcements concerning our competitors, or the biotechnology or pharmaceutical industries in general;

developments concerning our strategic alliances or acquisitions;

actual or anticipated variations in our operating results;

changes in recommendations by securities analysts or lack of analyst coverage;

deviations in our operating results from the estimates of analysts;

sales of our common stock by our executive officers or directors or sales of substantial amounts of common stock by us or others;

loss or disruption of facilities due to natural disasters;
changes in accounting principles; or
loss of any of our key scientific or management personnel.

The market price of our common stock may fluctuate significantly in response to factors which are beyond our control. The stock market in general has recently experienced extreme price and volume fluctuations. In addition, the market prices of securities of technology and pharmaceutical companies have also been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause a decline in the value of our common stock.

In the past, following periods of volatility in the market price of a particular company's securities, litigation has often been brought against that company. If litigation of this type is brought against us, it could be extremely expensive and divert management's attention and our company's resources.

We have broad discretion over the use of our cash and investments, and their investment may not always yield a favorable return

Our management has broad discretion over how our cash and investments are used and may from time to time invest in ways with which our stockholders may not agree and that do not yield favorable returns.

Executive officers, directors and principal stockholders have substantial control over us, which could delay or prevent a change in our corporate control favored by our other stockholders

Our directors, executive officers and principal stockholders, together with their affiliates, have substantial control over us. The interests of these stockholders may differ from the interests of other stockholders. As a result, these stockholders, if acting together, could have the ability to exercise control over all corporate actions requiring stockholder approval irrespective of how our other stockholders may vote, including:

- the election of directors;
- the amendment of charter documents;
- the approval of certain mergers and other significant corporate transactions, including a sale of substantially all of our assets; or

- the defeat of any non-negotiated takeover attempt that might otherwise benefit the public stockholders.

Our certificate of incorporation, our bylaws and Delaware law contain provisions that could discourage another company from acquiring us

Provisions of Delaware law, our certificate of incorporation and bylaws may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions include:

- authorizing the issuance of "blank check" preferred stock without any need for action by stockholders;

- providing for a classified board of directors with staggered terms;

- requiring supermajority stockholder voting to effect certain amendments to our certificate of incorporation and bylaws;

- eliminating the ability of stockholders to call special meetings of stockholders;

- prohibiting stockholder action by written consent; and

- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

DIRECTORS, EXECUTIVE OFFICERS AND SIGNIFICANT EMPLOYEES

The directors, executive officers and significant employees of the Company as of the date of this filing are as follows:

Executives and Key Advisors

Jim Segermark, President, Chief Executive Officer

Jim has been the founder, inventor, investor, and owner operator of numerous medical device ventures. Jim has as an extensive record of developing, managing and selling medical related companies. Jim has also established successful joint ventures and acted as a project consultant for strategic medical device opportunities. Jim is the President and Managing Governor of InSitu Biologics, Inc., St. Paul, Minnesota.

Jim was the founder of Eight Medical Corporation, a hyperthermic lavage system cleared by the FDA, which was sold in September of 2012. For three years prior to founding Eight Medical, Jim operated ThermaSolutions, Inc., a turnaround company in the hyperthermic lavage market. Jim was the Founder, Chairman (and first patient) of VMBC, LLC, TheVasclip Company, from 2001 - 2007. He founded

ViaMedics, LLC in 1998, a designer and manufacturer of proprietary medical devices. This company spun out The Vasclip Company and completed other product line based transactions. Jim served in various senior management positions at Microvena Corporation from 1991 until January of 1998. Jim served on the Board of Directors for Microvena from 1995-1997, and Infinity Extrusion and Engineering from 1995-1998.

Jim entered the medical device industry in 1987, marketing cardiac monitoring equipment for Circadian, Incorporated, and then marketed angioplasty products for the USCI Division of C.R. Bard.Jim founded his first company, Vascular Dynamics, Incorporated, a designer and manufacturer of exact medical models, in 1989. VDI was successfully sold and remains the industry standard for working vascular models today.

Jim holds dozens of patents and in the past 36 months has helped launch several new ventures. Jim recently helped launch AliveLock, Awestruck Medical and Capture Vascular.

Jim holds his MBA from Cardinal Stritch University, Milwaukee, Wisconsin with an emphasis in Finance and holds a B.S. from Carroll University, Waukesha, Wisconsin.

James Knapp, Chairman, Board of Directors

James Knapp, 40**,** CRPC, CFP, APMA is founder and President of Heritage Wealth Architects. He is responsible for leading all aspects of the firm. Earlier in his career, as a CFP, James led a franchise for one of the largest financial planning firms in the country. James specializes in advising executives, small business owners, and high net-worth individuals concerned with tax-planning, compensation, buying, growing or selling their businesses. James started HWA as a fee for service firm with a vision to provide clients with a personalized, flexible and thorough array of options to create and conserve wealth. At the center of his client-focused firm is the commitment to honor his fiduciary responsibilities, and really listen to each individual's goals and dreams. James is a Business Management graduate of Luther College, and lives in St. Paul, where he enjoys spending time with his family, traveling, hunting, fishing, climbing mountains and playing golf.

William J. Taylor, Chief Scientist

Bill is a successful medical device development program manager and scientist. Currently Bill leads multiple projects for ACIST Medical Systems including CVi – A2000V, CVi – CPT2000, and RXi rapid exchange FFR system and Navvus catheter; an ultrathin microcatheter pressure sensor. In 2007, Bill was recruited to lead a biohydrogel technology development program in cooperation with the Cleveland Clinic Foundation and was able to complete biocompatibility testing, fundamental physical and chemical property design package, initial application identification and start feasibility analysis. Bill was the lead project manager in the construction, qualification and validation of PDL Biopharma's (formerly Protein Design Labs, Inc.)state-of-the-art, $200 million production facility in Brooklyn Park, MN. Throughout his career he has been the program manager in medical device and biopharmaceutical product development including Retavase (Roche), Osteoarthritis

injectable, and several consumable kits. Prior to 2004, Bill was a principal scientist, inventor and program manager at Gradient Technology. Bill has authored industry papers in chemical remediation and demilitarization utilizing biological systems.

Bill has his Bachelor of Science from the University of Minnesota with a double major in Chemical Engineering and Biology.

Ryan Nunley, MD, Medical Advisor
Washington University School of Medicine - Associate Professor, Orthopedic Surgery

Dr. Nunley is an orthopedic surgeon at Washington University School of Medicine with a focus on hip and knee reconstructive surgery in adults. His clinical interests include: total hip and knee replacement surgery, minimally invasive hip replacement, minimally invasive knee surgery, arthroscopy of the hip, hip labral tears, femoral-acetabular impingement, hip disorders of the adolescent and young adult including hip dysplasia, Perthes deformities, avascular necrosis, and early arthritic hip joint problems. In that capacity, Dr. Nunley has extensive experience in perioperative pain management. He has a main focus on moving total joint surgery to a same day discharge procedure and avoiding having patients stay in the hospital after surgery.

Dr. Nunley received his undergraduate degree from Vanderbilt University in Nashville, TN, and his medical degree from the University of North Carolina School of Medicine in Chapel Hill, North Carolina. He completed his residency in Orthopedic Surgery at the Washington University School of Medicine. Dr. Nunley completed a Health Policy fellowship from the American Academy of Orthopedic Surgeons in Washington, DC as well as a fellowship in Joint Preservation, Resurfacing and Replacement at Washington University School of Medicine in St. Louis.

Dr. Nunley is a Consultant/Advisor to numerous healthcare companies including: Biocomposites, Blue Belt Technologies, Cardinal Health, Ethicon, Johnson & Johnson/DePuySynthes, Medical Compression Systems, Medtronic, Microport (Wright Medical Technologies), Mitek, Polaris, and Smith & Nephew.

Dr. Nunley has published over ninety scientific articles in Orthopedics and presented over 200 lectures across the United States and Internationally. He has authored eight book chapters. He serves on multiple Boards including the American Association of Hip and Knee Surgeons (AAHKS), the Southern Orthopaedic Association (SOA), and the Missouri State Orthopaedic Association (MSOA) and is an active member in the Mid-America Orthopaedic Association, Knee Society, and Hip Society.

Dr. Nunley has received numerous prestigious awards including:

- James A. Rand Award (most outstanding Paper in arthroplasty surgery presented at American Association of Hip and Knee Surgeons)

- AAHKS Poster Award winner
- Marshall R. Urist Young Investigator Award
- Harley and Betty Baxter Resident Research Award
- Knee Society Mark Coventry Award
- American Academy of Orthopaedic Surgeons Best Poster Award
- Best Doctors in America® list, 2011-present

Jacob Hutchins, MD, Medical Advisor, Principal Investigator for GLP Study Director of the Regional Anesthesia Acute Pain and Ambulatory Surgery division at the University of Minnesota

Dr. Hutchins is also the medical director for Maple Grove Ambulatory Surgery Center and the M Health Ambulatory Surgery Center. His current research interests include ultrasound-guided regional anesthesia in adult and pediatric acute postoperative pain as well as ambulatory anesthesia. His research also involves the use of liposomal bupivacaine for postoperative pain control in a variety of surgical procedures.

