Sorrento Therapeutics, Inc.
Form S-3
June 24, 2013
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As filed with the Securities and Exchange Commission on June 21, 2013

Registration No. 333-

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM S-3

REGISTRATION STATEMENT UNDER THE SECURITIES ACT

OF 1933

Sorrento Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	33-0344842
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

6042 Cornerstone Ct. West, Suite B San Diego, California 92121 (858) 210-3700

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Dr. Henry Ji Chief Executive Officer

Sorrento Therapeutics, Inc. 6042 Cornerstone Ct. West, Suite B San Diego, California 92121 (858) 210-3700

(Name, address including zip code, and telephone number, including area code, of agent for service)

With copies to:

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Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ¨

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ¨

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

Large accelerated filer ¨	Accelerated filer ¨ (Do not check if smaller reporting company)	Non-accelerated filer ¨	Smaller reporting company x

Title of Each Class of Securities to be Registered	**Amount to be Registered[1]**	**Proposed Maximum Offering Price Per Unit**	**Proposed Maximum Aggregate Offering Price[2]**	**Amount of Registration Fee[3]**
Common Stock, $.0001 par value per share				
Preferred Stock, $.0001 par value per share				
Warrants				
Units[4]				
Total			$100,000,000	$13,640

(1) There are being registered under this registration statement such indeterminate number of shares of common stock and preferred stock; such indeterminate number of warrants to purchase common stock, preferred stock, and/or units; and such indeterminate number of units as may be sold by the registrant from time to time, which together shall have an aggregate initial offering price not to exceed $100,000,000. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. The securities registered hereunder also include such indeterminate number of shares of common stock and preferred stock, and warrants as may be issued upon conversion of or exchange for preferred stock, upon exercise of warrants; or pursuant to the anti-dilution provisions of any such securities. In addition, pursuant to Rule 416 under the Securities Act of 1933, as amended (the Securities Act), the shares being registered hereunder include such indeterminate number of shares of common stock and preferred stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends, or similar transactions..

(2) Not required to be included in accordance with General Instruction II.D. of Form S-3 under the Securities Act.

(3) Calculated pursuant to Rule 457(o) under the Securities Act based on the proposed maximum aggregate offering price of all securities listed.

(4) Each unit will represent an interest in two or more other securities, which may or may not be separable from one another.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until this Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PROSPECTUS **SUBJECT TO COMPLETION,** **DATED JUNE 21, 2013**

SORRENTO THERAPEUTICS, INC.

$100,000,000

Common Stock

Preferred Stock

Warrants

Units

We may offer and sell, from time to time in one or more offerings, any combination of common stock, preferred stock, warrants or units having an aggregate initial offering price not exceeding $100,000,000. The preferred stock, warrants, and units may be convertible or exercisable or exchangeable for common stock or preferred stock or other securities of ours. When we decide to sell a particular class or series of securities, we will provide specific terms of the offered securities in a prospectus supplement.

We will provide specific terms of the offerings of our securities in supplements to this prospectus. The prospectus supplement may also add, update or change information in this prospectus. You should read this prospectus and any prospectus supplement, as well as the documents incorporated by reference or deemed to be incorporated by reference into this prospectus, carefully before you invest.

This prospectus may not be used to offer or sell our securities unless accompanied by a prospectus supplement relating to the offered securities.

Our common stock is presently traded on the OTC QB under the symbol SRNE. On June 20, 2013, the last reported sale price of our common stock was $0.35.

These securities may be sold directly by us, through dealers or agents designated from time to time, to or through underwriters, dealers or through a combination of these methods on a continuous or delayed basis. See Plan of Distribution in this prospectus. We may also describe the plan of distribution for any particular offering of our securities in a prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The net proceeds we expect to receive from any such sale will also be included in a prospectus supplement.

Investing in our securities involves various risks. See Risk Factors contained herein for more information on these risks. Additional risks will be described in the related prospectus supplements under the heading Risk Factors . You should review that section of the related prospectus supplements for a discussion of matters that investors in our securities should consider.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or passed upon the adequacy or accuracy of this prospectus or any accompanying prospectus supplement. Any representation to the contrary is a criminal offense.

The date of this Prospectus is , 2013.

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ABOUT THIS PROSPECTUS

This prospectus is part of a shelf registration statement that we filed with the Securities and Exchange Commission (the SEC) using a shelf registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings from time to time having an aggregate initial offering price of $100,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer securities, we will provide you with a prospectus supplement that describes the specific amounts, prices and terms of the securities we offer. The prospectus supplement also may add, update or change information contained in this prospectus. You should read carefully both this prospectus and any prospectus supplement together with additional information described below under the caption Where You Can Find More Information.

