
# Next-Generation Cancer Therapeutics

May 2014

# 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. 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, and by all other matters specified in Company's filings with the Securities and Exchange Commission, as well as risks inherent in funding, developing and obtaining regulatory approvals of new, commercially-viable and competitive products and product candidates. Sufficiency of the data for approval with respect to Cynviloq™ will be a review issue after NDA filing. 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 safe-harbor provisions of the PSLRA.

# Management Team

| | |
|---|---|
| **Henry Ji, Ph.D.**<br>President,<br>CEO & Director | Inventor of G-MAB® Technology<br>President & CEO of Stratagene Genomics<br>VP of CombiMatrix and Stratagene |
| **Vuong Trieu, Ph.D.**<br>CSO & Director | Founder and CEO of IgDraSol<br>Co-inventor of IP covering Abraxane®<br>Instrumental in the approval of Abraxane<br>Celgene acquired Abraxis Biosciences for > $3B |
| **Amar Singh**<br>EVP & CBO | Closed major business transactions on oncology products<br>Led Novacea global transaction (Asentar®) with Schering-Plough valued at >$500M<br>Led major deals at Spectrum Pharmaceuticals<br>Responsible for building Abraxis commercial organization<br>Led oncology franchise at Hoffmann-La Roche |
| **George Uy**<br>CCO | Directed the launches of Abraxane, Xeloda® & Fusilev®<br>Built commercial infrastructures and organizations in startup companies |
| **David Miao, Ph.D.**<br>CTO | President and CSO of Concortis BioSystems<br>Co-inventor of IP covering ADC technologies<br>Head of Chemistry at Ambrx |
| **Richard Vincent**<br>EVP & CFO | $430M sale of Elevation to Sunovion-Dainippon<br>Meritage Pharma option agreement with ViroPharma ($90M upfront + milestones)<br>$310M sale of Verus asthma program to AstraZeneca<br>Elan: various acquisitions and divestitures with aggregate values more than $300M |

## Board of Directors

**William S. Marth - Chairman**
Albany Molecular (President & CEO)
Teva – Americas (former President & CEO)

**Mark Durand**
Watson, Teva – Americas (former CFO)

**Cam Gallagher**
Nerveda, LLC (Managing Director)

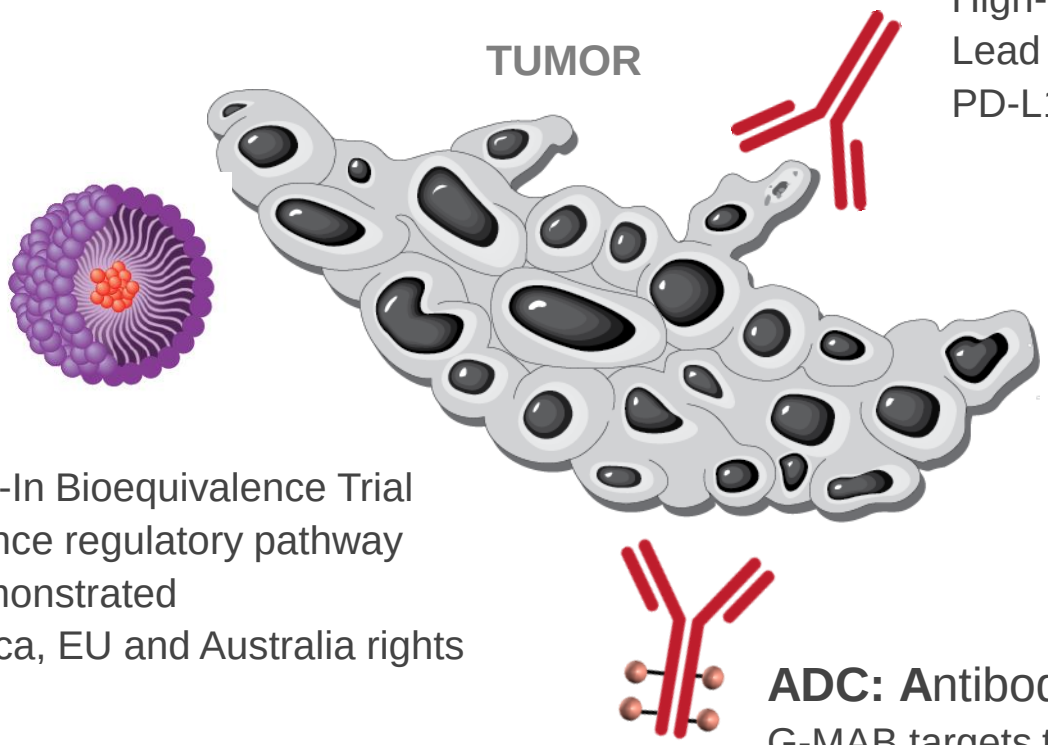
**Kim D. Janda, Ph.D.**
The Scripps Research Institute (Prof.)