Dr. Hutchins is the principal investigator for the AnestaGel GLP study, and he has been an investigator for several trials for EXPAREL for Pacira Pharmaceuticals. Dr. Hutchins also serves as a consultant and teacher for both Pacira and Halyard Heath. He has published numerous peer-reviewed publications on the topic of postoperative pain control.

Dr. Hutchins completed a cardiothoracic anesthesiology fellowship and his residency in anesthesiology at the University of Minnesota Medical School at University of Minnesota-Duluth, undergraduate studies in Biology and Physiology at the University of Minnesota and is currently enrolled in a Masters of Healthcare Administration at the University of Minnesota. He is originally from Rice, Minnesota.

Daniel Sipple, DO, Medical Advisor

Dr. Sipple graduated from the University of Minnesota Phi Beta Kappa and attended medical school at Des Moines University. He performed his internship at the University of Massachusetts Medical Center and his residency at the Rehabilitation Institute of Chicago/Northwestern University Medical School. After serving as a faculty instructor at Northwestern, Dr. Sipple completed his fellowship training in interventional pain medicine through Sinai Hospital of Baltimore, MD.

Dr. Sipple's research on musculoskeletal disorders has been published and presented at national meetings. Dr. Sipple is a member of numerous professional societies. He is board certified in Physical Medicine and Rehabilitation and sub-speciality board certified in Pain Medicine.

Dr. Sipple specializes in the diagnosis, treatment and rehabilitation of a variety of musculoskeletal and pain disorders, with an emphasis on spine care. Dr. Sipple is experienced in performing numerous interventions, including epidural steroid injections, radiofrequency, spinal cord stimulation and ultrasound guided procedures.

In addition to his administrative and clinical responsibilities, Dr. Sipple enjoys developing emerging medical device technology, and has completed provisional patent work in this area.

COMPENSATION OF DIRECTORS AND EXECUTIVE OFFICERS

From inception to the date of this Offering, the Company has paid no compensation to its officers or directors. The Company may hire additional officers in the future and pay them directly, and may choose to compensate its directors in the future.

Advisory Agreements

The Company has agreed to pay Manhattan Street Securities ("MSC"), a service fee equal to $25 per investor that invests through its platform. The Company will also pay $2,000 for web hosting and $25 in warrants per investor for the Company's Class A Common Shares. The warrants will be a cashless exercise and can be exercised for up to ten (10) years priced at $5.00 per share after the qualification of the Regulation A+ Offering by the Company. If the Regulation A+ does not complete within twelve (12) months of November 1, 2017, Client will deliver the Warrants promptly to MSC.

Employment Agreements

The Company has not entered into any employment agreements with its executive officers or other employees to date. It may enter into employment agreements with them in the future.

Stock Incentive Plan

In the future, the Company may establish a management stock incentive plan pursuant to which stock options and awards may be authorized and granted to our directors, executive officers, employees and key employees or consultants. Details of such a plan, should one be established, have not been decided upon as of the date of this Offering. Stock options or a significant equity ownership position in the Company may be utilized by us in the future to attract one or more new key senior executives to manage and facilitate our growth. We have entered into Advisory Board agreements with various individuals that include 2,500 shares of stock issued upon execution of the agreements and a provision for 10,000 stock options in the future.

Board of Directors

Our board of directors currently consists of three directors:

None of our directors are "independent" as defined in Rule 4200 of FINRA's listing standards. We may appoint an independent director(s) to our board of directors in the future, particularly to serve on appropriate committees should they be established.

Committees of the Board of Directors

We may establish an audit committee, compensation committee, a nominating and governance committee and other committees to our Board of Directors in the future, but have not done so as of the date of this Offering Circular. Until such committees are established, matters that would otherwise be addressed by such committees will be acted upon by the entire Board of Directors.

Director Compensation

We currently do not pay our directors any compensation for their services as board members, with the exception of reimbursing and board related expenses. In the future, we may compensate directors, particularly those who are not also employees and who act as independent board members, on either a per meeting or fixed compensation basis.

Limitation of Liability and Indemnification of Officers and Directors

Our Bylaws limit the liability of directors and officers of the Company. The Bylaws state that the Company shall indemnify, in accordance with and to the full extent now or hereafter permitted by law, any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (including, without limitation, an action by or in the right of the corporation), by reason of his or her acting as a director or officer of the corporation (or a director or officer serving at the request of the corporation in any other capacity for or on behalf of the corporation) against any expenses (including attorneys' fees, judgments, fines, ERISA or other excise taxes, penalties and amounts paid in settlement) actually and reasonably incurred by such director or officer in respect thereof; provided, however, that, the corporation shall not be obligated to indemnify any such director or officer with respect to proceedings, claims or actions initiated or brought voluntarily by such director and not by way of defense. Expenses that may be subject to indemnification hereunder shall be paid in advance of the final disposition of the action, suit or proceeding to the full extent permitted by Delaware law subject to the corporation's receipt of any undertaking required thereby. The provisions of this article of the Company's Bylaws shall be deemed to constitute a contract between the Company and each director or officer who serves in such capacity at any time while this article and the relevant provisions of Delaware law are in effect, and each such director or officer shall be deemed to be serving as such in reliance on the provisions of this article of the Company's Bylaws, and any repeal of any such provisions or of such article of the Company's Bylaws shall not affect any rights or obligations then existing with respect to any state of facts then or theretofore existing or any action, suit or proceeding theretofore or thereafter brought or threatened based in whole or in part upon any such state of facts. If a claim under this article of the Company's Bylaws is not paid in full within thirty (30) days after a written claim has been received by the corporation, the claimant may at any time thereafter bring suit against the corporation to recover the unpaid amount of the claim and, if successful in whole or in part, the claimant also shall be entitled to be paid the expense of prosecuting such claim. It shall be a defense to any such action (other than an action brought to enforce a claim for expenses incurred in defending any proceeding in advance of its final disposition where the required undertaking, if any, has been provided to the

corporation) that the claimant has not met the standards of conduct that make it permissible under Delaware law for the corporation to indemnify the claimant for the amount claimed, but the burden of proving such defense shall be on the corporation. Neither the failure of the corporation to have made a determination prior to the commencement of such action that indemnification of the claimant is proper under the circumstances because the claimant has met the applicable standard of conduct set forth in the Delaware law, nor an actual determination by the corporation that the claimant has not met such standard of conduct shall be a defense to the action or create a presumption that the claimant has not met the applicable standard of conduct. The rights of indemnification and advancement provided by this article of the Company's Bylaws are not exclusive of any other right to indemnification or advancement provided by law, agreement or otherwise, and shall apply to actions, suits or proceedings commenced after the date hereof, whether or not arising from acts or omissions occurring before or after the adoption hereof, and shall continue as to a person who has ceased to be a director or officer of the corporation and shall inure to the benefit of the heirs, executors and administrators of such a person.

There is no pending litigation or proceeding involving any of our directors or officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

For additional information on indemnification and limitations on liability of our directors and officers, please review the Company's Bylaws, which are attached to this Offering Circular.

CAPITALIZATION TABLE

Capitalization Table

The Company has completed two rounds of financing. The first financing was the sale of $300,000 in Convertible Notes, completed in October of 2015. Those Notes accrue interest at the rate of 10% per annum, and upon the first liquidity event related to the Product(s) Noteholders can elect to convert any or all of Note to shares at $12.00 / share (reverse split adjusted), receive a 3.3x payment, or a combination thereof. The Conversion Price will continue to adjust downward after the Company issues more than five million shares. The Notes Financing allowed the Company to complete characterization of the Matrix, perform literature searches, further develop intellectual property, and perform many bench top studies to prove successful capture and release of the drug, bupivacaine. The second financing was the sale of 1,500,000 LLC Membership Units at the price of $0.666 per Unit (reverse split adjusted). As part of this financing, the Company agreed to certain provisions with the Investor. A copy of that Addendum is attached as Appendix Three. This funding has allowed us to pay our five-year, renewable license fee, complete three separate animal studies, complete numerous toxicity and pathology tests, and fund all of our continued Product Development experiments and operations.