This prospectus does not contain all the information provided in the registration statement we filed with the SEC. You should read both this prospectus, including the section titled Risk Factors, and the accompanying prospectus supplement, together with the additional information described under the heading Where You Can Find More Information.

You should rely only on the information contained or incorporated by reference in this prospectus or a prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus is not an offer to sell securities, and it is not soliciting an offer to buy securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus or any prospectus supplement, as well as information we have previously filed with the SEC and incorporated by reference, is accurate as of the date on the front of those documents only. Our business, financial condition, results of operations and prospects may have changed since those dates.

OUR BUSINESS

Sorrento Therapeutics, Inc. is referred to throughout this prospectus as we, our or us. The discussion of our business in this section reflects, on a pro forma basis, our anticipated merger with IgDraSol, Inc. pursuant to the option agreement described below. In addition, the IgDraSol option agreement, initial services agreement, asset purchase agreement and development services agreement are collectively referred to in this prospectus as the IgDraSol Transactions.

Overview

We are a biopharmaceutical company engaged in the discovery, acquisition, development and commercialization of proprietary drug therapeutics for addressing significant unmet medical needs in the United States, Europe and additional international markets. Our primary therapeutic focus is oncology but we are also developing therapeutic products for other indications, including inflammation, metabolic disorders, and infectious diseases.

Our proprietary G-MAB® fully-human antibody library platform was designed to facilitate the rapid identification and isolation of highly specific antibody therapeutic product candidates that bind to disease targets appropriate for antibody therapy.

On March 7, 2013, we entered into an exclusive option agreement with IgDraSol, Inc., or IgDraSol, a private company focused on developing oncologic agents for the treatment of metastatic breast cancer, or MBC, non-small cell lung cancer, or NSCLC, and other cancers. IgDraSol granted us an irrevocable option to acquire IgDraSol by means of an agreement and plan of merger, and was paid a non-refundable lump sum payment of $200,000 in April 2013. IgDraSol s lead compound is Cynviloq , a micellar diblock copolymeric paclitaxel formulation drug product. Cynviloq is currently approved and marketed in several countries, including South Korea for MBC and NSCLC under the trade name Genexol-PM®.

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Our goal is to deliver innovative, highly effective and safe treatment options to patients throughout the world. By working closely with scientists, doctors, patient organizations and other health care specialists, we are committed to improving the lives of patients and assisting their caregivers in the fight against cancer, inflammatory and autoimmune diseases and other unmet medical needs.

G-MAB® Fully Human Antibody Library Platform

We believe our proprietary G-MAB® library is one of the industry s most diverse fully human antibody libraries. The theoretical diversity of our library has been calculated to be more than one quadrillion unique antibodies, making it, to our knowledge, the largest fully human antibody library available to pharmaceutical and biotechnology companies for drug discovery and development partnerships. Our objective is to leverage our library to develop both First-in-Class, or FIC, and/or Best-in-Class, or BIC, antibody drug candidates that we expect will possess greater efficacy and fewer side effects as compared to existing drugs.

We have experienced a high success rate when screening our diverse library to identify monoclonal antibodies, or mAbs, that have the potential to be used as drugs. Recently, we have selected several lead drug development candidates to advance into clinical trials in 2015, including anti-PD-L1 and anti-CCR2 mAbs.

The following is a chart of fully human mAbs we ve derived from our G-MAB® library. It includes antibodies that bind to a wide range of targets, from small molecular weight antigens to large protein complexes antigens, such as G-Protein Coupled Receptors, or GPCRs, a difficult class of antigens to raise therapeutic antibodies against.

In addition to employing our G-MAB® library to identify novel therapeutic antibodies, we also plan to: (i) develop potent antibody-formulated drug conjugates, or AfDCs, in therapeutic areas like oncology, auto-immune diseases and infectious diseases, armed using our proprietary TOCOSOL® technology (a tocopheryl polyethelyene glycol succinate (TPGS)-based drug formulation), and / or antibody drug conjugates, or ADCs, and (ii) create recombinant intravenous globulins, or rIVIG, for the treatment of certain auto-immune diseases as well as immunodeficiencies.

