Sorrento Therapeutics

Next-Generation Cancer Therapeutics

November 2013
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# Management Team

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Key Accomplishments</th>
</tr>
</thead>
</table>
| **Henry Ji, Ph.D.**   | President & CEO, Director    | • Inventor of G-MAB® Technology  
                           • President & CEO of Stratagene Genomics  
                           • VP of CombiMatrix and Stratagene                                                                 |
| **Vuong Trieu, Ph.D.**| CSO and Director             | • Founder and CEO of IgDraSol  
                           • Co-inventor of IP covering Abraxane®  
                           • Instrumental in the approval of Abraxane®  
                           • Celgene acquired Abraxis Biosciences for > $3 billion                                                                 |
| **George Uy**         | Chief Commercial Officer     | • CCO of IgDraSol  
                           • Directed the launches of Abraxane®, Xeloda® & Fusilev®  
                           • Built commercial infrastructures and organizations in startup companies                                                                 |
| **David (Zhenwei) Miao, Ph.D.** | CTO                           | • President and CSO of Concordis Biosystems  
                           • Co-inventor of IP covering ADC technologies  
                           • Head of Chemistry at Ambrx                                                                 |
| **Richard Vincent**   | EVP, CFO, Director           | • $430M sale of Elevation to Sunovion-Dainippon  
                           • Meritage Pharma option agreement with ViroPharma ($90M upfront + milestones)  
                           • $310M sale of Verus asthma program to AstraZeneca  
                           • Elan: various acquisitions and divestitures with aggregate values in excess of $300M |
Investment Highlights

Late Stage Oncology Drug with Exclusive US and EU Rights
- Addresses multi-billion dollar paclitaxel market
- Abbreviated regulatory pathway (“bioequivalence”) for approval
- Bioequivalence registration trial in 2014 (study direct costs ~ $5M)
- Product launch in 1H 2016

Intractable Pain in Advanced Cancer
- Ongoing Phase 1/2 study
- Orphan drug status received
- Two potential drug products from same API (Resiniferatoxin)

Therapeutic Antibody Engine
- Antibody market >$50B in 2012
- First antibody drug candidate in clinic 1H 2015

Targeted Drug Delivery (ADC)
- G-MAB® antibody as specific targeting warhead
- Proprietary toxins as potent tumor killing payload
- Selective conjugation chemistry for homogenous ADC generation
Sorrento’s Next-Generation Cancer Therapeutics

**Cynviloq™**
- Next-generation Abraxane®
  - Bioequivalence (BE) pathway for approval
  - Efficacy demonstrated
  - US and EU rights

**AfDC: Antibody formulated Drug Conjugate**
- G-MAB targets approved chemotherapeutics to the tumor
- Effective against heterogeneous tumors

**G-MAB®**
- High-diversity human Ab library
- Lead mAb programs include PD-L1, PD-1, and CCR2
- FTO and no stacking royalties

**ADC: Antibody Drug Conjugate**
- G-MAB targets toxin to cancer cell
- Programs include VEGFR2, c-Met
Cynviloq™

**INDICATION**

- Metastatic Breast Cancer
- Non-Small Cell Lung Cancer
- Pancreatic Cancer (BE* or sNDA)
- Bladder Cancer (sNDA)
- Ovarian Cancer (sNDA)

**Phase 1**

- 1H 2014

**Phase 2**

- 1H 2015

**Phase 3**

- 505(b)(2) Bioequivalence

**NDA Filing**

- 1H 2015

RTX

**INDICATION > TARGET**

- Refractory Pain in Cancer Patients

**Phase 1**

- 1H 2015

**Phase 2**

- In progress

G-MAB®

**INDICATION > TARGET**

- Oncology > PD-L1
- Oncology > PD-1
- Oncology/Inflammation > CCR2, CXCR3

**Phase 1**

- 1H 2015

**Phase 2**

- 2H 2015

**Phase 3**

- 2H 2015

**Preclinical**

- 2H 2015

**Partnership Opportunities**

- Multiple

- Strategic

* Abraxane® orphan drug status (FDA approval, September 2013)
Lead Product Opportunity

Cynviloq™

Registration Trial
Cynviloq is the 3rd Generation Paclitaxel Therapy

<table>
<thead>
<tr>
<th>Generation</th>
<th>Formulation</th>
<th>Maximum Tolerated Dose</th>
<th>Peak Product Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>Taxol® paclitaxel</td>
<td>Cremophor EL excipient: Polyoxylethylated castor oil</td>
<td>175 mg/m²</td>
</tr>
<tr>
<td>2nd</td>
<td>Abraxane® nab-paclitaxel</td>
<td>Biological polymer: Donor-derived human serum albumin (HSA)</td>
<td>260 mg/m²</td>
</tr>
<tr>
<td>3rd</td>
<td>Cynviloq™ paclitaxel polymeric micelle</td>
<td>Chemical polymer: Poly-lactide and polyethylene glycol diblock copolymer</td>
<td>&gt;300 mg/m² (up to 435 mg/m²)</td>
</tr>
</tbody>
</table>