**Henry Ji, Ph.D.**
Sorrento (CEO)

**Jaisim Shah**
PDL (former CBO)

**Vuong Trieu, Ph.D.**
Sorrento (CSO)

# Next-Generation Cancer Therapeutics




**G-MAB**

High-diversity human Ab library
Lead mAb programs include
PD-L1, PD-1, and CCR2

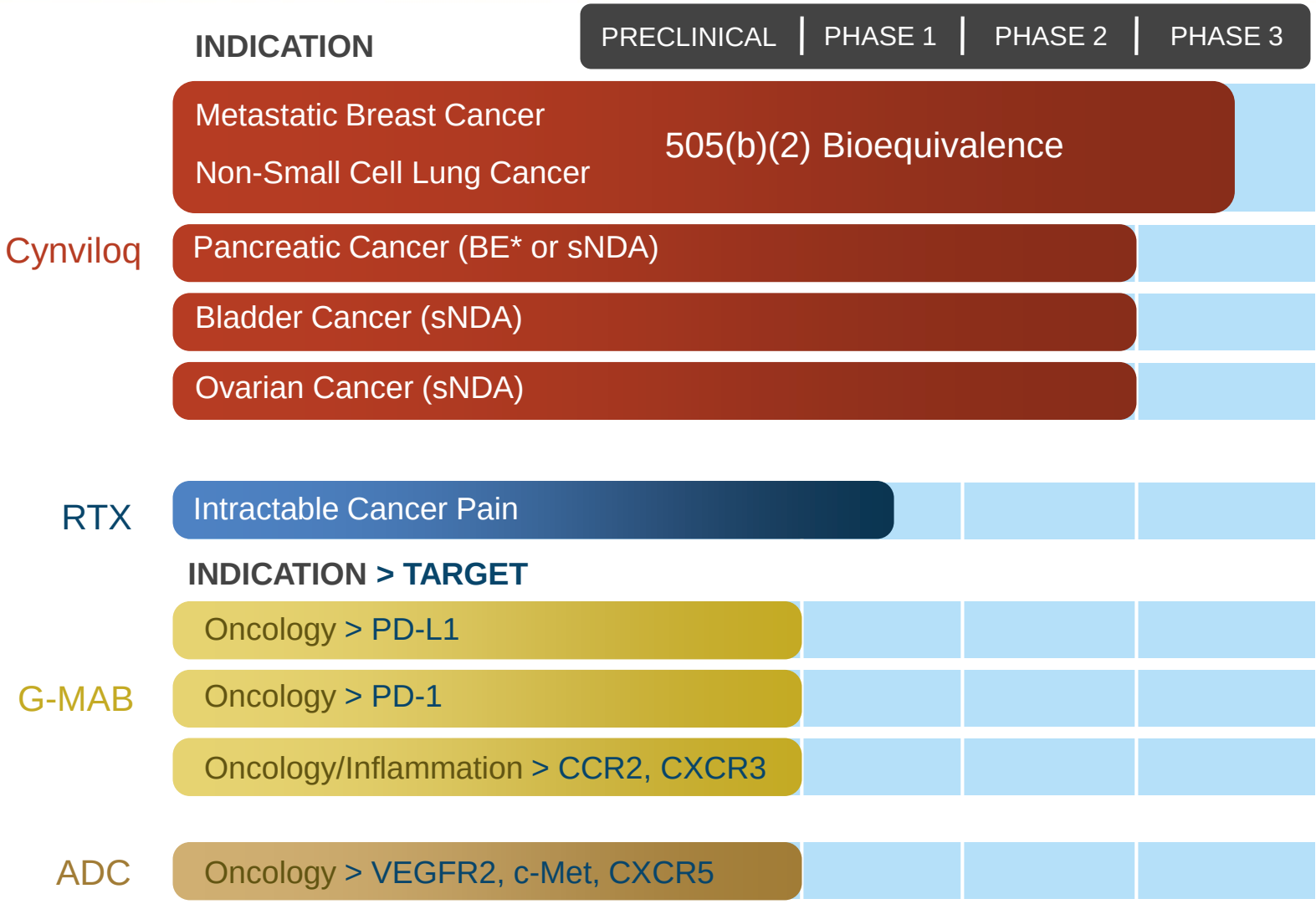
**Cynviloq**

First-Patient-In Bioequivalence Trial
Bioequivalence regulatory pathway
Efficacy demonstrated
North America, EU and Australia rights

**ADC: Antibody Drug Conjugate**

G-MAB targets toxin to cancer cell
Proprietary toxins and linkers
C-Lock and K-Lock conjugation chemistries

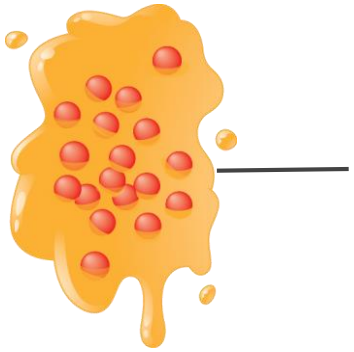
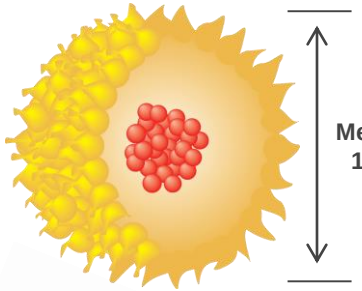
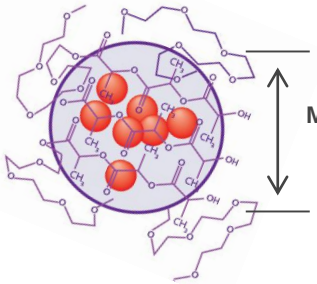
# Multiple Commercialization & Partnership Opportunities




* Abraxane orphan drug status (FDA approval, September 2013)

# Lead Oncology Product Opportunity

# Cynviloq: Next Generation Paclitaxel Therapy

| | Generation | | Formulation | Maximum Tolerated Dose | Peak Product Sales |
|---|---|---|---|---|---|
| 1st | **Taxol®**<br>paclitaxel |  | **Cremophor EL** excipient**:** Polyoxyethylated castor oil | **175 mg/m²** | ~ $1.6B (WW in 2000) |
| 2nd | **Abraxane**<br>*nab*-paclitaxel |  | **Biological** polymer: Donor-derived human serum albumin (HSA) | **260 mg/m²** | Est. ≥$1.7B* (US) ($430M in 2012) |
| 3rd | **Cynviloq**<br>paclitaxel polymeric micelle |  | **Chemical** polymer: Poly-lactide and polyethylene glycol diblock copolymer | **>300 mg/m²** **(up to 435 mg/m²)** | Conversion of Abraxane sales + new indications |

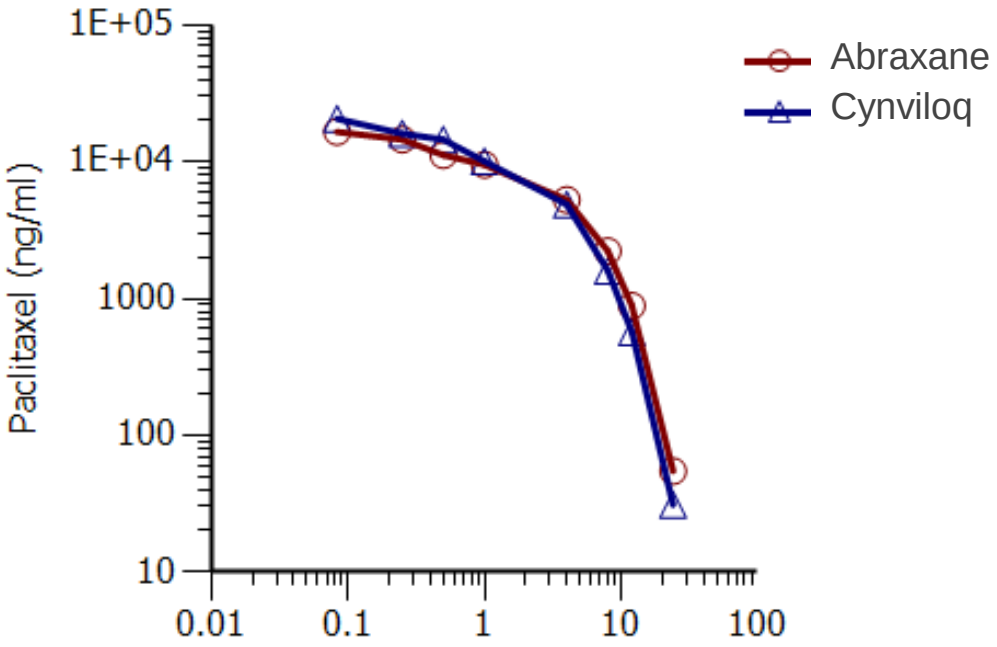
*Analyst projection; in MBC + NSCLC + PC

# 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)<br>>300 mg/m$^2$ (q3w) vs. 175 mg/m$^2$ (Taxol; weekly) and 275 mg/m$^2$ (Abraxane; q3w) |
| **Phase 2:** | Completed trials in MBC, NSCLC, PC, OC, BC; in US - Yale Cancer Center, Russia, S. Korea (total n=259)<br>Data suggestive of efficacy comparable to historic data for Abraxane and superior to historic Taxol data or Standard-of-Care<br>Possible Phase 3 sNDA programs in these tumor types |
| **Phase 3:** | Ongoing trial for MBC in S. Korea (total n=209; Cynviloq n=105)<br>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)<br>Interim analysis suggests ORR superior to Taxol and comparable to historic Abraxane efficacy<br>Efficacy and safety data supportive of 505(b)(2) BE submission |
| **PM-Safety:** | Completed for MBC and NSCLC (total n=502)<br>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)<br>230 mg/m$^2$ + cis (q3w) vs. Taxol 175 mg/m$^2$ + cis; non-inferiority established |
| **Phase 2 (IIS):** | 1st line treatment of OC vs Taxol in S. Korea (total n=100; Cynviloq n=50)<br>260 mg/m$^2$ + carbo (q3w) vs. Taxol 175 mg/m$^2$ + carbo; non-inferiority established |