Recent Developments IgDraSol Transactions and Cynviloq

On March 7, 2013, we entered into an exclusive option agreement with IgDraSol. IgDraSol granted us an irrevocable option to acquire IgDraSol by means of an agreement and plan of merger, and was paid a non-refundable lump sum payment of $200,000 in April 2013. The option must be exercised by the later of: (i) thirty (30) days after the receipt of the FDA End of Phase II meeting minutes for Cynviloq (the End of Phase II meeting is scheduled in July 2013), or (ii) September 30, 2013. If we exercise our option to acquire IgDraSol, we

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will immediately issue 76,199,198 shares of our common stock to the IgDraSol stockholders. If a specific regulatory milestone is achieved, we will issue an additional 32,656,799 shares of our common stock to the former IgDraSol stockholders. If we do not exercise our option to acquire IgDraSol, we will be required to invest $500,000 in IgDraSol *pari passu* with other new investors of IgDraSol.

IgDraSol s lead compound is Cynviloq , a micellar diblock copolymeric paclitaxel formulation drug product. Cynviloq is currently approved and marketed in several countries, including South Korea for MBC and NSCLC under the trade name Genexol-PM®. IgDraSol obtained exclusive distribution rights for Cynviloq in the United States and 27 countries of the European Union, or EU, from Samyang Biopharmaceuticals Corporation, a South Korean corporation.

We entered into an initial services agreement dated March 7, 2013 with IgDraSol, wherein IgDraSol has provided certain product development and technology services related to antibody-based nanotherapeutics. In March 2013, IgDraSol was paid a non-refundable payment of $1,000,000 and the related services were completed prior to May 31, 2013. There are no further obligations under the initial services agreement.

In addition, we entered into an asset purchase agreement with IgDraSol whereby we agreed to purchase all documentation, equipment, information and other know-how related to micellar nanoparticle technology encompassing Tocosol® and related technologies for a purchase price of $1,210,000, which was paid in April 2013. Also in April 2013, we entered into a development services agreement with IgDraSol related to the development of Tocosol® and related technologies. We will pay IgDraSol up to $3,000,000 for services provided.

Our Strategy

Assuming the consummation of our planned acquisition of IgDraSol in the third quarter of 2013, our mission is to improve the lives of cancer patients and assist their caretakers by delivering innovative, targeted therapies that improve outcomes while reducing the undesirable side effects of many current therapies. We intend to pursue this initially through the potential approval, launch and marketing of Cynviloq . We believe we have assembled a strong scientific team with in-depth domain knowledge in the nanomedicine and therapeutic antibody fields. We are fostering an integrated, multidisciplinary model for drug discovery, clinical development, manufacturing and commercialization. Our strategy is to discover, acquire, develop, and commercialize proprietary drugs for significant unmet medical needs, with a focus on cancer therapeutics. The key elements to our long-term oncology business strategy are illustrated and described below:

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Cynviloq is our next-generation oncolytic nanomedicine for effective tumor killing. Oncolytic agents are the predominant therapeutics for treating cancer patients, and paclitaxel is one of the most effective and widely used chemotherapeutic agents for multiple solid tumor indications. The first generation paclitaxel formulation, Taxol®, utilizes Cremophor, derived from castor oil, to solubilize paclitaxel. The second generation paclitaxel formulation, Abraxane®, utilizes human serum albumin, or HSA, to solubilize the paclitaxel in an injectable solution. We are developing a third generation injectable nanoparticle paclitaxel, Cynviloq™, that is both Cremophor-free and HSA-free. We believe our formulation offers a higher maximum tolerated dose, or MTD, for potential better efficacy, ease of administration, and may better enable personalized dosing regimens. We believe Cynviloq may provide cancer patients and oncology practitioners with a much needed alternative to the current paclitaxel-based chemotherapies and may offer the potential for improved patient outcomes. We intend to seek a partner to simultaneously develop a companion pharmacokinetic monitoring device to allow for personalized cancer therapy in combination with Cynviloq .

G-MAB® provides us with specific therapeutic antibodies for effective cancer cell targeting and killing. Our proprietary G-MAB® human antibody library has provided us with potent fully human therapeutic mAbs against many valuable cancer targets. The individual mAbs discovered from our G-MAB® library potentially gives us a multitude of therapeutic options to target and attack cancer cells, including, but not limited to, antibody-dependent cellular cytotoxicity, or ADCC for direct cancer cell killing, immunomodulation of T cell activity in the tumor, anti-angiogenesis for cutting off blood supplies to the tumor, and antagonist suppression of cellular processes required for cancer cell proliferation and metastasis. In addition, we intend to utilize our G-MAB® library-derived antibodies as the foundation for the development of companion diagnostics.