Figure 1: Capitalization Table. Pre-Offering

Name	Shares	Investment	% Owned	% Contributed
Founders	2,500,000	5,000	67.50%	0.005%
First Round	1,500,000	1,000,000	37.50%	99.995%
TOTAL	4,000,000	1,005,000	100.00%	100.00%

Figure 2: Capitalization Table. Post-Offering

Name	Shares	Investment	% Owned	% Contributed
Founders	2,500,000	5,000	59.52%	0.25%
First Round	1,500,000	1,000,000	35.62%	49.875%
Second Round	200,000	1,000,000	4.76%	49.875%
TOTAL	4,200,000	2,005,000	100.00%	100.00%

Continued Financing

In June 2017, the Company entered in to a line of credit ("LOC") for continued financing of the Company's operating expenses. This senior non-subordinated LOC provides for up to $130,000 of funding to be repaid at the non-usurious interest rate of 6%. As of October 1, 2017, the Company had accessed approximately $32,000 of the available funds.

In exchange for waiving all of the rights granted to 524 Investments, LLC in connection with their First Round Investment of $1,000,000 resulting in 99.95% of all equity purchased, with the exception of a board seat appointment, 524 Investments shall maintain shares which allow them 2 votes for every Class B Share.

INTEREST OF MANAGEMENT AND OTHERS IN CERTAIN RELATED-PARTY TRANSACTIONS AND AGREEMENTS

The Company has entered into agreements in the form of Promissory Notes with certain related parties as set out below. It is the intention of the Company to repay these promissory notes from the capital raised in this Offering, as set out in the Use of Proceeds herein.

From July through October 2014, we entered into a Convertible Loan Agreement (the "Loan Agreement") with five individuals. The principal loan amounts total $300,000 and accrue interest at a rate of 10% annually. The Notes are not secured, and have a 10-year term from the date of funding. The Noteholders have the option of conversion or a preferred repayment upon the sale or license of AnestaGel to a third party. The loan and interest, or any part thereof can be converted in to shares. There is no prepayment fee. The Loan Agreement may prove a burden to the Company as they become due.

Further, an initial investor 524 Investments, LLC was issued units originally in Insitu Biologics, LLC. In the conversion of the LLC to the current Delaware corporation, the Company has elected to issue Class B Common Shares to the 524 Investments, LLC.

Class B Common Shares are entitled to two votes for every share held by 524 Investments, LLC. Currently, 524 Investments, LLC holds 1,500,000 shares of Class B Common Stock. Further, 524 Investments, LLC, as the sole holder of Class B Common Stock, is entitled to appoint one director to the Board of Directors for an initial term. Thereafter, the board member must stand for reelection. The initial term shall be for three (3) years.

DESCRIPTION OF SECURITIES BEING SOLD

The Company is selling up to 200,000 shares of its Preferred Stock ("Preferred Shares") to Accredited Investors, as defined by the Securities and Exchange Commission ("SEC), accordingly:

20,000 Shares at $4.80 per Share
30,000 Shares at $4.90 per Share
100,000 Shares at $5.00 per Share
30,000 Shares at $5.10 per Share
20,000 Shares at $5.20 per Share

Pricing will be honored on a "first come-first serve basis" where earlier investors will enjoy lower pricing.

The Shares include Registration Rights. Because of the Registration Rights, the Shares may be considered "preferred" in the sense that at this time, only the Shareholders that purchase Shares in this Offering shall be afforded Registration Rights in the intended Regulation A+ offering that the Company hopes to conduct in

the coming months. Shareholders in this group of Owners shall have a 4.76% ownership stake and have paid 49.75% of the equity capital raised to as of the close of this Offering.

The Preferred Stock is convertible to the Class A Common Stock on a 1 to 1.1 basis meaning for every Preferred Share owned by a Shareholder, they may convert it into 1.1 shares of Class A Common Stock after the Regulation A+ offering is qualified by the Securities Exchange Commission.

The Class A Common Stock Shareholders will vote pari pasu on a share by share basis with the Preferred Stock Shareholders. The Class B Common Stockholders shall have two (2) votes for every share held. Currently there is one Class B Common Stockholder that holds 1,500,000 shares of stock.

The Company is offering Shares of its Preferred Stock. Except as otherwise required by law, the Company's Bylaws or its Certificate of Incorporation, each Preferred Stock shareholder shall be entitled to vote. The Shares of Preferred Stock, when issued, will be fully paid and non-assessable.

There are three classes of stock in the Company as of the date of this Offering Circular. The Company does not expect to create any additional classes of stock during the next 12 months, but the Company is not limited from creating additional classes which may have preferred dividend, voting and/or liquidation rights or other benefits not available to holders of its Preferred Stock if it chooses to do so.

The Company does not expect to declare dividends for holders of Preferred Stock in the foreseeable future. Dividends will be declared, if at all (and subject to the rights of holders of additional classes of securities, if any), in the discretion of the Company's Board of Directors. Dividends, if ever declared, may be paid in cash, in property, or in shares of the capital stock of the Company, subject to the provisions of law, the Company's Bylaws and the Certificate of Incorporation. Before payment of any dividend, there may be set aside out of any funds of the Company available for dividends such sums as the Board of Directors, in its absolute discretion, deems proper as a reserve for working capital, to meet contingencies, for equalizing dividends, for repairing or maintaining any property of the Company, or for such other purposes as the Board of Directors shall deem in the best interests of the Company.

There is no minimum number of 100,000 Shares that needs to be sold in order for funds to be released to the Company and for this Offering to close. The Company anticipates numerous closings to take place during the Offering.

The minimum subscription that will be accepted from an investor is Fifty Thousand Dollars ($50,000.00) (the "Minimum Subscription"). The Minimum Subscription may be waived by the Management at its election. A subscription for Fifty Thousand Dollars ($50,000.00) or more in the Shares may be made only by tendering to the Company the executed Subscription Agreement (via the Manhattan Street Securities Platform) delivered with the subscription price in a form acceptable to the Company, via check, wire, BitCoim or ACH (or other payment methods the Company may later add). The execution and tender of the documents required, as detailed in the materials, constitutes a binding offer to purchase the number of

Shares stipulated therein and an agreement to hold the offer open until the expiration date or until the offer is accepted or rejected by the Company, whichever occurs first. Manhattan Street Securities, LLC will hold and maintain such funds in escrow until (1) the Minimum Offering Amount has been sold; or (2) the Offering is terminated. If the Minimum Offering Amount of $100,000 in investments has not been subscribed on or before December 31, 2018, all funds on deposit with the escrow agent shall be promptly returned to subscribers in full, without deduction or charges. Thereafter, all additional subscription proceeds will be immediately transferred to the operating account of the Company.

The Company reserves the unqualified discretionary right to reject any subscription for Shares, in whole or in part. If the Company rejects any offer to subscribe for the Shares, it will return the subscription payment, without interest or reduction. The Company's acceptance of your subscription will be effective when an authorized representative of the Company issues you written or electronic notification that the subscription was accepted.

Aside from the right to first refusal and conversion rights previously discussed herein, there are no liquidation rights, preemptive rights, redemption provisions, sinking fund provisions, impacts on classification of the Board of Directors where cumulative voting is permitted or required related to the Preferred Stock, provisions discriminating against any existing or prospective holder of the Preferred Stock as a result of such Shareholder owning a substantial amount of securities, or rights of Shareholders that may be modified otherwise than by a vote of a majority or more of the Shares outstanding, voting as a class defined in any corporate document as of the date of filing. The Preferred Stock will not be subject to further calls or assessment by the Company. There are no restrictions on alienability of the Preferred Stock in the corporate documents other than a right of first refusal and those disclosed in this Offering Circular. The Company intends to engage a transfer agent and registrant for the Shares. For additional information regarding the Shares, please review the Company's Bylaws, which are attached to this Offering Circular. There are no restrictions on alienability other than the right of first refusal.

The right of first refusal is defined in the Company's Bylaws as follows:

Restrictions on Transfers of Shares. Until the Common Stock of the corporation is listed on an exchange and is made available for trading, no stockholder shall sell, assign, pledge or in any manner transfer any of the shares of Common Stock of the corporation or any right or interest therein, whether voluntarily or by operation of law, or by gift or otherwise, except by a transfer which meets the requirements hereinafter set forth in this Section.

If the stockholder receives from anyone a bona fide offer acceptable to the stockholder to purchase any of its shares of Common Stock, then the stockholder shall first give written notice thereof to the corporation. The notice shall name the proposed transferee and state the number of shares to be transferred, the price per share and all other terms and conditions of the offer.

For ten (10) days following receipt of such notice, the corporation shall have the option to purchase all (but not less than all) the shares specified in the notice at the price and upon the terms set forth in such bona fide offer. In the event the

corporation elects to purchase all the shares, it shall give written notice to the selling stockholder of its election and settlement for said shares shall be made as provided below in paragraph (c).

In the event the corporation elects to acquire the shares of the selling stockholder as specified in said selling stockholder's notice, the Secretary of the corporation shall so notify the selling stockholder and settlement thereof shall be made in cash within fifteen (15) days after the Secretary of the corporation receives said selling stockholder's notice; provided that if the terms of payment set forth in said selling stockholder's notice were other than cash against delivery, the corporation shall pay for said shares on the same terms and conditions set forth in said selling stockholder's notice.