# Equivalent PK in Mice




| Drug | HL (h) | T max (h) | AUCinf (h*ng/mL) | Vz (mL/kg) | Cl (mL/h/kg) |
|---|---|---|---|---|---|
| Abraxane | 2.99 | 0.08 | 61561.33 | 2103.71 | 487.32 |
| Cynviloq | 2.83 | 0.08 | 58151.31 | 2103.58 | 515.90 |

Data on file

IV bolus at 30 mg/kg; n = 3

# Comparable PK in Humans

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

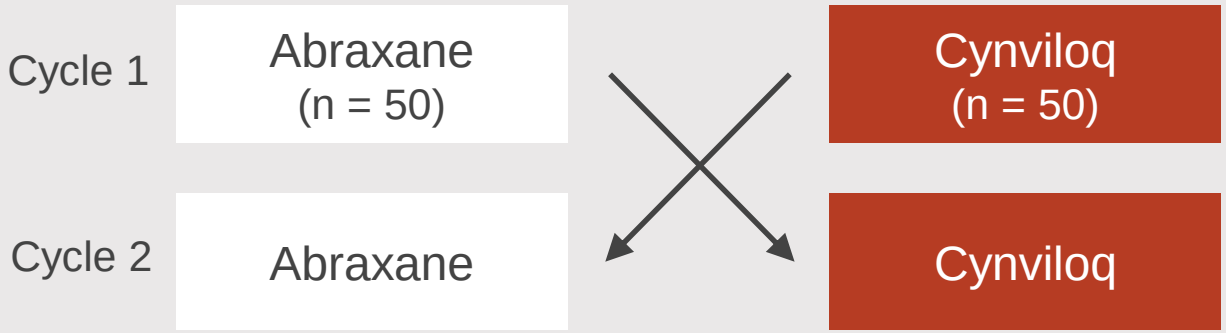
| | Cmax (ng/ml) | AUCinf (ng/ml*h) | Half-Life (hr) | Cl (L / hr / m$^2$) |
|---|---|---|---|---|
| Abraxane® | 1392 | 5654 | 12.9 | 27.4 |
| Cynviloq™ | 1357 | 5473 | 12.7 | 25.5 |

Abraxane data from: Nuhad K. Ibrahim, Phase I and Pharmacokinetic Study of ABI-007, a Cremophor-free, Protein-stabilized, Nanoparticle Formulation of Paclitaxel. Clinical Cancer Research 2002;8:1038-44

# Bioequivalence = Efficient Pathway to Market

TRIBECA™ (TRIal designed to evaluate BioEquivalence between Cynviloq™ and Abraxane®) (2014)

- Patients with MBC
- Duration = 12 months (including patient recruitment)




**Key Parameters:**

Dose: 260 mg/m$^2$

Infusion time: 30 min

Duration: 3 weeks + crossover for 3 weeks

Endpoints: AUC and Cmax (90% CI)

**First patient dosed** March 31, 2014

# Potential Cynviloq Advantages

| | Cynviloq | Abraxane | Taxol | Cynviloq Advantage |
|---|---|---|---|---|
| Maximum Tolerated Dose ($mg/m^2$) | >300 | 260 | 175 | Potential for higher efficacy |
| Rapid reconstitution: no foaming concerns | ● | | ● | Convenience for busy practices and pharmacies |
| No donor-derived human serum albumin (HSA) | ● | | ● | No viral / prion concerns |
| Convenient storage conditions | ● | | ● | No requirement for controlled temp storage |
| No microbial growth | ● | | ● | Chemical polymer |
| Cremophor-free | ● | ● | | Reduced side effects |
| Dosing | q3w | q3w* & weekly** | q3w & weekly | Exploits PK advantage @ higher dose |