Antibody formulated drug conjugates (AfDC) and antibody drug conjugates (ADC) for targeted tumor killing. Combining our proprietary nanotechnology with our proprietary mAbs or biosimilar mAbs, we are in a position to generate proprietary ADCs and/or AfDCs with potentially better efficacy and safety profiles than currently available therapies. We have the exclusive worldwide rights to the TOCOSOL® paclitaxel-nanoparticle formulation, which we believe is well suited for conjugation with a targeting mAb to generate an AfDC candidate. There are few competitors in the oncology space that offer the combination of targeting proprietary mAb warheads with an oncolytic payload, such as TOCOSOL®-paclitaxel. By combining this proprietary nanomedicine formulation encapsulating an oncolytic agent with our mAbs, we are positioning ourselves to become a leader in providing innovative, BIC targeted cancer therapeutics.

Combination therapy of oncolytic agents and therapeutic mAbs for cocktail-based tumor cell killing. There are a plethora of anti-cancer monotherapies available from many drug makers, including chemotherapeutics and therapeutic mAbs. There is a major trend to combine different monotherapeutics to attack cancer using different modes of action (MOA). Such combinations are often referred to as a cocktail treatment approach . We are positioned to develop both oncolytic agents for strong non-specific killing of tumor cells and therapeutic mAbs for specific targeted tumor killing. The mAbs provide an alternative MOA different from the oncolytic agents, such as anti-angiogenesis, in-tumor T cell activation, ADCC, etc. We believe we are well-positioned to provide such solutions by providing both modalities derived from our in-house, proprietary oncolytic and mAb therapeutics as proprietary combination therapies. Many of our competitors may have to collaborate to combine their existing drugs with other company s drugs in order to develop combination therapies. Cynviloq is well suited to be combined with our proprietary anti-angiogenesis mAbs and immunomodulatory mAbs to offer cancer patients with desirable anti-cancer cocktail treatments.

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Assuming the consummation of our planned acquisition of IgDraSol in the third quarter of 2013, we are advancing toward our goal of bringing new therapeutic options to patients and planning to continue to leverage the broad potential of our G-MAB® fully human antibody library. In the near term, we expect to:

- advance IgDraSol s late-stage, oncolytic drug candidate Cynviloq towards registration trials for multiple solid tumor cancer indications,

- progress selected drug development candidates from our proprietary G-MAB® fully human antibody library into clinical trials in 2015, including fully-human anti-PD-L1, anti-PD-1, and anti-CCR2 mAbs,

- develop AfDCs using our nanoparticle formulation (Tocosol® and/or related technologies) or ADCs,

- create rIVIG, using our proprietary G-MAB® fully human antibody library, and

- pursue combination therapies using Cynviloq and our proprietary fully-human mAbs.

Although we intend to retain ownership and control of some product candidates by advancing them further into preclinical or clinical development, we will also consider partnerships with pharmaceutical or biopharmaceutical companies in order to balance the risks associated with drug discovery and development and maximize our stockholders returns. Our partnering objectives include generating revenue through license fees, milestone-related development fees and royalties by licensing rights to our product candidates.

Product Candidates

We, through IgDraSol, currently have one late-stage oncology drug candidate, Cynviloq , in clinical development for multiple solid tumor indications. We are currently planning for registration trials pending the outcome of our planned End of Phase II meeting with the FDA in July 2013. Additionally, we have multiple mAb product candidates in preclinical development, such as our fully human anti-PD-L1 mAbs, anti-PD-1 mAbs, and anti-CCR2 mAbs, and a discovery effort advancing additional therapeutic mAb drug candidates. We believe these mAb product candidates, individually, as AfDC, as ADC, or as combination therapy, have the potential to address major unmet medical needs.

* Subject to EOP2 meeting with FDA scheduled in July 2013 and subject to FDA approval of Abraxane® for pancreatic cancer.

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Cynviloq

Cynviloq was secured by IgDraSol through an exclusive distribution agreement, as amended, for the United States and 27 countries of the EU, with Samyang Biopharmaceutical Corporation, a South Korean corporation, or Samyang. Cynviloq is currently approved and marketed by Samyang in South Korea for MBC, NSCLC and ovarian cancer, under the trade name Genexol-PM®. Cynviloq is also marketed in the Philippines, Vietnam, and India. Cynviloq consists of paclitaxel encapsulated within a polylactide and polyethylene glycol diblock copolymer micelle. A micelle is an aggregate of surfactant molecules, having hydrophobic and hydrophilic parts, in which the hydrophilic heads form the outside shell of the sphere with the hydrophobic tails at the center of the core. This hydrophobic core is able to effectively encapsulate hydrophobic drugs, such as paclitaxel.