*Analyst projection; in MBC + NSCLC + PC
Cynviloq is a High Value Proposition

1. Exclusive US and EU Rights

2. Cynviloq efficacy demonstrated in Phase 2 and Phase 3 studies
   a. Approved and marketed under brand name Genexol-PM in S. Korea

3. FDA concurred
   a. Available data support pursuing 505(b)(2) regulatory pathway
   b. Bioequivalence (BE) study sufficient for approval of indications in Abraxane label (MBC and NSCLC)

4. Large market opportunity
   a. Abraxis (Abraxane) sold to Celgene for > $3B
   b. $1.7B in projected US peak revenues for Abraxane
Clinical Efficacy & Safety Summary

Total number of patients across all trials: 1,260

Phase 1: Trials established higher MTD in US - Dana Farber Cancer Inst, Russia, & S. Korea (total n=80)
- >300 mg/m² (q3w) vs. 175 mg/m² (Taxol; weekly) and 275 mg/m² (Abraxane; q3w)

Phase 2: Completed trials in MBC, NSCLC, PC, OC, BC; in US - Yale Cancer Center, Russia, S. Korea (total n=259)
- Data suggestive of efficacy comparable to historic data for Abraxane and superior to historic Taxol data or Standard-of-Care
- Possible Phase 3 sNDA programs in these tumor types

Phase 3: Ongoing trial for MBC in S. Korea (total n=209; Cynviloq n=105)
- GPMBC301. An Open-label, Randomized, Parallel, Phase 3 Trial to Evaluate the Efficacy and Safety of Cynviloq compared to Genexol® (Paclitaxel with Cremophor EL) in Subjects with Recurrent or Metastatic Breast Cancer
- Interim analysis suggests ORR superior to Taxol and comparable to historic Abraxane efficacy
- Efficacy and safety data supportive of 505(b)(2) BE submission

PM-Safety: Completed for MBC and NSCLC (total n=502)
- Efficacy and safety data supportive of 505(b)(2) BE submission

Phase 2b (IIS): Chemo-naïve Stage IIIb/IV NSCLC vs Taxol in S. Korea (total n=276; Cynviloq n=140)
- 230 mg/m² + cis (q3w) vs. Taxol 175 mg/m² + cis; non-inferiority established

Phase 2 (IIS): 1st line treatment of OC vs Taxol in S. Korea (total n=100; Cynviloq n=50)
- 260 mg/m² + carbo (q3w) vs. Taxol 175 mg/m² + carbo; non-inferiority established
## Equivalent Pharmacokinetics in Mice

<table>
<thead>
<tr>
<th>Drug</th>
<th>HL (h)</th>
<th>T max (h)</th>
<th>AUCinf (h*ng/mL)</th>
<th>Vz (mL/kg)</th>
<th>Cl (mL/h/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abraxane</td>
<td>2.99</td>
<td>0.08</td>
<td>61561.33</td>
<td>2103.71</td>
<td>487.32</td>
</tr>
<tr>
<td>Cynviloq</td>
<td>2.83</td>
<td>0.08</td>
<td>58151.31</td>
<td>2103.58</td>
<td>515.90</td>
</tr>
</tbody>
</table>

IV bolus at 30 mg/kg; n = 3
## Comparable Pharmacokinetics in Human

Data from 2 separate studies  
(3 h infusion, 135 mg/m² dose, n=3)

<table>
<thead>
<tr>
<th></th>
<th>$C_{\text{max}}$ (ng/ml)</th>
<th>$AUC_{\text{inf}}$ (ng/ml*h)</th>
<th>Half-Life (hr)</th>
<th>Cl (L/hr/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cynviloq&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>1357</td>
<td>5473</td>
<td>12.7</td>
<td>25.5</td>
</tr>
<tr>
<td>Abraxane&lt;sup&gt;®&lt;/sup&gt;</td>
<td>1392</td>
<td>5654</td>
<td>12.9</td>
<td>27.4</td>
</tr>
</tbody>
</table>

Simulated PK Parameters Supportive of BE: Cynviloq vs. Abraxane

Comparison of mean non-compartmental pharmacokinetic parameters of Cynviloq (T) and Abraxane (260 mg/m²) at 30 min infusion time:

<table>
<thead>
<tr>
<th></th>
<th>Cmax (ng/mL)</th>
<th>Ratio Cmax(T)/Cmax(R)</th>
<th>AUCinf (ng*h/mL)</th>
<th>Ratio AUCinf(T)/AUCinf(R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cynviloq (Simulated PK)</td>
<td>19486</td>
<td>99.6%</td>
<td>22198</td>
<td>109.2%</td>
</tr>
<tr>
<td>Abraxane (Actual PK)*</td>
<td>19556</td>
<td></td>
<td>20324</td>
<td></td>
</tr>
</tbody>
</table>

* PK BE was calculated as 95% confidence interval (CI)

* Ratio T/R (Cmax and AUCinf) within 80-125% (FDA Guidance for establishing BE)

* Gardner et all, 2008
Bioequivalence = Efficient Pathway to Market

- Bioequivalence registration study in breast cancer patients (2014)
  - 12 months of duration (including patient recruitment)
  - Direct trial cost ~$5M

Key Parameters*:
- Dose: 260 mg/m²
- Infusion time: 30 min
- Duration: 3 weeks + crossover for 3 weeks
- Endpoints: AUC and Cmax (90% CI)

* Based on FDA "Draft Guidance on Paclitaxel" – September 2012
## Cynviloq Advantages

<table>
<thead>
<tr>
<th></th>
<th>Cynviloq™</th>
<th>Abraxane®</th>
<th>Taxol®</th>
<th>Cynviloq Advantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum Tolerated Dose (mg/m²)</td>
<td>&gt;300</td>
<td>260</td>
<td>175</td>
<td>Potential for higher efficacy</td>
</tr>
<tr>
<td>Rapid reconstitution: no foaming concerns</td>
<td></td>
<td></td>
<td></td>
<td>Convenience for busy practices and pharmacies</td>
</tr>
<tr>
<td>No donor-derived human serum albumin (HSA)</td>
<td></td>
<td></td>
<td></td>
<td>No viral / prion concerns</td>
</tr>
<tr>
<td>Convenient storage conditions</td>
<td></td>
<td></td>
<td></td>
<td>No requirement for controlled temp storage</td>
</tr>
<tr>
<td>No microbial growth</td>
<td></td>
<td></td>
<td></td>
<td>Chemical polymer</td>
</tr>
<tr>
<td>Cremophor-free</td>
<td></td>
<td></td>
<td></td>
<td>Reduced side effects</td>
</tr>
<tr>
<td>Dosing</td>
<td>q3w</td>
<td>q3w* &amp; weekly**</td>
<td>q3w &amp; weekly</td>
<td>Exploits PK advantage @ higher dose</td>
</tr>
</tbody>
</table>

* = MBC; ** = NSCLC & PC
Cynviloq Market Opportunity

~70,000 patients treated with paclitaxel-based regimen in 1st line

# of Patients Treated in 1st line (US Only; 2012)

- Other regimens
- PAC+ treated

NSCLC n = 93,800
- 30,766

MBC n = 38,000
- 9,880

Pancreatic Cancer n = 27,000
- 15,903

Ovarian Cancer n = 17,700
- 14,479

~55,000 patients with paclitaxel as 1st line therapy in MBC, NSCLC & OC

15,903 PC patients eligible for treatment with Abraxane® + Gemcitabine combination

Note: In Pancreatic Cancer, the blue portion represents # patients treated with gem-based Rx in 2012


1st Line patient estimates from IntrinsiQ 2012 Monthly LOT Diag Combo.
Potential to Expand Label Indications – For Example: 2nd Line Bladder Cancer

<table>
<thead>
<tr>
<th></th>
<th><strong>Cynviloq</strong></th>
<th><strong>Best Supportive Care</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phase 2 (Korea)*</td>
<td>Phase 2 (Japan)<strong>/ Phase 3 (EU)</strong>*</td>
</tr>
<tr>
<td></td>
<td>260-300 mg/m² q3w</td>
<td>n=23** / n=108***</td>
</tr>
<tr>
<td></td>
<td>n=34#</td>
<td></td>
</tr>
<tr>
<td>Overall Response Rate (ORR)</td>
<td>21%</td>
<td>- / 0%***</td>
</tr>
<tr>
<td>Progression Free Survival</td>
<td>2.7 M</td>
<td>- / 1.5 M***</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>6.5 M</td>
<td>2.3 M** / 4.3 M***</td>
</tr>
</tbody>
</table>