In the event the corporation does not elect to acquire all of the shares specified in the selling stockholder's notice, said selling stockholder may, within a sixty-day period following the expiration of the rights granted to the corporation herein, sell elsewhere the shares specified in said selling stockholder's notice which were not acquired by the corporation, in accordance with the provisions of paragraph (c) of this Section provided that said sale shall not be on terms and conditions more favorable to the purchaser than those contained in the bona fide offer set forth in said selling stockholder's notice. All shares so sold by said selling stockholder shall continue to be subject to the provisions of this Section in the same manner as before said transfer.

Anything to the contrary contained herein notwithstanding, the following transactions shall be exempt from the provisions of this Section:

A stockholder's transfer of any or all shares held either during such stockholder's lifetime or on death by will or intestacy to such stockholder's immediate family. "Immediate family" as used herein shall mean spouse, lineal descendant, father, mother, brother, or sister of the stockholder making such transfer and shall include any trust established primarily for the benefit of the stockholder or his immediate family.

(ii) A stockholder's bona fide pledge or mortgage of any shares with a commercial lending institution, provided that any subsequent transfer of said shares by said institution shall be conducted in the manner set forth in this Section.

(iii) A stockholder's transfer of any or all of such stockholder's shares to the corporation.

(iv) A corporate stockholder's transfer of any or all of its shares to an affiliate thereof or pursuant to and in accordance with the terms of any merger, consolidation, or reclassification of shares or capital reorganization of the corporate stockholder.

(v) A corporate stockholder's transfer of any or all of its shares to any or all of its stockholders.

(vi) A transfer by a stockholder which is limited or general partnership to any or all of its partners or retired partners, or to any such partner's or retired partner's estate. In any such case, the transferee, assignee or other recipient shall receive and

hold such Common Stock subject to the provisions of this Section 8.14, and there shall be no further transfer of such Common Stock except in accordance with this Section.

The provisions of this Section may be waived with respect to any transfer either by the corporation, upon duly authorized action of the Board of Directors, or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the corporation (excluding the votes represented by those shares to be sold by the selling stockholder). This Section may be amended or repealed only upon the express vote or written consent of the owners of a majority of the voting power of each outstanding class of voting securities of the corporation or by the duly authorized action of the Board of Directors.

Any sale or transfer, or purported sale or transfer, of securities of the corporation shall be null and void unless the terms, conditions, and provisions of this Section are strictly observed and followed.

The foregoing right of first refusal shall automatically terminate upon the date securities of the corporation are first offered to the public pursuant to a registration statement filed with, and declared effective by, the United States Securities and Exchange Commission under the Securities Act of 1933, as amended, or upon the listing of the securities of the corporation on any stock exchange subject to the Securities Exchange Act of 1934. These provisions of this Section shall also not apply to the corporation's securities that are sold or granted to shareholders in any private placement or securities prior to the date securities of the corporation are first offered to the public pursuant to a Regulation A offering qualified by the United States Securities and Exchange Commission.

DISQUALIFYING EVENTS DISCLOSURE

Recent changes to Regulation D promulgated under the Securities Act prohibit an issuer from claiming an exemption from registration of its securities under such rule if the issuer, any of its predecessors, any affiliated issuer, any director, executive officer, other officer participating in the offering of the Preferred Shares, general partner or managing member of the issuer, any beneficial owner of 20% or more of the voting power of the issuer's outstanding voting equity securities, any promoter connected with the issuer in any capacity as of the date hereof, any investment manager of the issuer, any person that has been or will be paid (directly or indirectly) remuneration for solicitation of purchasers in connection with such sale of the issuer's Preferred Shares, any general partner or managing member of any such investment manager or solicitor, or any director, executive officer or other officer participating in the offering of any such investment manager or solicitor or general partner or managing member of such investment manager or solicitor has been subject to certain "Disqualifying Events" described in Rule 506(d)(1) of Regulation D subsequent to September 23, 2013, subject to certain limited exceptions. The Company is required to exercise reasonable care in conducting an inquiry to determine whether any such persons have been subject to such Disqualifying Events and is required to disclose any Disqualifying Events that occurred prior to September 23, 2013 to investors in the Company. The Company believes that it has exercised reasonable care in conducting an inquiry into Disqualifying Events by the foregoing persons and is aware of the no such Disqualifying Events.

It is possible that (a) Disqualifying Events may exist of which the Company is not aware and (b) the SEC, a court or other finder of fact may determine that the steps that the Company has taken to conduct its inquiry were inadequate and did not constitute reasonable care. If such a finding were made, the Company may lose its ability to rely upon exemptions under Regulation A, and, depending on the circumstances, may be required to register the Offering of the Company's Preferred Stock with the SEC and under applicable state securities laws or to conduct a rescission offer with respect to the securities sold in the Offering.

ERISA CONSIDERATIONS

Trustees and other fiduciaries of qualified retirement plans or IRAs that are set up as part of a plan sponsored and maintained by an employer, as well as trustees and fiduciaries of Keogh Plans under which employees, in addition to self-employed individuals, are participants (together, "ERISA Plans"), are governed by the fiduciary responsibility provisions of Title 1 of the Employee Retirement Income Security Act of 1974 ("ERISA"). An investment in the Shares by an ERISA Plan must be made in accordance with the general obligation of fiduciaries under ERISA to discharge their duties (i) for the exclusive purpose of providing benefits to participants and their beneficiaries; (ii) with the same standard of care that would be exercised by a prudent man familiar with such matters acting under similar circumstances; (iii) in such a manner as to diversify the investments of the plan, unless it is clearly prudent not do so; and (iv) in accordance with the documents establishing the plan. Fiduciaries considering an investment in the Shares should accordingly consult their own legal advisors if they have any concern as to whether the investment would be inconsistent with any of these criteria.

Fiduciaries of certain ERISA Plans which provide for individual accounts (for example, those which qualify under Section 401(k) of the Code, Keogh Plans and IRAs) and which permit a beneficiary to exercise independent control over the assets in his individual account, will not be liable for any investment loss or for any breach of the prudence or diversification obligations which results from the exercise of such control by the beneficiary, nor will the beneficiary be deemed to be a fiduciary subject to the general fiduciary obligations merely by virtue of his exercise of such control. On October 13, 1992, the Department of Labor issued regulations establishing criteria for determining whether the extent of a beneficiary's independent control over the assets in his account is adequate to relieve the ERISA Plan's fiduciaries of their obligations with respect to an investment directed by the beneficiary. Under the regulations, the beneficiary must not only exercise actual, independent control in directing the particular investment transaction, but also the ERISA Plan must give the participant or beneficiary a reasonable opportunity to exercise such control, and must permit him to choose among a broad range of investment alternatives.

Trustees and other fiduciaries making the investment decision for any qualified retirement plan, IRA or Keogh Plan (or beneficiaries exercising control over their individual accounts) should also consider the application of the prohibited transactions provisions of ERISA and the Code in making their investment decision. Sales and certain other transactions between a qualified retirement plan, IRA or Keogh Plan and certain persons related to it (*e.g.,* a plan sponsor, fiduciary, or service provider) are prohibited transactions. The particular facts concerning the sponsorship, operations and other investments of a qualified retirement plan, IRA or Keogh Plan may cause a wide range of persons to be treated as parties in interest or disqualified persons with respect to it. Any fiduciary, participant or beneficiary considering an investment in Shares by a qualified retirement plan IRA or Keogh Plan should examine the individual circumstances of that plan to determine that the investment will not be a prohibited transaction. Fiduciaries, participants or beneficiaries considering an investment in the Shares should consult their own legal advisors if they have any concern as to whether the investment would be a prohibited transaction.

Regulations issued on November 13, 1986, by the Department of Labor (the "Final Plan Assets Regulations") provide that when an ERISA Plan or any other plan covered by Code Section 4975 (*e.g.*, an IRA or a Keogh Plan which covers only self-employed persons) makes an investment in an equity interest of an entity that is neither a "publicly offered security" nor a security issued by an investment company registered under the Investment Company Act of 1940, the underlying assets of the entity in which the investment is made could be treated as assets of the investing plan (referred to in ERISA as "plan assets"). Programs which are deemed to be operating companies or which do not issue more than 25% of their equity interests to ERISA Plans are exempt from being designated as holding "plan assets." Management anticipates that we would clearly be characterized as an "operating company" for the purposes of the regulations, and that it would therefore not be deemed to be holding "plan assets."

Classification of our assets of as "plan assets" could adversely affect both the plan fiduciary and management. The term "fiduciary" is defined generally to include any person who exercises any authority or control over the management or disposition of plan assets. Thus, classification of our assets as plan assets could make the management a "fiduciary" of an investing plan. If our assets are deemed to be plan assets of investor plans, transactions which may occur in the course of its operations may constitute violations by the management of fiduciary duties under ERISA. Violation of fiduciary duties by management could result in liability not only for management but also for the trustee or other fiduciary of an investing ERISA Plan. In addition, if our assets are classified as "plan assets," certain transactions that we might enter into in the ordinary course of our business might constitute "prohibited transactions" under ERISA and the Code.