Cynviloq has been clinically tested in over 900 patients in the United States, Russia, and South Korea in Phase I, Phase II, and Phase III clinical trials, and post-marketing surveillance studies in MBC, NSCLC, ovarian, pancreatic and bladder cancer. Cynviloq has demonstrated comparable clinical efficacy and tolerability compared to historical albumin-bound paclitaxel (*nab*-paclitaxel; Abraxane®/Celgene Corporation) clinical data. Samyang is currently conducting an ongoing open-label Phase III MBC study in South Korea, randomizing patients with recurrent or advanced MBC to Cynviloq using a dosing regimen of 260mg/m^2 every 3 weeks, or q3w, as compared to Cremophor-paclitaxel (Taxol®) given at a standard 175 mg/m^2 q3w dose. Interim results have shown statistically significant improvement in the objective response rate (ORR) with Cynviloq when compared to Taxol®. We believe the superior ORR for Cynviloq versus Taxol® is comparable to data generated from the pivotal registration studies submitted for Abraxane® that was the basis for Abraxane® s approval in the United States and in China for the MBC indication.

Cynviloq Differentiation versus Taxol® and Abraxane®

Paclitaxel is a water insoluble drug that requires a solvent formulation. The first generation paclitaxel formulation, Taxol®; developed by Bristol-Myers-Squibb, or BMS, utilizes a Cremophor solvent, a castor oil-based emulsion. Known dose-limiting toxicities of Cremophor restrict the overall dose of Taxol® that can be safely administered to patients. Cremophor also causes the entrapment of paclitaxel in the bloodstream, thereby allowing less freely-available paclitaxel to reach the tumor sites. Furthermore, patients receiving Taxol® require pre-medication with steroids and antihistamines to allay the toxic side effects associated with Cremophor.

Abraxane® is a second generation paclitaxel formulation that utilizes a biological polymer, namely donor-derived HSA to encapsulate paclitaxel. Abraxane® does not contain the Cremophor solvent and thus, enables administration of ~50% more paclitaxel than with Taxol®.

Cynviloq is a next generation paclitaxel formulation comprised of paclitaxel encapsulated in a non-biological polymeric micelle composed of a polylactide and polyethylene glycol diblock copolymers resulting in an injectable suspension of paclitaxel. This polymeric micelle formulation of paclitaxel achieves an increased MTD of paclitaxel of potentially greater than 300 mg/m^2. This is significantly greater than the MTDs of Taxol® (175 mg/m^2) and Abraxane® (260 mg/m^2). We believe Cynviloq is easier to prepare and administer for clinical practices, and has no special storage requirements in contrast to Abraxane®. Cynviloq also avoids certain biohazardous safety issues, such as potential prion or viral contamination and subsequent transmission that could be associated with the use of donor-derived HSA required for the Abraxane® formulation.

Clinical Strategy: Basis for bioequivalence

Cynviloq utilizes a proprietary, non-biological, chemical polymeric-micellar nanoparticle technology to solubilize paclitaxel. This is a different formulation from Abraxane®, where paclitaxel is solubilized in HSA nanoparticles. Particle dissociation studies comparing Abraxane® and Cynviloq have shown that both formulations rapidly disintegrate under physiologically-relevant conditions, suggesting that both formulations

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release their paclitaxel payloads shortly after intravenous administration. Our analysis of pharmacokinetic (PK) data (see table below) from three Phase I trials with Cynviloq , suggests Cynviloq is bioequivalent to Abraxane® under the FDAs bioequivalence (BE) guidance. Both paclitaxel formulations showed substantially identical PK parameters at the approved Abraxane® dose range of 100-260 mg/m^2 paclitaxel (administered intravenously over 30 minutes). If we receive the FDA s concurrence, we plan to utilize a 505(b)(2) new drug application, or NDA, submission process to show the BE of Cynviloq as compared to Abraxane®.

We believe the following analysis demonstrates BE between Cynviloq and Abraxane®:

1. Large volume of distribution (suggestive of rapid tissue penetration),

2. Dose proportional PK profile of doses ranging up to 350 mg/m^2,

3. Similar PK parameters at 135 mg/m^2 dose level for Abraxane® (Ibrahim, 2002) and Cynviloq (Study GXLPM-01) both infused over 180 minutes.

