# sorrento

## Next-Generation Cancer Therapeutics

April 2015



### Safe Harbor Statement NASDAQ: SRNE

This presentation contains "forward-looking statements" as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), including statements regarding expectations, beliefs or intentions regarding our business, technologies and products strategies or prospects. Such forward-looking statements are characterized by future or conditional verbs such as "may," "will," "expect," "intend," "anticipate," "believe," "estimate" and "continue" or similar verbs. Actual results may differ from those projected due to a number of risks and uncertainties, including, but not limited to, the possibility that some or all of the pending matters and transactions being considered by the Company may not proceed as contemplated, as well as risks inherent in additional financing, developing and obtaining regulatory approvals of new, commercially-viable and competitive products and product candidates, including timelines, the size of clinical trials, sufficiency of data from those trials and the requirements of the FDA for potential approval of Cynviloq<sup>™</sup> and by all other matters described in the Company's filings with the Securities and Exchange Commission, including the risk factors set forth therein. These statements are made based upon current expectations that are subject to risk and uncertainty and information available to the Company as of the date of this presentation. The Company does not undertake to update forward-looking statements in this presentation to reflect actual results, changes in assumptions or changes in other factors affecting such forward-looking information. Assumptions and other information that could cause results to differ from those set forth in the forward-looking information can be found in the Company's filings with the Securities and Exchange Commission, including its most recent periodic report. We intend that all forward-looking statements be subject to the safeharbor provisions of the PSLRA.



### A Comprehensive Oncology Company

**Deep and Complementary Pipeline Creates Significant Opportunities-**Novel breakthrough combination therapeutic regimens and modalities to attack cancer Significant reduction in clinical development costs and timeline Significant commercial edge in future drug pricing



CYNVILOQ, CAR.TNK, CAR.TNK (Chimeric Antigen Receptor Tumor-attacking Neukoplast) are trademarks owned by Sorrento Therapeutics, Inc. Neukoplast is a trademark owned by Conkwest, Inc.





#### RTX

Intractable **Cancer Pain** 

## **Corporate Events Validate and Advance Sorrento Pipeline Unlocking Significant Value**

CYNVILOQ NANTIBODY Joint Venture R&D Collaboration

Patient enrollment in TRIBECA registration trial completed. Pilot PK suggests bioequivalence (BE) between Cynviloq and albumin-bound paclitaxel

Exclusive global partnership with Conkwest to develop next generation anti-cancer cellular immunotherapy with "Off-the-Shelf" CAR.TNK™ (Chimeric Antigen Receptor *T*umor-attacking *N*eu*K*oplast)

First joint venture with NantWorks and Abraxis BioScience Inc. founder, Dr. Patrick Soon-Shiong, to develop next generation immunotherapies for the treatment of cancer and autoimmune disease.

**NantCell** global collaboration to discover and develop novel anti-cancer immunotherapies against neoepitopes of tumor-specific antigens discovered using NantWorks' proprietary panomics based, precision medicine approach

Licensing agreement to develop and commercialize anti-PD-L1 mAb with Lee's **Pharmaceutical** for greater Chinese Market

Exclusive research and option agreement to generate and develop antibody-drug conjugates (ADCs) with Morphotek / Eisai



## Deep and Complementary Pipeline Creates Significant Opportunities

	<b>INDICATION</b> > TARGET	PRECLINICAL	PHASE 1	PHASE 2
CYNVILOQ™	Metastatic Breast Cancer Non-Small Cell Lung Cancer	r	TRIE Registration	B E C A* trial completed
RTX	Intractable Cancer Pain			
G-MAB Bi-Specific Ab CARTINE Chineric Analgen Receptor Tunor-attacking Neukoplast	Immuno-oncology > PD-L1, P PD-L1/c-MET; PD-L1/CTLA-4, PD- PD-L1.TNK, CD123.TNK, ROR1.T	D1, CD47, CD137 L1/EGFR NK, PSMA.TNK		
ADC	VEGFR2, c-MET, CXCR5			
<b>MYC</b> Inhibitor	Solid tumors and hematological ma	alignancies		

\* TRIBECA 505 (b)(2) Bioequivalence trial versus albumin-bound paclitaxel (Abraxane<sup>®</sup>) (paclitaxel albumin-bound particles for injectable suspension) (albuminbound), Abraxane<sup>®</sup> is a registered trademark of and marketed by Celgene Corp. PDL1.TNK, CD123.TNK, ROR1.TNK, PSMA.TNK are trademarks owned by Sorrento Therapeutics, Inc.