* = MBC; ** = NSCLC & PC

# Next Steps for Cynviloq

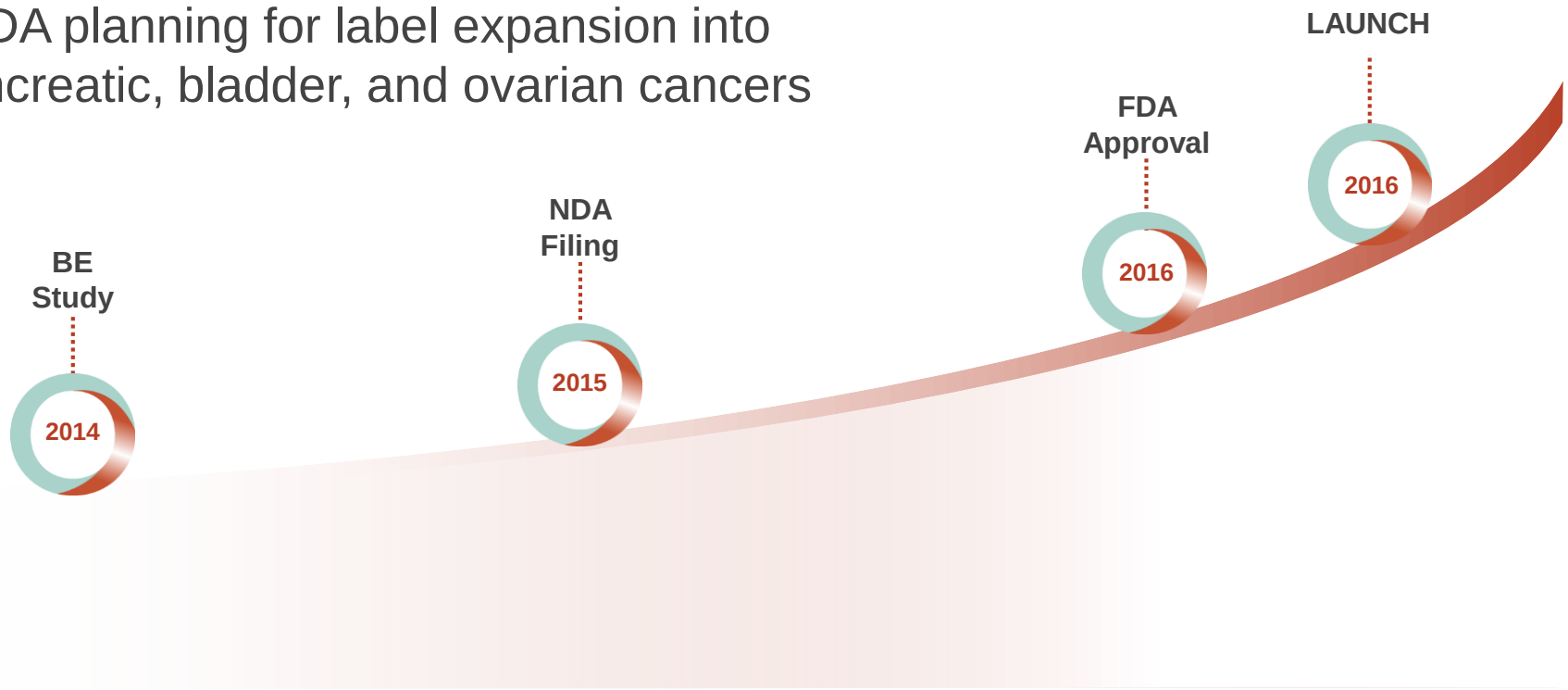
First patient dosed: **March 31, 2014**

NDA filing: **2015**

Product launch (MBC and NSCLC): **2016**

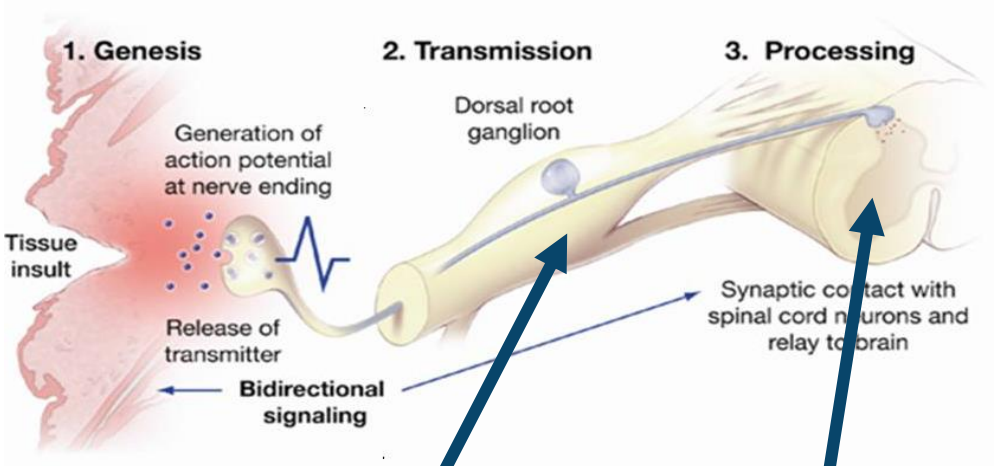
sNDA planning for label expansion into pancreatic, bladder, and ovarian cancers

Cynviloq™
(paclitaxel polymeric micelle)
for Injectable suspension



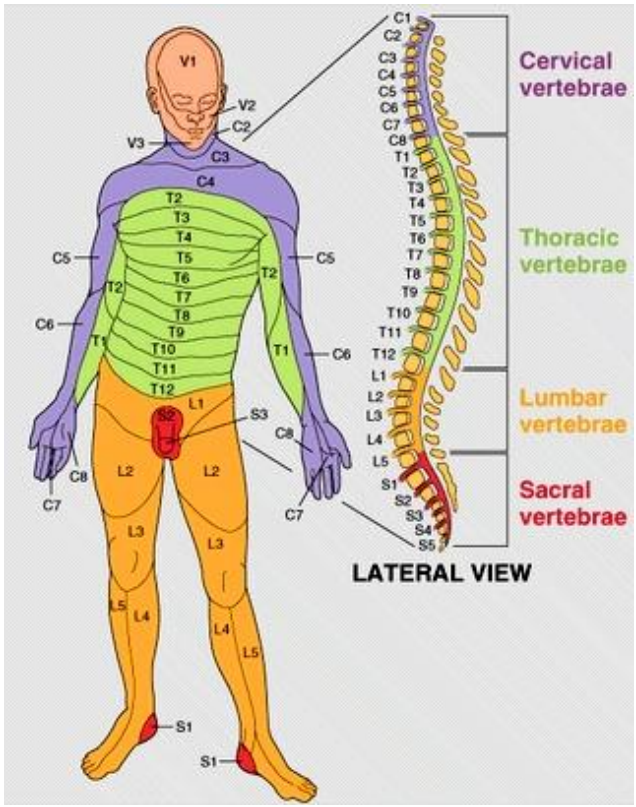
# Clinical Stage Pain Management Asset

# Two Injection Sites = Two Products for Human Use

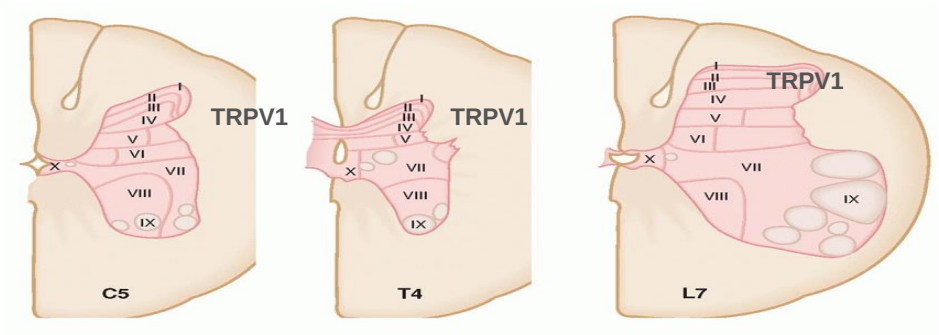


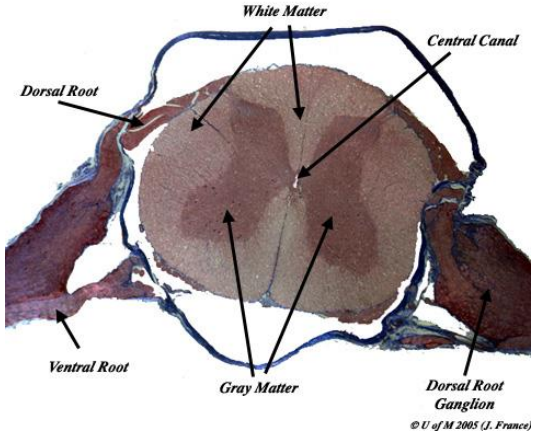

***Intraganglionic***
*(injection into or near the ganglion)*

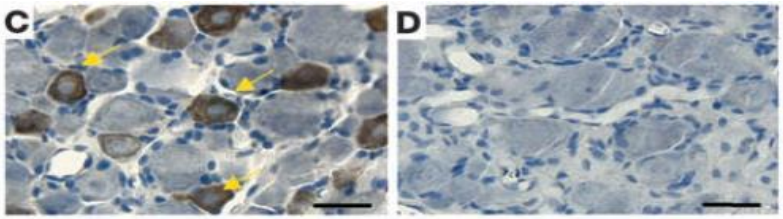
***Intrathecal***
*(injection into the cerebrospinal fluid space)*