Under Code Section 408(i), as amended by the Tax Reform Act of 1986, IRA trustees must report the fair market value of investments to IRA holders by January 31 of each year. The Service has not yet promulgated regulations defining appropriate methods for the determination of fair market value for this purpose. In addition, the assets of an ERISA Plan or Keogh Plan must be valued at their "current value" as of the close of the plan's fiscal year in order to comply with certain reporting obligations under ERISA and the Code. For purposes of such requirements, "current value" means fair market value where available. Otherwise, current value means the fair value as determined in good faith under the terms of the plan by a trustee or other named fiduciary, assuming an orderly liquidation at the time of the determination. We do not have an obligation under ERISA or the Code with respect to such reports or valuation although management will use good faith efforts to assist fiduciaries with their valuation reports. There can be no assurance, however, that any value so established (i) could or will actually be realized by the IRA, ERISA Plan or Keogh Plan upon sale of the Shares or upon liquidation of us, or (ii) will comply with the ERISA or Code requirements.

The income earned by a qualified pension, profit sharing or stock bonus plan (collectively, "Qualified Plan") and by an individual retirement account ("IRA") is generally exempt from taxation. However, if a Qualified Plan or IRA earns "unrelated business taxable income" ("UBTI"), this income will be subject to tax to the extent it exceeds $1,000 during any fiscal year. The amount of unrelated business taxable income in excess of $1,000 in any fiscal year will be taxed at rates up to 36%. In

addition, such unrelated business taxable income may result in a tax preference, which may be subject to the alternative minimum tax. It is anticipated that income and gain from an investment in the Shares will not be taxed as UBTI to tax exempt shareholders, because they are participating only as passive financing sources.

APPENDIX ONE

Financial Pro Forma – Year One Operating Expenses

Cost Center Expenses	1	2	3	4	5	6	7	8	9	10	11	12	First 12 Months
Compensation & Benefits	71,750	71,750	71,750	71,750	71,750	71,750	71,750	71,750	71,750	71,750	71,750	71,750	861,000
Travel	1,980	1,980	1,980	1,980	1,980	1,980	1,980	1,980	1,980	1,980	1,980	1,980	23,760
Communications & Utilities	665	665	665	665	665	665	665	665	665	665	665	665	7,980
Office Supplies & Support	200	200	200	200	200	200	200	200	200	200	200	200	2,400
Laboratory Supplies and Suppo	7,133	7,133	7,133	7,133	140,164	140,164	140,164	140,164	140,164	140,164	140,164	140,164	1,149,842
Facility	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	12,000
Marketing & Promotion													0
Corporate Items	5,500	5,500	5,500	5,500	5,500	5,500	5,500	5,500	5,500	5,500	5,500	5,500	66,000
Total	88,228	88,228	88,228	88,228	221,259	221,259	221,259	221,259	221,259	221,259	221,259	221,259	2,122,982

Financial Pro Forma – Year Two Operating Expenses

Cost Center Expense	13	14	15	16	17	18	19	20	21	22	23	24	Mos. 13-24
Compensation & Benefits	77000	77000	77000	77000	77000	77000	77000	77000	77000	77000	77000	77000	924000
Travel	3144	3144	3144	3144	3144	3144	3144	3144	3144	3144	3144	3144	37725
Communications & Utilities	1745	1745	1745	1745	1745	1745	1745	1745	1745	1745	1745	1745	20940
Office Supplies & Support	200	200	200	200	200	200	200	200	200	200	200	200	2400
Laboratory Supplies and Support	140664	140664	4300	44800	44800	44800	44800	44800	44800	61050	61050	61050	737577
Facility	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	8333	19333
Marketing & Promotion													0
Corporate Items	5500	6917	6917	6917	6917	6917	6917	6917	6917	253917	6917	6917	328583
Regulatory Fees and Consultants	15000	15000	25000	25000	25000	25000	25000	25000	155000	155000	155000	155000	800000
Total	229252	230669	94305	134805	134805	134805	134805	134805	134805	398055	151055	158389	2870559

Financial Pro Forma – Year Three Operating Expenses

Cost Center Expenses	25	26	27	28	29	30	31	32	33	34	35	36	Mos 25-36
Compensation & Benefits	87,500	87,500	87,500	87,500	87,500	87,500	87,500	87,500	87,500	87,500	87,500	87,500	1,050,000
Travel	3,256	3,256	3,256	3,256	3,256	3,256	3,256	3,256	3,256	3,256	3,256	3,256	39,075
Communications & Utilities	795	795	795	795	795	795	795	795	795	795	795	795	9,540
Office Supplies & Support	200	200	200	200	200	200	200	200	200	200	200	200	2,400
Laboratory Supplies and Support	53,133	48,133	48,133	48,133	8,133	8,133	8,133	53,133	48,133	48,133	8,133	8,133	387,600
Facility	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	8,333	19,333
Marketing & Promotion													0
Corporate Items	5,500	6,917	6,917	6,917	6,917	6,917	6,917	6,917	6,917	53,917	6,917	6,917	128,583
Regulatory Fees and Consultants	140,000	40,000	25,000	15,000	15,000	15,000	15,000	15,000	15,000	15,000	15,000	15,000	340,000
Total	151,384	147,801	147,801	147,801	107,801	107,801	107,801	152,801	147,801	194,801	107,801	115,135	1,976,531

APPENDIX ONE

Financial Pro Forma – Year One Capital Expenses

Computers and Software	$ 10,000
Laboratory Equipment	$ 61,500
Work Benches	$ 10,000
Total	$ 81,500

Financial Pro Forma – Year Two Capital Expenses

Computers and Software	$ 12,000
Lab Equipment Consumables	$ 10,000
Environmental Chamber 2	$ 15,000
HPLC/GPC	$ 20,000
Filtration	$ 3,000
Work Benches	$ 7,500
Total	$ 67,500

Financial Pro Forma – Year Three Capital Expenses

Computers and Software	$ 8,000
Environmental Chamber	$ 15,000
IR Spectometer	$ 14,500
Filtration	$ 3,000
Work Benches	$ 7,500
Total	$ 48,000

APPENDIX TWO

AnestaGel Feasibility Study

AnestaGel – P™ Provides Greater Analgesia in a Rat Model of Post-Operative Incisional Pain with Mechanical Allodynia than Exparel® at 24 and 48 Hours

Authors: William Taylor, Daniel P. Sipple, D.O., F.A.B.P.M.R., D.A.B.P.M., Stefano M. Sinicropi, M.D., F.A.A.O.S.

ABSTRACT

The feasibility and duration of AnestaGel-P™, a novel hydrogel-based drug delivery system to provide sustained analgesia was evaluated in a post-operative incisional pain rat model when compared to a positive control, Exparel®. Twenty-eight male Sprague-Dawley rats were prepared for surgery and an approximately 1 cm long incision was made in the left hind paw. The incision was closed and the animals were treated with either AnestaGel–P or Exparel in a randomized manner. The animals recovered from the procedure and monitored until euthanasia at 96 hours post-surgery. Tissues were taken at the injection site and local lymph nodes, and analyzed to determine tissue impact as a result of sample injection. No abnormal tissue response was detected from or in either test sample and was generally well tolerated. AnestaGel–P delivered a statistically significant greater analgesic effect at 24 and 48 hours post incision and AnestaGel–P provided an equivalent analgesic effect at < 24 hours post-surgical incision, and equivalent analgesic effect at >72 hours.

INTRODUCTION

Pain is one of the few medical conditions that affects nearly every human being in the world. The development of opiates, cocaine and derivatives of these compounds has done much to reduce human suffering. The coca leaf's importation to Europe in the 1880s, combined with the emergence of modern organic chemistry, led to an explosion in regional anesthesia, the foundations of modern pre-operative, peri-operative and post-operative pain management. Cocaine, while effective, was highly addictive, short-acting, and not without central nervous system and cardiovascular toxicity. Early local anesthetic derivatives of cocaine were also of limited duration, leaving opium derivatives, such as cocaine, highly addictive, and as the mainstay of post-operative pain management.

Over 100 million Americans suffer from chronic pain each year. The annual economic impact of pain in the U.S. is estimated to exceed $635 billion (Stith Butler, Adrienne ; Xi, Jing ;Cox, Thelma L; Pope, Andrew M.; Randall, Donna; Bowman, Victoria), affecting more lives than heart disease, diabetes and cancer combined. The NIH has declared development of new, safer medications to alleviate pain with lower risk a top priority. Pain is a major reason for physician visits, prescription medications, disability claims and a significant decrement to economic productivity and quality of life. Appropriate management of pain is high-risk and time intensive for trained specialists, who are in short supply.