## Lead Oncology Product Opportunity



### Registration Trial

## **Cynviloq: Next Generation Paclitaxel Therapy**



\*Celgene Presentation at JPM Healthcare Conference Jan 2015

#### Peak Product Sales

#### ~ \$1.6B (WW in 2000)

#### \$ 2.2 B\* (2020) MBC, NSCLC, PC

#### Conversion of paclitaxel sales + new indications

## **Cynviloq Clinical Development Summary**

	Total number of patients across all trials: 1,260
Phase 1:	Trials established MTD at >300 mg/m <sup>2</sup> - Dana Farber Cancer Inst, Russia, & S. Korea (total n=80) >300 mg/m <sup>2</sup> (q3w) vs. 175 mg/m <sup>2</sup> (Taxol; weekly)
Phase 2:	Completed trials in MBC, NSCLC, PC, OC, BC; in US - Yale Cancer Center, Russia, S. Korea (total n=2 Possible Phase 3 sNDA programs in these tumor types
Phase 2b*:	Chemo-naïve Stage IIIb/IV NSCLC vs Taxol in S. Korea (total n=276; Cynviloq n=140) 230 mg/m <sup>2</sup> + cis (q3w) vs. Taxol 175 mg/m <sup>2</sup> + cis; non-inferiority established
Phase 2*:	1st line treatment of OC vs Taxol in S. Korea (total n=100; Cynviloq n=50) 260 mg/m <sup>2</sup> + carbo (q3w) vs. Taxol 175 mg/m <sup>2</sup> + carbo; non-inferiority established
Phase 3:	MBC in S. Korea (total n=209; Cynviloq n=105 vs Taxol n=104) GPMBC301. An Open-label, Randomized, Parallel, Phase 3 Trial to Evaluate the Efficacy and Safety of Cynviloq compared to Genexol® with Cremophor EL) in Subjects with Recurrent or Metastatic Breast Cancer)
PM-Safety:	Completed for MBC and NSCLC (total n=502) Efficacy and safety data supportive of 505(b)(2) submission





### **Comparative Phase 3 MBC Clinical Results**



\* Trieu et al. 2013. IG-001 for Metastatic Breast Cancer- Interim Analysis of a Phase 3 Trial. 4th Nanomedicine Conference, Sydney, Australia.

\*\* Gradishar et al. 2005. J Clin Oncol, 23:7794-7803.

\*\*\* Guan et al. 2007. ASCO Annual Meeting Proceedings Part I. Jun 20;25 (Suppl 18):1038.



9

### **Bioequivalence = Accelerated Pathway to Market**

### $TRIBECA^{TM}$

(TRIal establishing BioEquivalence between Cynvilog<sup>™</sup> and Albumin-bound paclitaxel)

### - Patients with MBC



**Note:** Previous trial size estimate of 100 patients was based on **PK simulation** of albumin-bound paclitaxel and Cynviloq historical data with both drugs given at different doses and infusion rates. Based on the recent positive initial PK data and subject to FDA guidance, 53 patients may be sufficient to establish BE.

T R I B E C A<sup>™</sup> (TRIal establishing BioEquivalence between Cynviloq<sup>™</sup> and Albumin-bound paclitaxel) is a trademark owned by Sorrento Therapeutics, Inc.