Cynviloq vs Abraxane® PKs at 135 mg/m^2 on a 3 hr Infusion Regimen

	Cmax (ng/mL)	AUC inf (ng/mL*h)	T1/2 (hr)	CL (L/hr/m2)
Cynviloq	1357	5473	12.7	25.5
Abraxane®	1392	5654	12.9	27.4

4. Overlapping 95% confidence interval (CI) for AUCinf/D, T1/2, CL, and Vz. There were 78 patients in the Abraxane® dataset, and 32 patients in the Cynviloq dataset.

5. When the Cynviloq infusion was performed over 60 minutes instead of 180 minutes, the ranges for AUCinf/D, T1/2 and Vz overlapped with 95% CI of both Abraxane® and Cynviloq , suggesting that a shorter infusion time does not negatively impact Cynviloq PK properties as predicted by simulation modeling.

Cynviloq vs Abraxane®- Dose Adjusted PK Parameters

	Infusion Time	AUCinf/D (ng/hr/mL/D)	T1/2 (hr)	CL (L/hr/m2)	Vz (L/m2)
		Mean (95% confidence interval)			
Abraxane®	30 min	53	17	22	536
(N=14)		(20-86)	(10-24)	(11-33)	(145-928)
Cynviloq	180 min	48	14	25	631
(N = 9)		(11-84)	(8-19)	(9-40)	(252-1010)
Cynviloq *	60 min				
(N = 7)		(26-61)	(6.0-18.6)		(249-1512)

* Lim, et al, 2009, the AUC, T1/2, CL or Vz were not reported.

6. PK studies were initially conducted using a 180 minute infusion administration of Cynviloq , the same administration schedule as Taxol®, which was the only approved comparator product available when Genexol-PM® was approved (Studies GPMP1 and SAY00101US). The approved dosage administration for Abraxane® is a 30 minute infusion time. A simulation analysis of Cynviloq administered in a 30 minute infusion time is shown in the table below. The simulated data were compared to historical data for Abraxane® to assess similarity (point estimates) for AUC0-t and AUCinf between Cynviloq and Abraxane® (Study Camargo1).

Simulated mean PK Parameter Values after Administration of 260 mg/m^2 Cynviloq in 30 minutes and Summary of Abraxane® s PK Parameter Values

Cmax	**AUC_{inf}**	**Point Estimate for Cmax**	**Point Estimate for AUC_{inf}**
(ng/mL)	**(ng hr/mL)**	**(Difference in %)**	**(Difference in %)**
19486	22198	0.36	9.22
19556	20324		

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Cynviloq Regulatory Strategy

Manufacturers can obtain FDA approval of NDAs for new formulations of approved drugs with the same active pharmaceutical ingredient (API) using an FDA 505(b)(2) BE application process. The 505(b)(2) BE application process relies, in part, on the FDA s findings for a prior approved drug. This avoids costly and time consuming clinical trials. We believe this process might apply to Cynviloq as paclitaxel is the approved API for both of the Abraxane® and Taxol® formulations. According to the Section 505(b)(2) guidelines, an NDA approval can be obtained for a new drug without conducting the full complement of safety and efficacy trials and without a right of reference from the original applicant. In cases where different formulations of the same API are found to be bioequivalent, a BE trial comparing the PK parameters (Cmax and AUC) of both drugs may be sufficient to obtain FDA approval. The Draft Guidance (September 2012) for *nab*-paclitaxel (Abraxane®) states that measurements of both total and unbound paclitaxel should be made to establish BE. Given that both Cynviloq and Abraxane® release free paclitaxel upon intravenous administration, we believe that this is an appropriate method of comparison for marketing approval.

In July 2013, IgDraSol will meet with the FDA to discuss, among other items, using a FDA 505(b)(2) BE application process for Cynviloq on the basis of BE versus Abraxane® as the reference drug. If the FDA concurs with our approach, we plan to initiate a BE trial as well as a Phase III bladder trial. We are also considering other cancer trials. Subject to the FDA s concurrence, a single BE trial is planned to treat MBC patients with Abraxane® in the first cycle and then with Cynviloq (or vice versa) in the next cycle in a cross-over trial designed to use the patients as their own controls to measure the PK parameters between the two drug formulations, and thus establish BE.

Subject to the FDA s concurrence and our conducting the BE trial, an NDA filing under 505(b)(2) is expected to be completed in the first half of 2015, with potential approval in the first half of 2016. If Cynviloq and Abraxane® are found to be bioequivalent and FDA approval is granted, Cynviloq will receive the same label indications as Abraxane®, including MBC and NSCLC, in addition to potentially other future indications for which Abraxane® may be approved, such as advanced pancreatic cancer (upon expiration of Abraxane® s marketing exclusivity). Subject to the FDA s concurrence, a Phase III registration trial for Cynviloq as second-line treatment for bladder cancer as compared to the best supportive care (BSC) is planned as a sNDA application, with approval targeted in 2017.