Opiates, the mainstay of treatment for severe pain, have been utilized for centuries. Persons over 65, representing the largest demographic of consumers of health care in the United States, tolerate opiates poorly (Manchikanti M. D., Pampati MSc and Boswell). Opiate related constipation, bowel obstruction, respiratory suppression, and delirium increase length of stay, cost, mortality and reduce patient satisfaction. Declared an epidemic by the Centers for Disease Control, over 47,000 deaths were reported in 2014, a 6.5 % increase from the previous year and a 200% increase since 2000. (Rudd MSPH, Aleshire JD and Zibbel PhD.) In addition, opiates are mostly ineffective in treating neuropathic pain and headache, which constitutes a disproportionate sample of the most painful conditions known: cluster headache, complex regional pain syndrome, migraine headache, phantom limb pain and trigeminal. Patients with these conditions often remain collateral damage from the opiate epidemic, as fear of opiates coinciding with a limited pharmacological armamentarium limits effective treatment options.

By 1957, the effective duration of local anesthetics was significantly increased with the introduction of bupivacaine. While infusion pumps with bupivacaine are utilized to deliver continuous nerve block, until the arrival of liposome-based Exparel, there was not a significant improvement in the duration of action of local anesthetics for over fifty years. Exparel is a leading analgesic used to treat post-operative pain. It has been shown to be an effective analgesic up to 72 hours. Exparel is a liposomal formulation that is injected directly into the target tissue and placed in the interstitial spaces. Its action depends on the breakdown of the carrier liposomes and subsequent elution of Bupivacaine into the surrounding

tissues. It has been reported that in some cases the product does not last the full 72 hours (Schnacky PharmD and Kelley PharmD) (VHA Pharmacy Benefits Management Services, Medical Advisory Panel and VISN Pharmacist Executives). Migration from the injection site, tissue type, and mechanical action may all play a role in causing variability in liposome breakdown and duration.

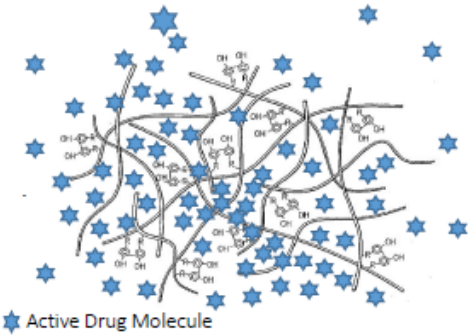
Matrix™ BioHydrogel is a tunable, biocompatible and physiologically neutral platform technology. This flexible implantable carrier platform can be used in stem cell and drug delivery, soft tissue, nerve, bone and other regenerative applications. Via customized tunable unique crosslinking, Matrix BioHydrogel engineered AnestaGel-P exceeds Exparel in efficacy, in a pre-clinical study. It performed as well as Exparel < 24hrs and exceeded Exparel analgesic effectiveness at 24 and 48 hours, and again matched performance > 48 hrs. AnestaGel-P also remained present in the injection location while Exparel was no longer present at the end of the study. Due to its consistency, AnestaGel-P will not migrate from the injection site.

AnestaGel-P utilizes a new approach to elution of analgesics into target tissues. AnestaGel-P utilizes the tried and true method of using a hydrogel as a drug reservoir, but is unique in that it is able to crosslink in the presence of the drug molecule without interacting or reacting with it. This allows for a much higher drug load capacity for the drug reservoir and allows for tuning the material to target desired properties in delivery rate, persistence, duration and stability. AnestaGel-P also ensures that the material stays in place where it is delivered into the target tissues. This is due to its physical form that resists extrusion from the injection site and migration through interstitial tissue spaces.

MATERIALS AND METHODS

The test article for this study was AnestaGel-P, a bupivacaine-loaded injectable hydrogel mixture indicated for administration into a surgical site to produce post-surgical analgesia. AnestaGel–P was administered to animals assigned to one test group and compared to a positive control arm that was administered Exparel. AnestaGel-P is comprised of 35 mg/mL bupivacaine-dense hydrogel sustained release particle contained in a loose continuous phase binding hydrogel matrix. The positive control article for this study was Exparel (1.33%, NDC 65250-266-20), a bupivacaine liposome injectable suspension indicated for administration into a surgical site to produce post-surgical analgesia. The test and control articles were in a sterile, ready-to-use form prior to study procedures. Exparel 13.3 mg/mL was used for the positive control and supplied as a vial. 1mL BD syringes with 0.1mL demarcations were used to deliver the test articles to the sciatic nerve between the greater trochanter and ischial tuberosity. AnestaGel-P was supplied in gel form in 1mL BD syringes with 0.1mL demarcations. Animals were transferred to the procedure room, anesthetized, and the left hind paw prepared for aseptic surgery. Surgical creation of a 1 cm longitudinal incision along the plantar aspect of the foot was performed and the incision closed in standard fashion. At the completion of the 96-hour testing session, animals were humanely euthanized and submitted for gross necropsy by a testing facility veterinarian. The injection sites of each animal and local lymph nodes were collected, processed for histology, and submitted to a board certified veterinary pathologist for analysis.

The key to Matrix BioHydrogel technology is its tunable, three-dimensional amino acid crosslinking. Through crosslinking density, AnestaGel's viscosity is intentionally tailored to a consistency approaching peanut butter, less prone to migration. Unlike Exparel, whose lipid structure is compartmentalized, Matrix BioHydrogel-based AnestaGel possesses contiguous three-dimensional molecular uniformity in a three-dimension lattice. Such molecular precision produces precise, reliable elution mechanics. In contrast, Exparel's lobulated, fat globule reservoir is amorphous, its surface to volume ratio, being in liquid form, is variable, affecting degradation, elution and migration. This raises concerns for Marcaine toxicity through bolus release, migration away from the surgical site.



Active Drug Molecule

AnestaGel-P particles are created by crosslinking a high molecular weight polysaccharide in the presence of a drug molecule. The relatively mild crosslinking reaction allows the drug to be captured within the crosslinked molecular mass at a desired concentration. The newly

formed drug reservoirs are then processed to form a uniform particle size and then bound in a loose second formulation of hydrogel that binds the particles together forming a thick gelatinous mass ready for delivery to target tissues.

Rat Model and Methods

The Sprague-Dawley rat is a widely used and established animal model for behavioral and nociceptive research. Rats are suitable for testing and widely accepted by the appropriate regulatory agencies.

This study was designed to evaluate the effects of AnestaGel-P on mechanical allodynia in a post-operative incisional pain model when compared to a positive and negative control. The model was based on an allodynia assessment technique in which an incision is created in the hind paw of a rat and pain response was assessed using pressure applied to the wound site using von Frey hairs. (Brennan) (Chaplan, Bach and Yaksh). Two arms of this study utilized sixteen (16) male rats (Sprague-Dawley), weighing approximately 150-250 grams on the day of the implant procedures. Age was dependent on weight for all animals. They were verified to be in good health through a physical exam performed by testing veterinary care staff at the time of arrival and within two days prior to the study procedure. Any animals showing signs of disease, which may affect the outcome of the study, were excluded from the study.

Animals must have met the following criteria in order to be enrolled in the study:

- Pre-injury baseline 50% response threshold of ≥ 7 grams of force on both the ipsilateral and contralateral paws
- Full recovery from the surgical procedure

Animals were given free access to food and water. Prior to dosing and surgery, each animal underwent a baseline behavioral test assessing the 50% response threshold to mechanical stimulation using von Frey filaments.

Sixteen (16) animals meeting inclusion criteria were assigned to treatment groups (test group I (n=8) or positive control (n=8), ensuring even distribution based on the pre-injury baseline 50% response thresholds.

Animals were transferred to the procedure room, anesthetized, and the left hind paw prepared for aseptic surgery. A 1 cm longitudinal incision along the plantar aspect of the foot was performed and the incision closed in standard fashion. Following the incisional procedure, each animal received an injection of the corresponding treatment (with the exception of the negative control group who did not receive an injection) targeting the sciatic nerve between the greater trochanter and the ischial tuberosity. All animals recovered from anesthesia and returned to general housing.

The 50% response threshold was measured for all groups at 3, 6, 9, 24, 48, 72, and 96 hours post-dosing according to the up-down method using von Frey filaments. Animal observations occurred at least once daily for the duration of the study. Analgesic and antibiotic therapy was not administered during the conduct of the study. At the completion of the 96-hour testing session, animals were humanely euthanized and submitted for gross necropsy by a testing facility veterinarian. The injection sites of each animal and local lymph nodes were collected, processed for histology and analysis.