#### **Key Parameters:**

 Dose: 260 mg/m<sup>2</sup> Infusion time: 30 min Duration: 3 weeks + crossover for 3 weeks Endpoints: AUC and C<sub>max</sub> (90% CI)

### Pilot PK Data Analyses Suggest **BE vs. Albumin-Bound Paclitaxel**



#### **BE Assessment and Sample Size Estimate**

Parameters	Ratio of Cynviloq/ Albumin-bound paclitaxel (%)	90% Cl
Ln(AUC <sub>0 to ∞</sub> )	109.1	93.98 – 126.58
Ln(C <sub>max</sub> )	102.5	83.10 – 126.35
Point estimate 110 - Ln(AUC <sub>0 to ∞</sub> )	N = 53 with 90% power	



### **TRIBECA** Patient Enrollment Completed

111 patients recruited from Eastern Europe, USA and Asia Initial reported AEs consistent with historical nab-paclitaxel toxicity profile



**Enrollment and Active Sites** 



### **Estimated Timeline and Next Steps\***

First patient dosed: March 31, 2014

Last patient in: January 2015

NDA filing: Q3 2015

Product launch (MBC and NSCLC): 2016



\*Estimates, subject to discussions with the FDA.





#### LAUNCH





### Resiniferatoxin (RTX): A Novel, Non-opiate Analgesic



### Intractable Cancer Pain

## Two Injection Sites = Two Products for Human Use



#### \* Adapted from Karai et al., 2004





### TRPV1-positive cells (dark brown)



Absence of TRPV1positive cells after RTX treatment

## Summary of Interim Data from the Phase 1/2 NIH **Sponsored Trial**

### **DESIGN OVERVIEW**

6 advanced cancer patients with severe refractory pain received a single injection of RTX. Neuropathic pain, visceral and bone pain 2° to bone metastases (49-61 years; 4 M/2F, MBC, H&N, pancreatic, lymphoma, SCLC, endometrial cancer).

No unexpected toxicities

All 6 patients had near complete relief postinjection

Clinically meaningful improvement in QOL 100% of non-ambulatory patients could walk post injection (n=2)

> Improved pain scores with increased activity





#### MTD not reached, additional dose optimization being explored

### **Next Steps for RTX Development**

Complete intractable cancer pain clinical Phase 1/2 trial (**intrathecal injection**) under Sorrento IND; n=45-60 patients; optimization of dosing study

OBJECTIVES for 2015 and 2016 End of Phase 2 meeting with FDA (for intrathecal injection)

Initiate Phase 3 (intrathecal injection)

Phase 1/2 trial(s) (intraganglionic injection)

End of Phase 2 meeting with FDA (for intraganglionic injection)

~3 years for clinical development



## Immunotherapy Programs





## **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 x 10<sup>16</sup> distinct antibodies

Fully human antibodies

High successful screening hit rate (over 70 targets screened)

**Ideal for CAR-Generation** 

**Difficult Targets: Small Peptides** 



**High Value Oncology Targets:** Immune modulation: PD-1, PD-L1, CD47 Antibody Drug Conjugates: VEGFR2, c-Met







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





## **Anti-PD-L1 mAb Exhibits Potent Activity**

#### Immune Modulation\*

Tumor Mouse Model\*\*



\* mAbs @ 0.05 mg/mL

\*\* 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





## **Anti-PD1 mAb Exhibits Excellent Activity**

**Immune Modulation\*** 





### **Target Specificity**

## **Proprietary K-Lock and C-Lock Conjugation Chemistries Enable Homogeneous ADCs**

### K-Lock

**Current industry** standard

**Proprietary** 



purified

#### Sorrento's homogenous ADC



No need for:

non-natural amino acids genetic re-engineering enzymatic posttranslational modification

### C-Lock

#### Maleimide conjugation

Destabilizes antibody structure Drug-antibody linkage not stable Altered PK profile Off-target drug effects Antibody **C-Lock conjugation** Enhances ADC stability Prolongs PK profile Reduces off-target effects