# RTX Ablates TRPV1-positive Neurons after Intrathecal Injection



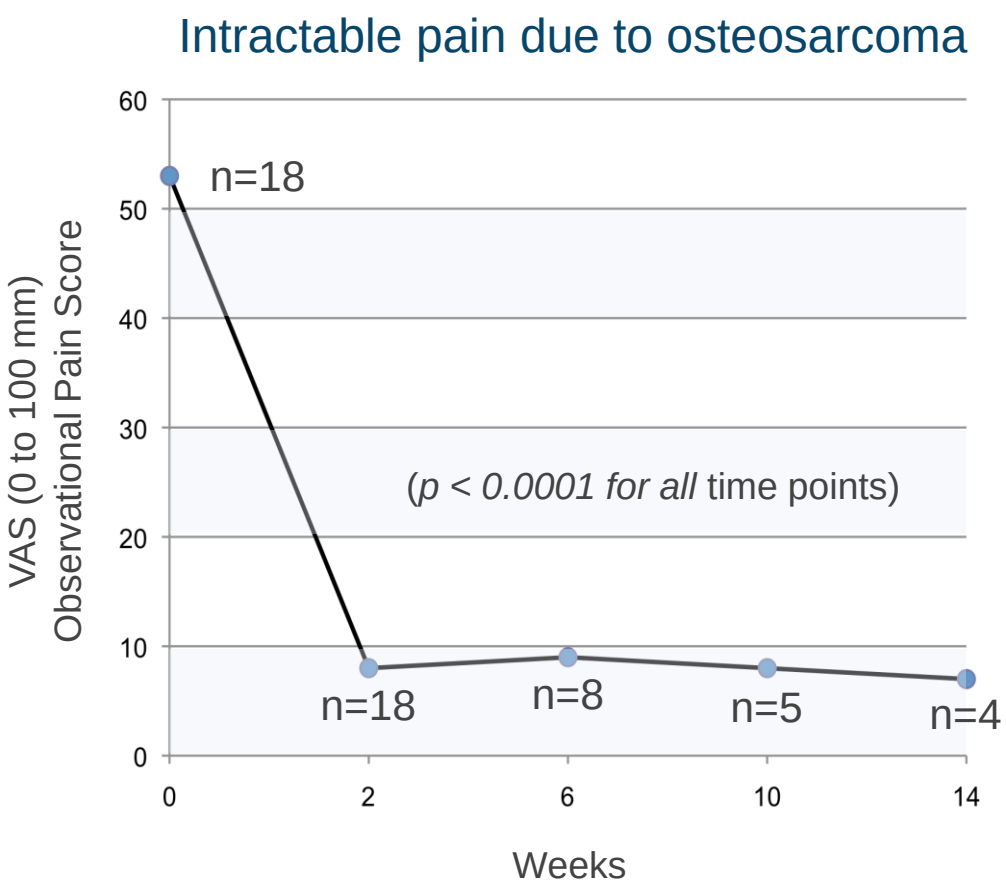




**Fore limb**
TRPV1 positive

**Hind limb**
TRPV1 negative

Adapted from Karai et al. 2004

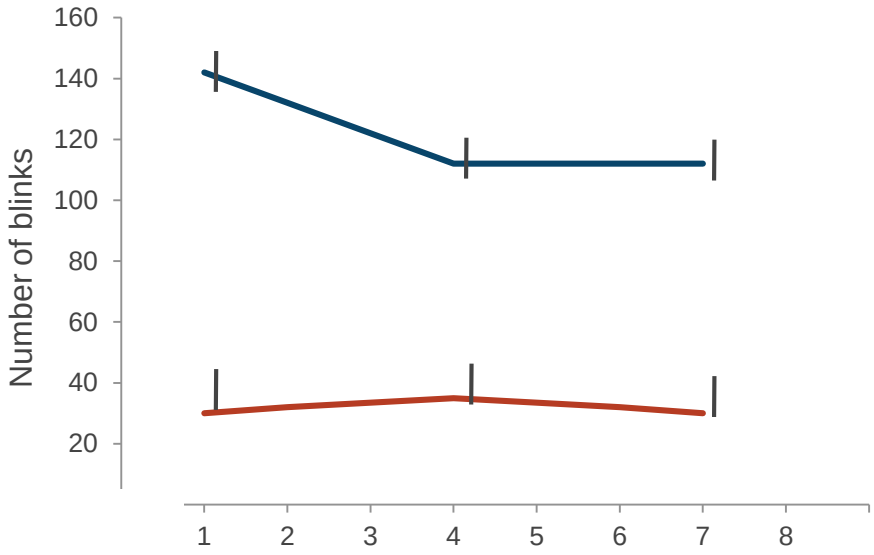
# Open-Label Study in Companion Dogs




- 100% response rate with single intrathecal injection
- 12 dogs reduced or discontinued analgesics
- Dogs passed away due to underlying osteosarcoma, not RTX treatment
- Permanent analgesic effect
  - Personality intact
  - Gait and mood visibly improved
- Lack of serious adverse events
  - No opioid-like side effects
- Animal health market represents separate licensing opportunity

Brown et al, 2005

# Unilateral Effect Following Trigeminal Injection




Left eye (blue) vs
Right eye (red)

Nociceptive neuron-mediated
neurogenic inflammation
(Evans blue)

Adapted from Tender et al. 2005

# Interim Data from the Phase 1/2 NIH sponsored trial

- 6 advanced cancer pts with severe refractory pain dosed with no unexpected toxicity
- MTD not reached, additional dose escalation being explored
- Clinically meaningful improvement in QOL
- Improved pain scores with increased activity

| Demographics at Study Entry | Cancer Diagnosis | Target Pain Area |
|---|---|---|
| **49 y (f)** | Metastatic breast cancer | Low back and bilateral leg pain 2º bone mets |
| **56 y (m)** | Metastatic supraglottic squamous cell cancer | Low back and bilateral hip pain 2º bone mets |
| **57 y (m)** | Metastatic pancreatic cancer | Bilateral abdominal (visceral) pain |
| **68 y (m)** | Lymphoma, small fiber monoclonal gammopathy | Bilateral hip and buttocks (neuropathic) pain |
| **55 y (m)** | Metastatic small cell lung cancer | Left hip pain 2º bone mets |
| **61 y (f)** | Metastatic endometrial cancer | Low back and left hip/groin pain 2º bone mets |

| Patient | Pre RTX | Injection Date | Last NRS PI score | %NRS PI improvement | Details |
|---|---|---|---|---|---|
| **1** | **7.3** | **5/9/11** | **6.1 (6 mo)** | **15.5** | **Bedridden to walking; nearly Y3 post RTX; cancer has progressed** |
| **2** | **8.3** | **5/10/12** | **3.8 (2 wk)** | **54.0** | **Died D35 of pneumonia 2º cancer** |
| **3** | **8.4** | **8/3/12** | **6.0 (1 mo)** | **28.8** | **Died just past D30 of cancer** |
| **4** | **8.0** | **10/23/12** | **5.4 (6 mo)** | **32.1** | **Wheelchair-bound to walking; Y1.5 post RTX; cancer has progressed** |
| **5** | **9.0** | **2/13/13** | **8.1 (1 mo)** | **9.6** | **Died W6 of cancer** |
| **6** | **8.6** | **9/23/13** | **7.9 (1 mo)** | **8.3** | **Breakthrough pain meds reduced by half by M1; ET from study just after M1 due to cancer progression; died just after M3** |
| | **Baseline average NRS = 8.27** | | **Average NRS reduction = 2.05 (24.7% Improvement)** | | **Average 1.6 point improvement across BPI pain interference items.** |

Data presented May 1, 2014 at 33rd Annual Scientific Meeting of the American Pain Society; Tampa, FL