HISTOLOGY/PATHOLOGY

Sixteen (16) male Sprague-Dawley rats were prepared for surgery and an approximately 1 cm long incision was made in the left hind paw. The incision was closed and the animals were treated as appropriate for their assigned group (AnestaGel–P or Exparel). The animals recovered from the surgical procedure, then were tested and monitored per the protocol until euthanasia at 96 hours post-surgery. The animals were then humanely euthanized and tissues were taken from the injection site and nearby local lymph nodes for histology. Tissue samples were prepared and hematoxylin and eosin (HE) slides were made. Samples of the injection site and nearby lymph nodes were collected for analysis.

AnestaGel-P

Eight injection sites were evaluated. Three sections of muscle were normal. Five sections had minimal to moderate histiocytic inflammation in the muscle fascia and occasionally in the muscle. Within the inflammation, there were a few to multiple, small irregularly shaped deposits of pale blue, acellular, non-birefringent material consistent with the test article. Three sections had minimal myofiber regeneration.

Eight sections of lymph node were evaluated. All of the sections of lymph node were normal.

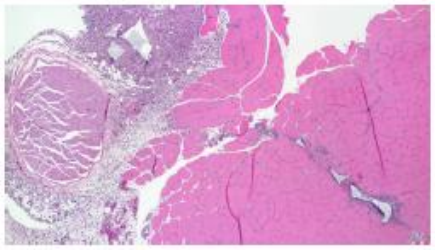


Figure 1. AnestaGel-P, Animal #16V144, Slide 1, Overview of the muscle and facia with inflammation and test article material. HE stain, 40x total magnification.

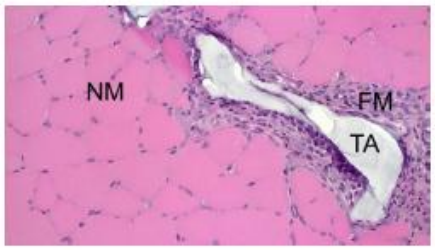


Figure 2. AnestaGel-P, Animal #16V144, Slide 1, Higher magnification of Figure 5 showing normal muscle (NM) infiltrated by foamy macrophages (FM) surrounding test article material (TA). HE stain, 200x total magnification.

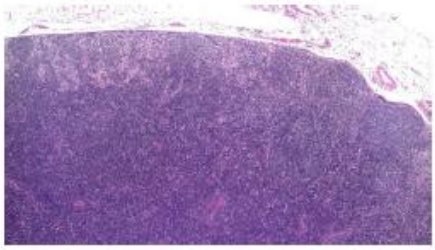


Figure 3. AnestaGel-P, Animal #16V157, Slide 2, Overview of the lymph node. HE stain, 40x total magnification.

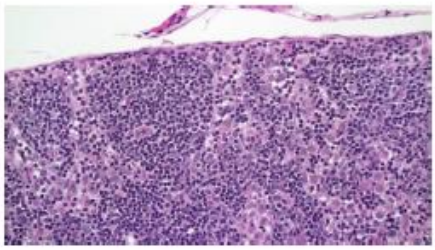


Figure 4. AnestaGel-P, Animal #16V157, Slide 2, Higher magnification of Figure 7 showing normal lymph node. HE stain, 200x total magnification.

Exparel

Eight injection sites were evaluated. Five sections of muscle were normal. Three sections had minimal to mild histiocytic inflammation in the muscle fascia.

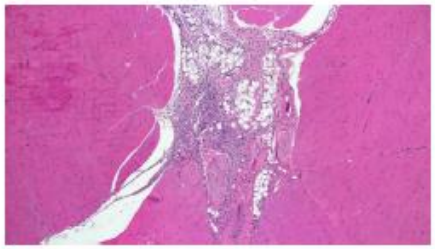


Figure 5. Exparel, Animal #16V150, Slide 1, Overview of the muscle and facia with inflammation. HE stain, 40x total magnification.

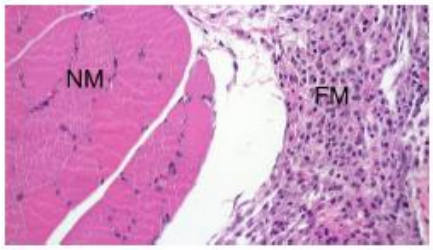


Figure 6. Exparel, Animal #16V150, Slide 1, Higher magnification of Figure 9 showing normal muscle (NM) adjacent to fascia infiltrated by foamy macrophages (FM). HE stain, 200x total magnification.

Histiocytic inflammation was present in the fascia of the muscle at the injection site in the test group and the positive control group. This is not an unexpected finding at a site in which a vehicle suspended drug has been injected. The AnestaGel-P had more histiocytic inflammation and also had deposits of an extracellular material consistent with the test material in the area of inflammation. No extracellular material was seen in the Exparel group sites.

All of the lymph nodes were normal in both test groups.

Eight sections of lymph node were evaluated. All of the sections of lymph node were normal.

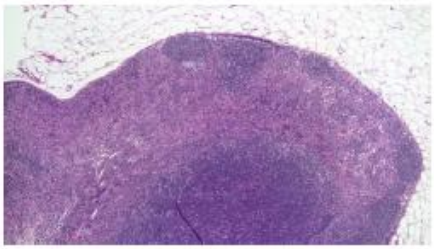


Figure 7. Exparel, Animal #16V161, Slide 2, Overview of the lymph node. HE stain, 40x total magnification.

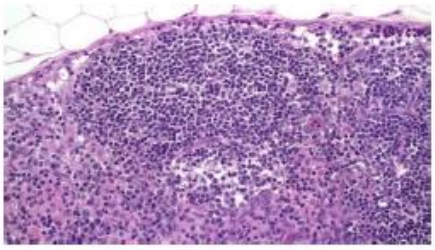
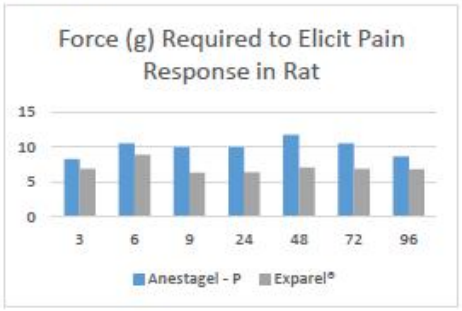


Figure 8. Exparel, Animal #16V161, Slide 2, Higher magnification of Figure 11 showing normal lymph node. HE stain, 200x total magnification.

RESULTS



Force applied within 1mm of incision wound of a Male Sprague-Dawley Rat. $p<0.05$ at 24 and 48 hr. time points. AnestaGel-P consistently exceeded Exparel in efficacy at every time interval from 3 to 96 hours and maintained the 10 g force threshold from 6 to 72 hours.

DISCUSSION

AnestaGel-P provided superior analgesic effectiveness 24 and 48 hours post administration of the hydrogel to Exparel Liposome suspended solution. Histology results demonstrate the AnestaGel-P test article was still present at conclusion of the study, but the Exparel was not present in tissue samples. Delivery vehicle migration away from the injection site will reduce analgesic drug delivery to the surgical site as it will carry the drug material within it as it migrates away.

AnestaGel-P was loaded with more bupivacaine and demonstrated it was able to supply pain relief superior to Exparel up to 72 hours. AnestaGel-P is designed to quickly release drug from the binding matrix short term and then continuously supply the drug to the injection site by elution from the dense hydrogel particle reservoirs. Exparel is dependent upon the continuous degradation of the liposomes and is dosed at a lower concentration.

CONCLUSION

AnestaGel-P was determined to be a superior drug delivery vehicle for pain treatment when compared to Exparel. The physical properties of a homogenius, densely crosslinked molecular structure facilitate superior elution mechanics. Demonstrating non-Newtonian fluid properties, the viscosity of AnestaGel-P increases with resistance, retarding migration from the targeted site of placement. Exparel, in contrast, possesses classical low viscosity fluid mechanics, freely migrating through the interstitial space away from the target tissue, diminishing efficacy.

AnestaGel-P is a tunable bio-hydrogel, offering customizable concentrations of local anesthetics with consistent elution mechanics of superior duration. Liposomal delivery systems are not crosslinked. Low viscosity exposes greater surface area relative to volume, accelerating degradation, with resultant less consistent elution mechanics.

REFERENCES

Brennan, Timothy J. "Postoperative Models of Nociception." *ILAR Journal* (1999): 129-136. Journal.

Chaplan, Sandra R., et al. "Quantitative assessment of tactile allodynia in the rat paw." *Journal of Neuroscience Methods* (1994): 55-63.

Manchikanti M. D., Lamaiah, et al. "Analysis of the Growth of Epidural Injections and Costs in the Meidcare Population: A Comparative Evalutation of 1997,2002, and 2006 Data." *Pain Physician* (2010): 199-212.

Rudd MSPH, Rose, et al. "Increases in Drug and Opiod Overdose Deaths - United States, 2000 - 2014." *Morbity and Mortality Weekly Report* (2016): 1378-1382. US Dept. of Health and Human services Weekly Report.