## **Proprietary High Potency Duostatin Toxins**

ЕС <sub>50</sub> (рМ)	Cancer	Her-2	DM1	MMAE	Duostati
SBKR3	Breast	+++	95	72	30
HCC1954	Breast	+++	124	78	68
BT474	Breast	+++	818	126	214
MDA-MB-361	Breast	+++	218	151	35
ZR75	Breast	+++	215	298	264
HCC1419	Breast	+++	391	271	332
MDA-MB-453	Breast	++	1,877	>100,000	452
MDA-MB-175	Breast	+	>100,000	1,348	425
N87	Gastric	+++	368	139	260
OE-19	Gastric	+++	176	164	130
SKOV-3	Ovarian	+++	150	251	144





## In Vivo Proof-of-Concept of Sorrento ADCs

### **VEGFR2-ADC STI-D0168**

### c-MET-ADC STI-D0602





A431 squamous-cell carcinoma cells; ^indicates dosing

U87 xenograft; dosing twice weekly; maytansinoid drug conjugates



### "Nantibody, LLC- The Immunotherapy Antibody JV Company"







Independent company focused

on advancing next generation immunotherapies against cancer and autoimmune diseases.

Both companies will contribute to its pipeline of clinical and preclinical assets of novel and proprietary immunotherapies, ADCs, and bispecific antibodies.

Nantworks will contribute phase 3 antibody.

Nantibody will draw from NantWorks' proteomic and genomic capabilities and Sorrento's industry-leading, highly diverse G-MAB library.







Chimeric Antigen Receptor Tumor-attacking Neukoplast<sup>®</sup>

## AN EXCLUSIVE JOINT PARTNERSHIP conkwest • NANTWORKS • Sorrento

CAR.TNK is a trademark owned by Sorrento Therapeutics, Inc. Neukoplast is a trademark owned by Conkwest, Inc.

## **Advancing Cellular Immunotherapy Beyond CAR-T Cell Therapies**

### conkwest



## sorrento



Neukoplast® NK cell line ("off-the-shelf")

Broad anti-cancer activity in solid and liquid tumors

No clinical DLTs/SAEs in over 40 patients treated

Vast diversity human antibody library

High successful screening rate (over 70 targets screened)

Proprietary technologies with **FTO** 



technology





#### Single-patient, disposable Cartridge, containing

- Cell culture chamber
- Associated fluidics
- Medium

#### Advanced proteomics platform

#### Proprietary gene insertion (without use of lentiviruses)

### 'GMP in a Box' production

### **CAR.TNK vs CAR-T: Key Differentiators**

	CAR.TNK	CAR-T
Cell Production	Simple: Off-the-shelf universal product CAR-modified Neukoplast cells	Invasive: Autologo invasive procedure/
Transduction characteristics	<b>100%:</b> Master cell bank with 100% of cells expressing CAR	Variable %: Variable transfection & expression
MOA	<b>Broad:</b> Multiple MOAs, targeting and killing through CAR-dependent and innate mechanisms ("off-target / on-tumor")	Limited: Requires ( (CD80, CD86) not p solid tumors
Safety	Good: On-target / off-tumor effects limited due to short half life and lack of IL-6 production	<b>Poor:</b> Cytokine rele Prolonged bone ma Cardiotoxicity; Repo encephalitis; Death
COGS	Low: large scale bioreactor manufacturing for many patients	High: requires indiv

#### vidual patient processing

#### ease syndrome, ICU; arrow suppression; orted cases of

#### co-stimulators present in many

#### le CAR ession

#### us (patient-derived) /leukapheresis



## **Unmodified Neukoplast Clinically Validated In Several Phase 1 Studies**

More than 40 patients treated

Advanced metastatic disease refractory to chemo, biologics, cytokines, radiation, and surgery

Many patients received multiple dosing regimens (up to 6 months)

Promising activity against different cancer types, including acute myelogenous leukemia (AML), lymphoma (NHL, HL), melanoma, renal cell cancer (RCC), and lung cancers (SCLC, NSCLC)

No DLTs; only 1 "grade 4 SAE" (hypoglycemia likely related to tumor lysis)