# Next Steps for RTX Development

## Under NIH CRADA

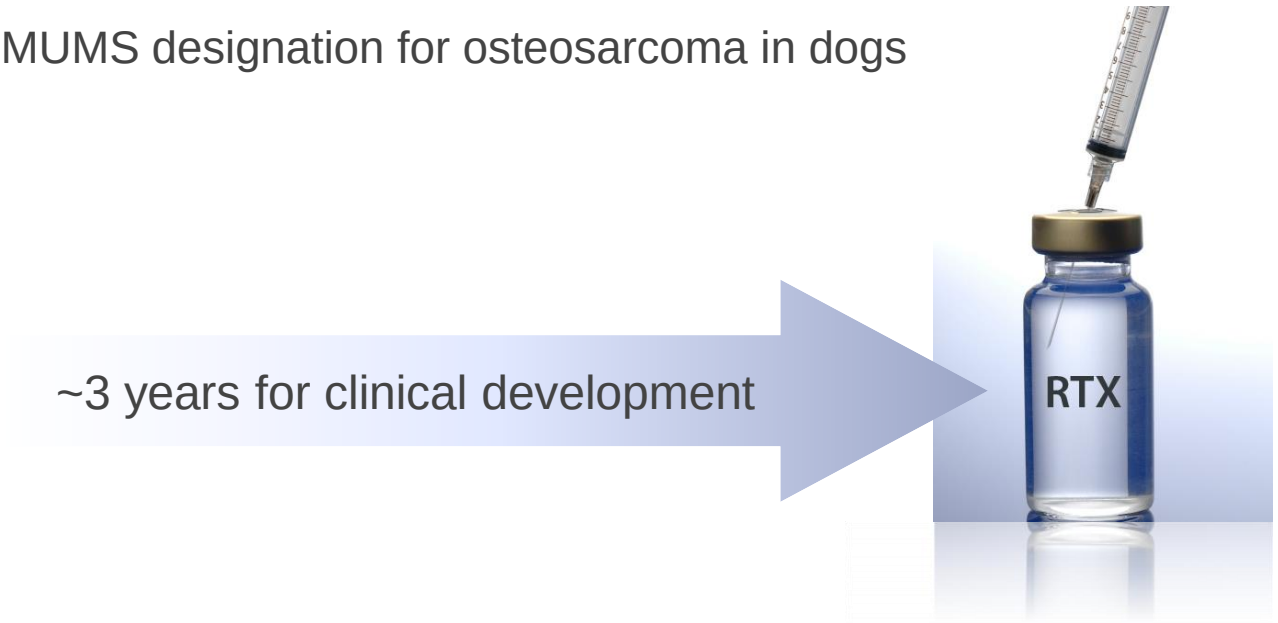
Intractable cancer pain clinical Phase 1/2 trial (**intrathecal injection**); n~13 patients

Phase 1/2 trial for osteosarcoma (**intraganglionic injection**); n~15 patients

## Under Sorrento IND

Intractable cancer pain clinical Phase 1/2 trial (**intrathecal injection**); n~40 patients

Filing for MUMS designation for osteosarcoma in dogs



# Immunotherapy Programs

# G-MAB: Library of Therapeutic Antibodies

Proprietary technology:

- RNA amplification used for library generation
- Freedom-To-Operate

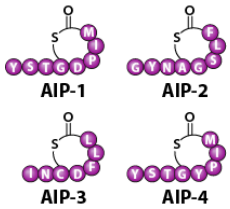
No stacking royalties

Very high library diversity:
**2.1 x $10^{16}$** distinct antibodies

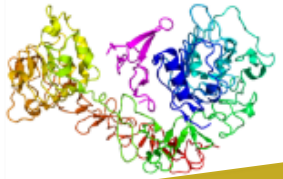
Fully human antibodies

High successful screening hit rate

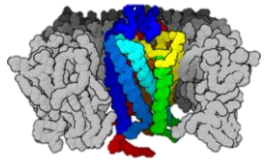
**Difficult Targets:**
Small Peptides




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



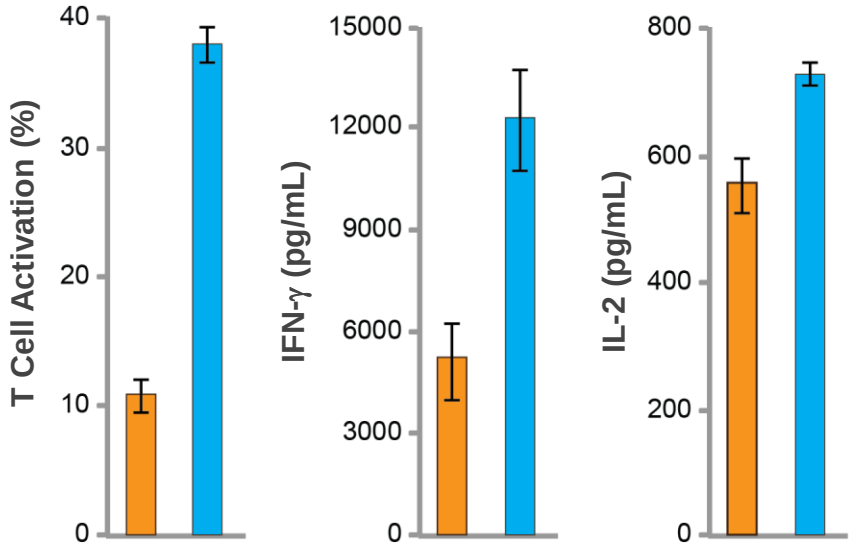
**Most Difficult Targets:**
G Protein-Coupled Receptors (GPCRs)