Market Opportunity

Cynviloq

According to the 2012 IMS NSP, the taxane market in the United States is estimated to be one billion dollars in 2012, and is comprised of Abraxane®, generic paclitaxel (Taxol®; BMS) and generic docetaxel (Taxotere®; Sanofi-Aventis). Abraxane® had approximately 40% market share in the United States in 2012. In the rest of the world, the taxane market is estimated to be worth at least $2.4 billion, driven primarily by sales of generic paclitaxel and docetaxel, with Abraxane® sales of approximately $90 million. Taxanes are one of the most widely used chemotherapies in the world and play a significant role in the treatment of various solid tumors, including breast, lung, prostrate and ovarian cancers. Taxanes are often the standard of care as monotherapy or in combination with other chemotherapy or biological agents when used in the metastatic setting, although it also being used in the adjuvant/neo-adjuvant settings as well. Historically, taxanes were rarely used in pancreatic cancer. However, the survival benefit seen in the MPACT study combining Abraxane® with gemcitabine is predicted to become the standard of care, replacing gemcitabine monotherapy in this highly aggressive tumor with limited treatment options.

MBC[1]

It is estimated that over 230,000 new cases of invasive breast cancer will be diagnosed among women in the United States during 2013, along with over 2,000 new cases in men. Excluding skin cancers, breast cancer is the most frequently diagnosed cancer in women. An estimated 40,000 breast cancer deaths are expected in 2013. Breast cancer ranks second as a cause of cancer death in women, after lung cancer. Taking into account tumor

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size, extent of spread, and other characteristics, as well as patient preference, treatment usually involves breast-conserving surgery (surgical removal of the tumor and surrounding tissue) or mastectomy (surgical removal of the breast). Treatment may also involve radiation therapy, chemotherapy (before or after surgery), hormone therapy (e.g., selective estrogen response modifiers, aromatase inhibitors, ovarian ablation), and/or targeted therapy. Postmenopausal women, with early stage breast cancer, that test positive for hormone receptors may benefit from treatment with an aromatase inhibitor (e.g., letrozole, anastrozole, or exemestane) or tamoxifen. For women whose cancer tests positive for HER2/neu, approved targeted therapies include trastuzumab (Herceptin®; Genentech), and, for advanced disease, lapatinib (Tykerb®; GSK), and pertuzumab (Perjeta®; Genentech). In February 2013, the United States FDA approved Kadcyla® (ado-trastuzumab emtansine) from Roche-Genentech, a new therapy for patients with HER2-positive, late-stage MBC. Kadcyla® is an ADC product with trastuzumab as the targeting warhead and the anti-tubulin toxin DM1 as the payload. Kadcyla® is intended for patients who were previously treated with trastuzumab, another anti-HER2 therapy, and taxanes. The safety and effectiveness of Kadcyla were evaluated in a clinical study of 991 patients randomly assigned to receive Kadcyla® or lapatinib plus capecitabine (Xeloda®; Roche-Genentech). Results showed that patients treated with Kadcyla® had a median progression-free survival of 9.6 months compared to 6.4 months in patients treated with lapatinib plus capecitabine. The median overall survival was 30.9 months in the Kadcyla group and 25.1 months in the lapatinib plus capecitabine group.

In 2012, approximately 330,000 patients diagnosed with breast cancer were treated with drugs in the United States and the top five (5) EU countries (Germany, France, Italy, Spain, United Kingdom). Half of these patients live in the United States, and approximately 100,000 of these patients were treated in the advanced or metastatic settings in first, second or third-line therapy. The National Comprehensive Cancer Network (NCCN) treatment guidelines list of preferred single agent drugs include paclitaxel & paclitaxel albumin-bound (Abraxane®), among other drugs, for the treatment of patients with Stage IV advanced breast cancer. Preferred combination chemotherapy agents include among others paclitaxel plus Herceptin, paclitaxel plus gemcitabine, Herceptin® plus paclitaxel & carboplatin and Perjeta® plus Herceptin® & paclitaxel. It is estimated that about 25-30% of all patients treated in MBC received a paclitaxel-based regimen. In addition, paclitaxel in combination with other targeted therapies are recommended in neo-/adjuvant breast cancer treatment as well.