**Summary:**
- High unmet need - no FDA-approved 2nd line drug
- Demonstrated clinical Overall Response Rate (ORR)
- Phase 3-ready for development as 2nd line chemotherapy in patients refractory to platinum-based therapy

# advanced urothelial carcinoma patients refractory to gemcitabine and cisplatin
** AUA- San Diego May 4th-8th; *** JCO (2009): 4454-61
Next Steps for Cynviloq

1. Bioequivalence (BE) trial: 2014
2. NDA filing: 2015
3. Approval: 2016
   a. MBC and NSCLC
   b. Future Abraxane indications (Pancreatic cancer and Melanoma)
5. sNDA planning for label expansion into Bladder and Ovarian cancers
Expanded Clinical Pipeline with Multiple Opportunities

RTX

Intractable Pain in Advanced Cancer
Resiniferatoxin (RTX):
Non-opiate Drug Candidate for Treating Cancer Pain

“Prickly Painkiller: An experimental plant extract may end intractable pain with a single injection”*

RTX Ultra Potent and Selective Toxin

Pharmacology:

Ultra potent agonist of the TRPV1 receptor
- < 2 pM TRPV1 receptor binding

Binding in primate ex-vivo spinal cord
- dorsal root ganglion
  resiniferatoxin Ki = 309 pM
- dorsal horn
  resiniferatoxin Ki = 349 pM

RTX induces apoptosis of TRPV1-expressing afferent nerves.

“ADC”-like killing, but no antibody-mediated targeting needed

* Adapted from Karai et al. 2004
Single Injection Addresses Cancer Pain in Dogs

- Single intrathecal injection
- Permanent ablation of nerves
- Attractive therapeutic effect
  - All subjects responded
  - Personality & mood of animals visibly improved
  - No opioid-associated side effects

Veterinary Market: Strategic Partnership Opportunity
Next Steps for Dual Pathway of RTX Development

2014

1. Intractable cancer pain clinical trial (*intrathecal injection*); n~40 patients
2. Phase 1/2 trial for *intraganglionic injection* (osteosarcoma); n~15 patients

~3 years for clinical development
Pre-IND Immunotherapy Programs

G-MAB® ADC

Antibodies + Proprietary Toxins
G-MAB®: Library of Therapeutic Antibodies

- Proprietary technology
  - RNA amplification used for library generation
  - Freedom-To-Operate
- No stacking royalties
- Very high library diversity: $2.1 \times 10^{16}$ distinct antibodies
- Fully human antibodies
- High successful screening hit rate

Difficult Targets:
- Small Peptides

High Value Oncology Targets:
- Immunomodulation: PD1 and PD-L1
- Antibody Drug Conjugates: VEGFR2 and c-Met

Most Difficult Targets:
- G Protein-Coupled Receptors (GPCRs)

Size of Target Antigen
Anti-PD-L1 mAbs Exhibit Potent Activity

Immune Modulation*

- T Cell Activation (%)
- IFN-γ (pg/mL)
- IL-2 (pg/mL)

Tumor Mouse Model**

- Tumor Growth Inhibition (%)

** xenograft model using H1975 human NSCLC cells; % inhibition relative to control mAb treatment
*** p<0.05, mean tumor volumes are significantly reduced in STI-A1010 group versus control groups as determined by Mann-Whitney u-test
Potent Antibody against Difficult GPCR Target*

<table>
<thead>
<tr>
<th>mAb</th>
<th>Cell Binding (EC₅₀ – nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorrento</td>
<td>0.17</td>
</tr>
<tr>
<td>Competitor</td>
<td>21</td>
</tr>
</tbody>
</table>

* Sorrento mAb against C-C Chemokine Receptor 2 (CCR2)
** Experimental Auto-immune Encephalomyelitis (EAE) = murine model of Multiple Sclerosis
Antibody Drug Conjugates (ADC)

Key Components:
1. Target-specific internalizing antibody
2. Potent cytotoxic prodrugs
3. Linker and conjugation chemistries

Drug released in CANCER CELL
Proprietary ADC Screening and Optimization Panels

- **20-panel for discovery of lead ADCs**
  - 3 benchmark ADCs for rapid POC studies
  - 20 ADCs by rationale design with linker/conjugation technologies and payload pool

- **50-panel for generation of ADC candidates**
  - Optimization of payloads
  - Optimization of linkers and conjugation methods
  - Expansion to new MOA payloads, if needed
K-lock Conjugation Enables Homogeneous ADCs

- Selective ADC chemistry
- Fewer positional isomers
- Better control of DAR
Irreversible C-lock-stabilized ADCs

- C-lock enhances ADC stability leading to:
  - Prolonged PK profile
  - Reduced off-target effects
Proprietary Toxin Potency Higher than DM1