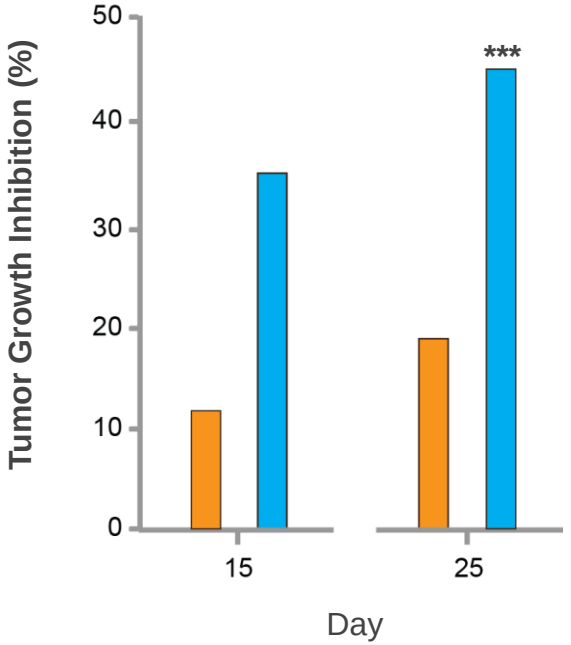
Size of Target Antigen

# Anti-PD-L1 mAbs Exhibit Potent Activity

## Immune Modulation*




## Tumor Mouse Model**




Competitor mAb

**Sorrento mAb**

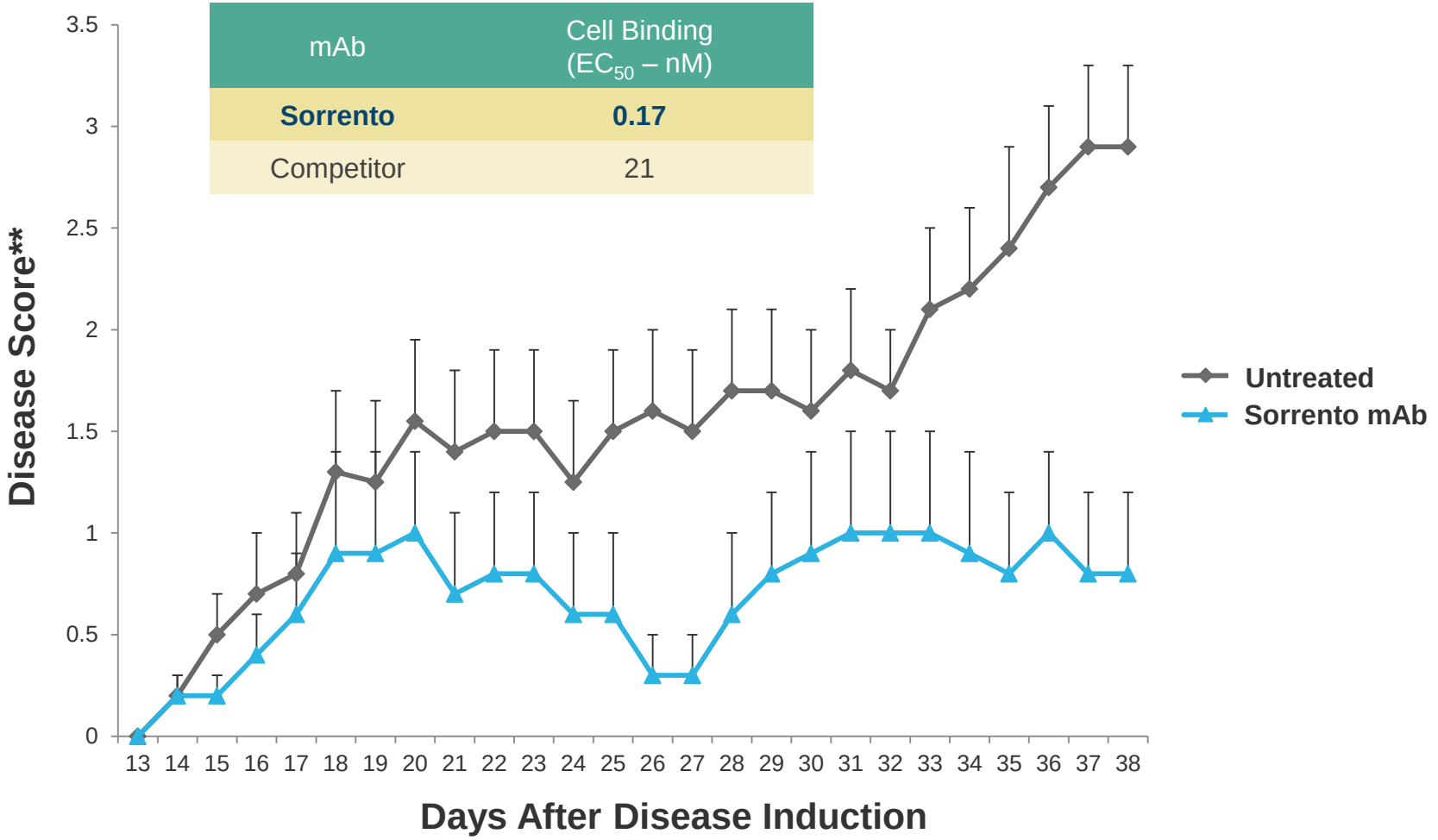
* mAbs @ 0.05 mg/mL

** 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

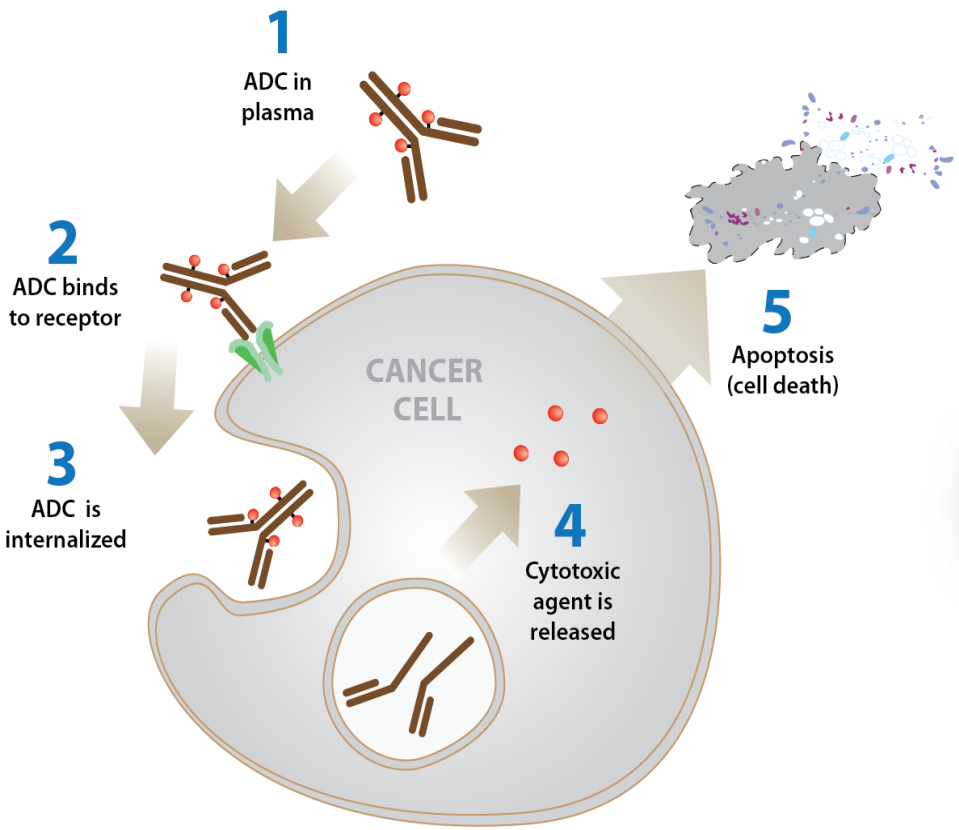
# Potent Antibody against Difficult GPCR Target*

| mAb | Cell Binding ($EC_{50}$ – nM) |
|---|---|
| **Sorrento** | **0.17** |
| Competitor | 21 |




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

# Antibody Drug Conjugates (ADCs)




## Key Components:

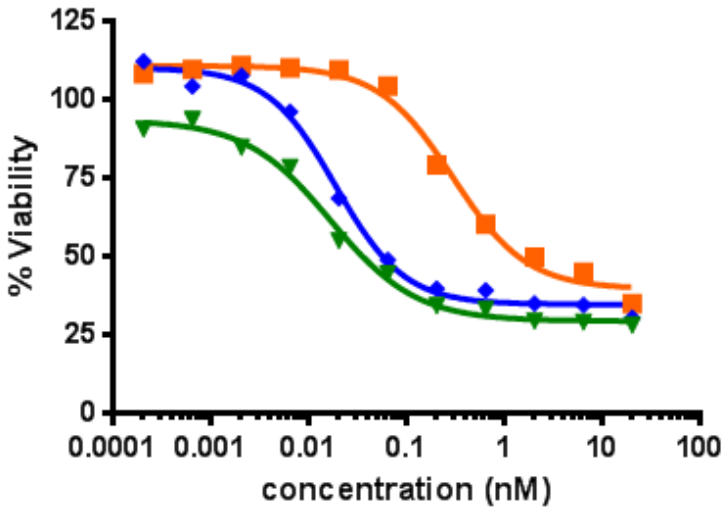
1. Target-specific internalizing antibody
2. Potent cytotoxic prodrugs
3. Linker and conjugation chemistries