Lung cancer[1]

In the United States, lung cancers are expected to represent approximately 14% of new cancer diagnoses, or an estimated 223,000 new cases in 2013. Lung cancer accounts for more deaths than any other cancer in both men and women. An estimated 160,000 deaths, accounting for about 27% of all cancer deaths, are expected in 2013.

Lung cancer is classified as small cell (15%) or non-small cell (84%) for the purposes of treatment. Based on type and stage of cancer, treatments include surgery, radiation therapy, chemotherapy, and targeted therapies such as bevacizumab (Avastin®/Roche-Genentech), erlotinib (Tarceva®), and crizotinib (Xalkori®). Advanced-stage non-small cell lung cancer patients are usually treated with chemotherapy, targeted drugs, or some combination of the two. Approximately 134,000 patients with locally advanced or metastatic Stage IIIB/IV NSCLC were diagnosed in the United States last year. Approximately 70% of these patients were treatment eligible. The NCCN s list of systemic therapy for advanced or metastatic NSCLC includes paclitaxel and Abraxane®, among other recommendations. Paclitaxel is often used in combination with a platinum agent (carboplatin or cisplatin). It is estimated that about a third of patients treated in the first-line and second-line settings received a paclitaxel-based therapy.

Ovarian cancer[1]

Approximately 48,500 women were diagnosed with ovarian cancer last year in the United States and the top 5 EU countries. More than 70% of women diagnosed with ovarian cancer will present with advanced disease, and up to 80% of them will experience disease recurrence and eventually die from this disease. Treatment includes surgery and usually chemotherapy. Among patients with early ovarian cancer, complete surgical staging has been

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associated with better outcomes. For women with advanced disease, surgically removing all abdominal metastases larger than one centimeter (debulking) enhances the effect of chemotherapy and helps improve survival. For women with stage III ovarian cancer that has been optimally debulked, studies have shown that chemotherapy administered both intravenously and directly into the abdomen (intraperitoneally) improves overall survivial, or OS.

In 2012 in the United States and the top 5 EU countries, approximately 36,000 patients were treated with front-line chemotherapy, and approximately17,000 patients were treated with second-line chemotherapy. Paclitaxel in combination with a platinum compound plays a significant role in the treatment of ovarian cancer with the NCCN recommending taxanes plus platinum to be used in both the adjuvant and metastatic settings. It is estimated that 75% of the patients treated in the United States, in 2012, were treated with paclitaxel-based chemotherapy as front-line therapy.

Pancreatic cancer[1]

Even though pancreatic cancer is a relatively uncommon form of cancer making up only 2.1% cancer cases it is one of the leading causes of cancer related deaths, killing around 38,000 people in the United States each year. It is one of the most difficult forms of cancer to treat, especially as it is usually detected at very late stages. It is estimated that around 65,000 patients were diagnosed with pancreatic cancer (mainly adenocarcinoma) in the United States and the top 5 EU countries. In 2013, an estimated 45,000 new cases of pancreatic cancer will be diagnosed in the United States. Pancreatic cancer accounts for about 7% of all cancer deaths and ranks fourth as a cause of cancer death among both men and women in the United States. In 2013, an estimated 38,000 people are expected to die from pancreatic cancer in the United States. The treatment choice is largely determined by whether the tumor can be surgically removed. Surgery remains the only treatment that offers a chance of cure for pancreatic cancer patients. Approximately 20% of all pancreatic cancer patients are candidates for surgery.

Approximately 56,000 of patients with pancreatic cancer were treated in the first-line setting in the United States and top 5 EU countries, with the United States accounting for 27,000 of these patients. Another 26,000 patients were treated in the second-line setting in the United States and top 5 EU countries, with the United States accounting for 15,000 of these patients. Gemcitabine-and fluoro-pyrimidine based therapy are the standard of care both in the adjuvant and metastatic settings. The NCCN recommendation for patients with unresectable, locally advanced or metastatic adenocarcinoma of the pancreas includes Abraxane® plus gemcitabine, gemcitabine (Gemzar®/Lilly) monotherapy, or in combination with erlotinib (Tarceva®/Astellas), folfirinox, capecitabine (Xeloda®/ Roche-Genentech) or fluorouracil (Efudex/Valeant) as a continuous infusion. Last year, before the results of the MPACT study with Abraxane® plus gemcitabine data were reported, approximately 65% of patients were treated with gemcitabine-based regimens in first-line settings, and 30% of patients were treated with gemcitabine-based regimens in second-line settings. Wi