**SKBR3**
(Breast Cancer Cell Line)

- Duo6 (K-lock)
- Duo3 (K-lock)
- DM1 (NHS)
- MMAE (C-lock)
- MMAE (maleimide) cleavable MC-vc-PAB linker

**IC₅₀ (nM)**
- 0.017
- 0.019
- 0.3 (0.24 nM reported)
- 0.025
- 0.035

**HCC1954**
(Breast Cancer Cell Line)

- Duo6 (K-lock)
- Duo3 (K-lock)
- DM1 (NHS)
- MMAE (C-lock)
- MMAE (maleimide) cleavable MC-vc-PAB linker

**IC₅₀ (nM)**
- 0.035
- 0.052
- 0.25 (0.24 nM reported)
- 0.091
- 0.091
### G-MAB® and ADC Pipeline

#### Oncology

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Stage</th>
<th>Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1</td>
<td>Preclinical</td>
<td>1H 2015</td>
</tr>
<tr>
<td>PD-1</td>
<td>Preclinical</td>
<td>1H 2015</td>
</tr>
<tr>
<td>VEGFR2-ADC</td>
<td>Preclinical</td>
<td>2H 2015</td>
</tr>
<tr>
<td>EGFR</td>
<td>ADC</td>
<td></td>
</tr>
<tr>
<td>c-Met</td>
<td>ADC</td>
<td></td>
</tr>
<tr>
<td>Her2</td>
<td>ADC</td>
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</tr>
</tbody>
</table>

#### Oncology / Inflammation (GPCR)

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Stage</th>
<th>Timeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCR2</td>
<td>ADC</td>
<td>2H 2015</td>
</tr>
<tr>
<td>CCR2</td>
<td>ADC</td>
<td></td>
</tr>
<tr>
<td>CXCR3</td>
<td>ADC</td>
<td></td>
</tr>
<tr>
<td>CXCR5</td>
<td>ADC</td>
<td></td>
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</tbody>
</table>

#### Multiple Strategic Partnership Opportunities
Positioned to Become Oncology Leader

- Cynviloq™
  - Registration Trial
  - Intractable Pain in Advanced Cancer
  - Antibodies + Proprietary Toxins
- RTX
- G-MAB® ADC
# Small Molecule Oncology Drug, Antibody Library and ADC Company Valuations

<table>
<thead>
<tr>
<th>Company</th>
<th>Small Molecule Oncology Drug</th>
<th>Antibody Platform</th>
<th>Targeted Drug Delivery</th>
<th>Mkt Cap*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puma: PBYI</td>
<td>MBC (Phase 3)</td>
<td></td>
<td></td>
<td>~$1.2B</td>
</tr>
<tr>
<td>Clovis: CLVS</td>
<td>NSCLC, MBC (Phase 1)</td>
<td></td>
<td></td>
<td>~$1.6B</td>
</tr>
<tr>
<td>MorphoSys: MOR.DE</td>
<td></td>
<td>Antibody Library</td>
<td></td>
<td>~$1.6B</td>
</tr>
<tr>
<td>Seattle Genetics: SGEN</td>
<td>NSCLC, MBC</td>
<td>ADC</td>
<td></td>
<td>~$5.1B</td>
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<tr>
<td>ImmunoGen: IMGN</td>
<td></td>
<td>ADC</td>
<td></td>
<td>~$1.3B</td>
</tr>
<tr>
<td>Sorrento: SRNE</td>
<td>NSCLC, MBC (Ph3/Registration Trial)</td>
<td>ADC &amp; AfDC</td>
<td></td>
<td>~$180M</td>
</tr>
</tbody>
</table>

*M based on publicly-available information (11/14/13)
Investment Highlights

**Late Stage Oncology Drug with Exclusive US and EU Rights**
- Addresses multi-billion dollar paclitaxel market
- Abbreviated regulatory pathway (“bioequivalence”) for approval
- Bioequivalence registration trial in 2014 (study direct costs ~ $5M)
- Product launch in 1H 2016

**Intractable Pain in Advanced Cancer**
- Clinical Phase 1/2 study ongoing at NIH
- Potential patients for treatment: ~150,000 in the U.S. annually
- Two potential drug products from same API

**Therapeutic antibody engine**
- Antibody market >$50B in 2012
- First antibody drug candidate in clinic 1H 2015

**Targeted Drug Delivery (ADC)**
- G-MAB® antibody as specific targeting warhead
- Proprietary toxins as potent tumor killing payload
- Selective conjugation chemistry for homogenous ADC generation
Sorrento Therapeutics

Next-Generation Cancer Therapeutics

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