### Neukoplast do not stimulate allogeneic T cells

**T cell Proliferation measured using** Mixed Lymphocyte Reaction (MLR) Culture Assay



Lymphocytes from 2 healthy donors co-cultured with each other  $\rightarrow$  vigorous proliferation Co-cultured with Neukoplast (7 days)  $\rightarrow$  *no proliferation* 



### **CAR.TNK: CAR-modified Neukoplast**

Clonal cell lines expressing one or more CARs to establish a range of distinct products

Multiple killing mechanisms - CAR-targeted as well as broad intrinsic anti-cancer activity of Neukoplast ("off-target / on-tumor")

Engages the adaptive immune system through cytokine secretion and immune cell recruitment

Titratable: repeat dosing option; controllable dose exposure to manage safety risk



## Serial Killing of Her2+ Cells by Her2.TNK Cells

### **IN VIVO PRECLINICAL MOUSE DATA**



Homing to Her2 expressing tumors

Inhibition of Her2+ RCC metastasis

Growth inhibition and killing correlate with Her2 expression levels

"Serial killing" of Her2+ target cells even after gamma radiation with 10 Gy

Selective cytotoxicity (spares normal cells)

Schoenfeld et al. Mol Therapy, in press

![](_page_31_Picture_9.jpeg)

## **Her2.TNK Demonstrate Tumor Homing and Potent Anti-Glioma Activity in Mice**

#### Intracranial LN-319 glioblastoma xenografts in NSG mice

![](_page_32_Figure_2.jpeg)

### Tumor homing of CAR.TNKs

![](_page_32_Figure_4.jpeg)

![](_page_32_Figure_5.jpeg)

![](_page_32_Figure_6.jpeg)

Schoenfeld et al. Mol Therapy, in press

![](_page_32_Picture_8.jpeg)

## **Prospective CAR.TNKs for Development** (Initial List)

Target	Potential Indication(s)	
EGFRviii.TNK	Glioma	
EphA3.TNK	Glioma, AML	
L1CAM.TNK	Gastric, pancreatic, NSCLC	
CSPG4.TNK	H&N, breast, mesothelioma	
BCMA.TNK	Myeloma	
ROR1.TNK	CLL, ALL, MCL, breast, lung, pancreas	
PSMA or PSCA.TNK	Prostate	
PDL1.TNK	Myeloma, RCC, NSCLC, TNBC	
CS1.TNK	Myeloma	
CD123.TNK	AML	
CD19.TNK	CLL, ALL	
CD22.TNK	CLL, ALL	

CAR targets jointly selected by the **Steering Committee** 

Lead company will be responsible for all pre-clinical and clinical development, regulatory filings, and commercialization

Profit sharing on all CAR.TNKs revenues proportional to contribution

![](_page_33_Picture_6.jpeg)

### Next Steps for CAR.TNK Development

- H1 2015 Generation of CARs
- H2 2015 Generation and evaluation of stable CAR.TNK cell lines
- 2016 IND-enabling studies, IND submission, and initiation of Phase 1 studies

![](_page_34_Picture_4.jpeg)

### A Comprehensive Oncology Company

**Deep and Complementary Pipeline Creates Significant Opportunities-**Novel breakthrough combination therapeutic regimens and modalities to attack cancer Significant reduction in clinical development costs and timeline Significant commercial edge in future drug pricing

![](_page_35_Figure_2.jpeg)

CYNVILOQ, CAR.TNK, CAR.TNK (Chimeric Antigen Receptor Tumor-attacking Neukoplast) are trademarks owned by Sorrento Therapeutics, Inc. Neukoplast is a trademark owned by Conkwest, Inc.

![](_page_35_Picture_4.jpeg)

![](_page_35_Picture_6.jpeg)

#### RTX

Intractable **Cancer Pain** 

## sorrento **Next-Generation Cancer Therapeutics**

### CONTACT:

George Uy **Executive Vice President and CCO** guy@sorrentotherapeutics.com (661) 607-4057

Henry Ji, Ph.D. President and CEO hji@sorrentotherapeutics.com (858) 668-6923

![](_page_36_Picture_4.jpeg)

![](_page_36_Picture_5.jpeg)