Schnacky PharmD, Kim and Cathy Kelley PharmD. "Bupivacaine Liposome Inejectable Suspension (Exparel) National Drug Monograph June 2013." Drug Monograph. 2013.

Stith Butler, Adrienne ; Xi, Jing ;Cox, Thelma L; Pope, Andrew M.; Randall, Donna; Bowman, Victoria. "Relieving Pain in America. A Blueprint for Transforming Prevention, Care, Education, and Research ." Report Brief. 2011.

VHA Pharmacy Benefits Management Services, Medical Advisory Panel and VISN Pharmacist Executives. "Bupivacaine Liposome Injectable Suspension (Exparel) Update March 2016." 2016.

Disclosure: Authors Taylor, Sipple and Sinicropi are shareholders and advisors to InSitu Biologics, LLC.

This research was funded by InSitu Biologics, LLC, St. Paul, MN

APPENDIX THREE
ADDENDUM TO INVESTMENT

ADDENDUM TO
SUBSCRIPTION AGREEMENT AND INVESTMENT LETTER
AND MEMBER CONTROL AGREEMENT

ADDENDUM, made this _____ day of June, 2015, by and between the Company, Investor and Founding Members, as hereinafter defined.

WHEREAS, InSitu Biologics, Inc., a Minnesota limited liability company (the "Company") and 524 Investments, LLC, a Delaware limited liability company (the "Investor") have signed that certain Subscription Agreement and Investment Letter of even date (the "Subscription Agreement") for the purchase of 3,000,000 Units of Membership Interest (the "Units") of the Company; and

WHEREAS, the Company and the Company's Members and Investor have agreed to the terms of this Addendum as part of negotiating, signing and funding the Subscription Agreement.

NOW, THEREFORE, the Subscription Agreement is finalized and the Member Control Agreement is amended by including the following terms and conditions:

1. Full Ratchet Price Protection. In the event the Company issues any additional Units (including, but not limited to, warrants, rights to subscribe for Units and securities convertible into Units) for a consideration per Unit that is less than Investor's subscription price per Unit (as adjusted for any Unit splits and similar events), the subscription price of the Units issued hereby shall be adjusted on a full ratchet basis. The adjustment will be made through the issuance of additional Units to Investor so that the Investor's consideration per Unit shall be the same as the price per Unit of the dilutive issuance.

2. Transfer to Third Party by Founding Member. Notwithstanding any other term and condition contained in this Agreement, the Investor's Units shall be subject to the following rights:

(a) **Drag Along**. If a Founding Member receives a bona fide offer to transfer thirty five percent (35%) or more of the Founding Member's Units to a third party in a single transaction or a series of related transactions, then, the Founding Member shall have the right to compel the Investor to transfer to such third party on the same terms and conditions, all, but not less than all, of the Investor's Membership Units (a "Drag Along Right"). The Founding Member shall provide to Investor a written notice (the "Drag Along Notice") of the Founding Member's decision to exercise the Drag Along Right. The Drag Along Notice must set forth the identity of the third party, the sale price and all other material terms and conditions of the offer. Within Twenty (20) days of receipt of the Drag Along Notice, the Investor must deliver to the Founding Member any documents required to be executed in connection with the third party offer. If the Investor fails to deliver any such documents, the Company shall cause the books and records of the Company to show that Investor's Membership Units are bound by this Section 2 and such Units shall be transferred to the third party offeror.

(b) **Tag Along Rights**. If a Founding Member receives a bona fide offer to transfer thirty-five percent (35%) or more of the Membership Units of the Founding Member to a third party in a single transaction or a series of related transactions, then, as a condition of the transfer of the Founding Member's Units pursuant to such offer, the Investor shall be, at the Investor's option (a "**Tag Along Right**") entitled to transfer to such third party on the same terms and conditions, all, but not less than all, of such Investor's Membership Units. The Founding Member shall provide to the

Investor a written notice of the offer (a "**Tag Along Notice**"). The Tag Along Notice must set forth the identity of the third party, the sale price and all other material terms and conditions of the offer. The Tag Along Right must be exercised by the Investor by providing written notice to the Founding Member, at the principal office of the Company, within twenty (20) days of the receipt by such Investor of the Tag Along Notice. If a Investor fails to exercise Investor's Tag Along Right during such twenty (20) day period, such failure shall be deemed to be an election by such Investor not to exercise the Tag Along Right.

3. Board Seat. So long as the Investor continues to own 37.5% of the issued and outstanding Units of the Company, the Founding Members agree that they will vote their Membership Units to elect James S. Knapp to the Board of Governors of the Company on behalf of the Investor.

4. Certain Veto Rights. The following is a list of actions that require advance written consent from the Investor before the actions may be undertaken by the Company.

a. Disposition of all or substantially all of the Company's assets

b. Issuing any additional Units of Membership Interest of the Company;

c. Reorganization of the Company in any manner;

d. Dissolving or liquidating the Company;

e. Amending the Company's Articles of Organization or the Member Control Agreement;

f. Changing the Company's accounting policies;

g. Not paying any governmental charge lien, tax, hold fee or other similarly required governmental payment; and

h. Entry into or altering the line of business of the Company as it is currently operated.

5. Investor's Preemptive Rights. Before the Company offers to sell or sells any additional Units or warrants or rights to subscribe for Units or securities convertible into Units (the "Offering"), the Company shall first offer to Investor the right to purchase a pro rata proportion (based upon Investor's percentage of ownership of all of the Company's outstanding Units) of such Offering. The Company shall provide Investor with written notice of the Offering. Upon receipt of such notice, Investor shall have twenty (20) days to exercise Investor's preemptive rights. If Investor fails to exercise Investor's preemptive rights during such twenty (20) day period, such failure shall be deemed an election by Investor not to exercise preemptive rights.

6. Miscellaneous. The following miscellaneous provisions are part of this Addendum: 3

(a) **Governing Law**. This Addendum and the rights of the parties hereunder will be governed by, interpreted, and enforced in accordance with the laws of the State of Minnesota.

(b) **Severability**. If any provision of this Addendum is held to be illegal, invalid, or unenforceable under the present or future laws effective during the term of this Addendum, such provision will be fully severable, and this Addendum will be construed and enforced as if such illegal, invalid, or unenforceable provision had never comprised a part of this Addendum, and the remaining provisions of this Addendum will remain in full force and effect.

(c) **Counterparts**. This Addendum may be executed in several counterparts, each of which will be deemed an original, but all of which will constitute one and the same instrument.

(d) **Notices**. Any notice to be given or to be served pursuant to this Addendum will be in writing and may be delivered personally or by mail to the party at the address set forth in the Subscription Agreement and Investment Letter.

(e) **Company Documents**. Investor has reviewed and is familiar with the Company's Articles of Organization and Member Control Agreement (the "Company Documents"). By signing this Addendum, Investor agrees to be bound by the Company Documents. To the extent of any conflict between this Addendum and the Company Documents, the latter shall be controlling; provided, however, with respect to Investor's preemptive rights, the provisions of paragraph 5 of this Addendum shall control.

(f) **Member Control Agreement**. The Founding Members and 524 Investments, LLC by execution of this Addendum intend and specially agree that the provisions of this Addendum, as applicable, amend the provisions of the Company's Member Control Agreement, and this Addendum and the Member Control Agreement shall read as one integrated document.

(g) **Entire Agreement**. This Addendum is the final integration of the agreement of the parties with respect to the matters covered by it and supersedes any prior understanding or agreement, oral or written, with respect thereto.

(h) **Founding Member.** The term "Founding Member" means the following owners of Units of the Company: James Segermark, Daniel Sipple, Stefano Sinicropi, William Taylor, Joseph Glab.

[Signature Page Follows] 4

IN WITNESS WHEREOF, the undersigned have executed this Addendum to be made effective on the date first above written.

COMPANY:
InSitu Biologics, Inc.

_____
James Segermark
President and Chief Manager
INVESTOR:
524 Investments, LLC
By_____
James Knapp
Its_____
Founding Members:

_____
James Segermark

_____
Daniel Sipple

_____
Stefano Sinicropi

_____
William Taylor

_____
Joseph Glab 5

EXHIBIT A

TO ADDENDUM

Upon purchase of the 3,000,000 Units by Investor as set forth in this Subscription Agreement, Investment Letter and Addendum, the ownership of Units of the Company shall be as follows:

James Segermark: 1,000,000 Units

Daniel Sipple: 1,000,000 Units

Stefano Sinicropi: 1,000,000 Units

William Taylor: 1,000,000 Units

Joseph Glab: 1,000,000 Units

524 Investments, LLC: 3,000,000 Units

Total: 8,000,000 Units

I:\DATA\Jule\InSitu Biologics, Inc.\2015-06-04 Subscription Agreement Investment Letter Addendum.docx