**Drug released in CANCER CELL**

# Proprietary High Potency Duostatin Toxins

**SKBR3**
**(Breast Cancer Cell Line)**

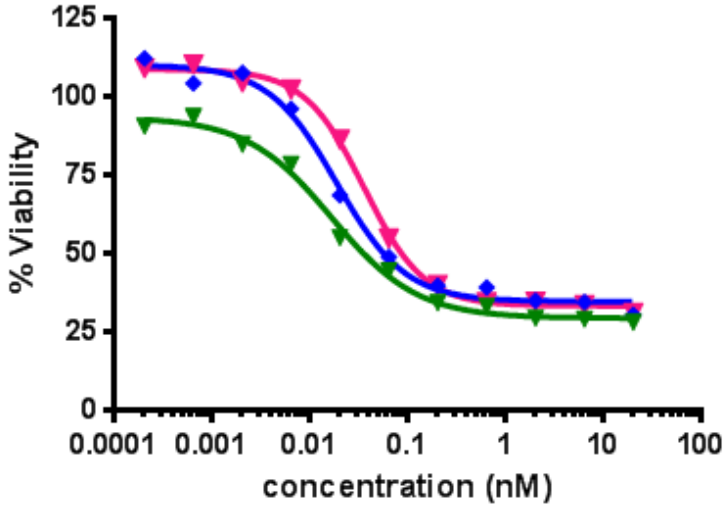
## Duostatins vs. DM1




- Duostatin toxin 1 (K-lock)
- Duostatin toxin 2 (K-lock)
- DM1 (conventional; NHS)

>15x higher potency

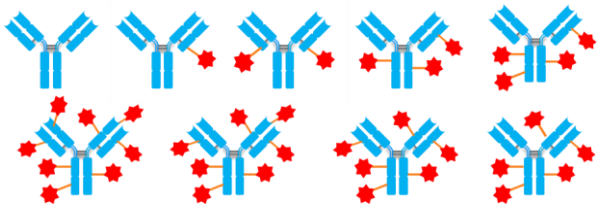
## Duostatins vs. MMAE

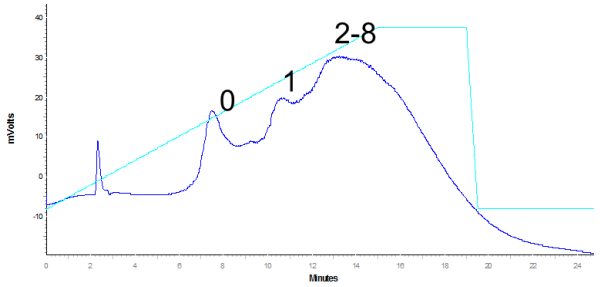



- Duostatin toxin 1 (K-lock)
- Duostatin toxin 2 (K-lock)
- MMAE (conventional; maleimide)

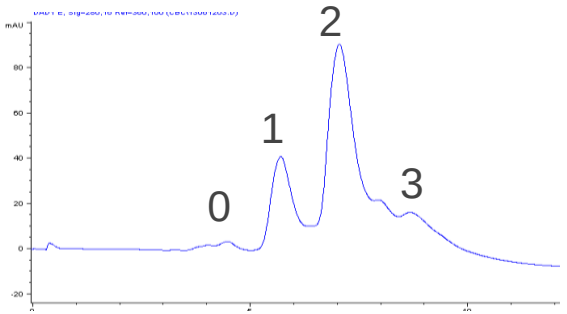
# K-Lock Conjugation Enables Homogeneous ADCs

**Current industry standard chemistry**






**Proprietary K-Lock chemistry**

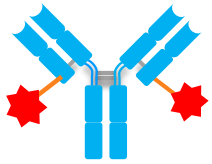


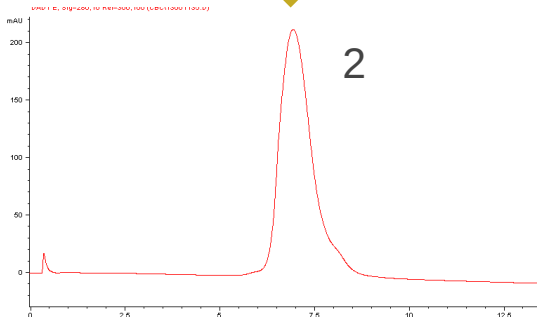

purified

**Sorrento's homogenous ADC**

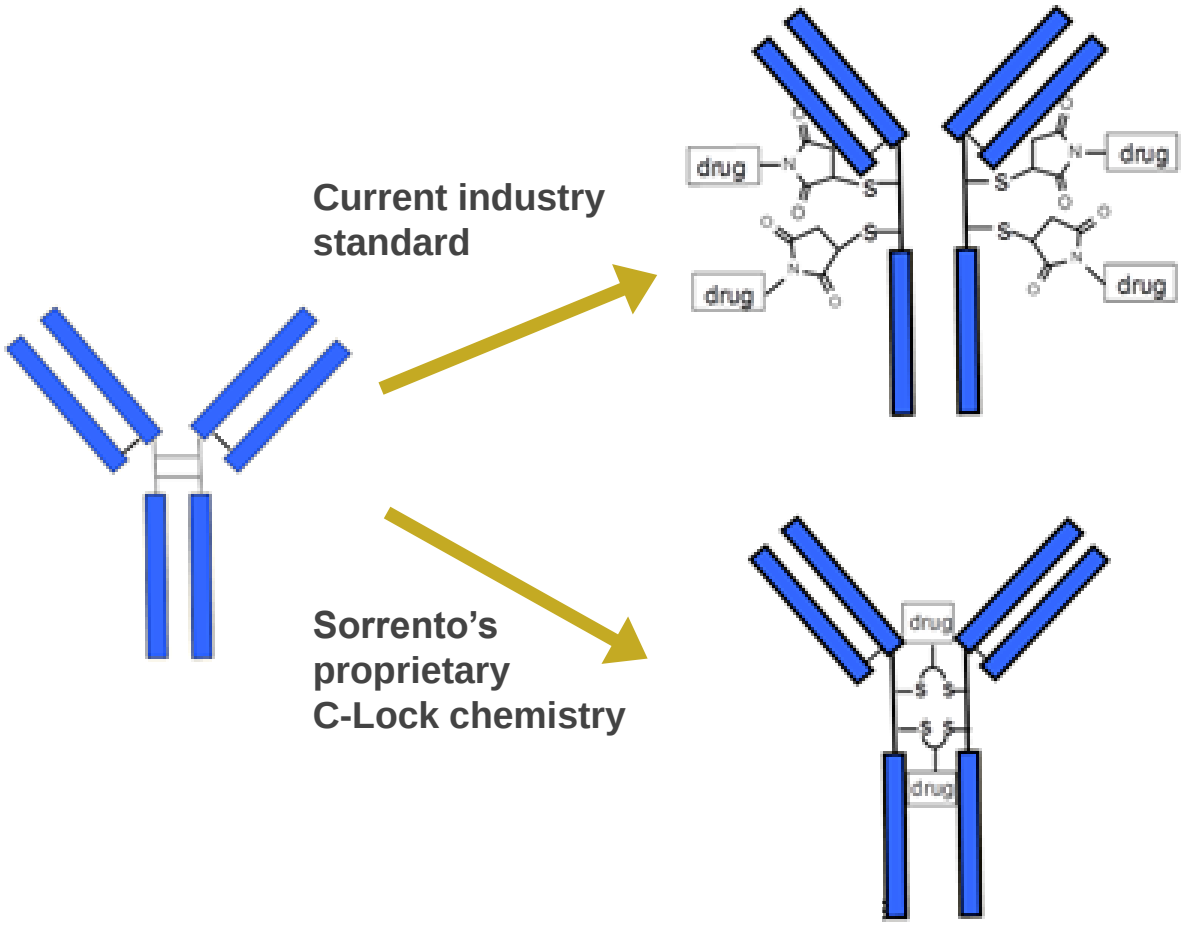
No need for:

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





# C-Lock Conjugation Stabilizes ADCs




**Maleimide conjugation**

Destabilizes antibody structure

Reduced target specificity

Altered PK profile

Drug-antibody linkage not stable

Off-target drug effects

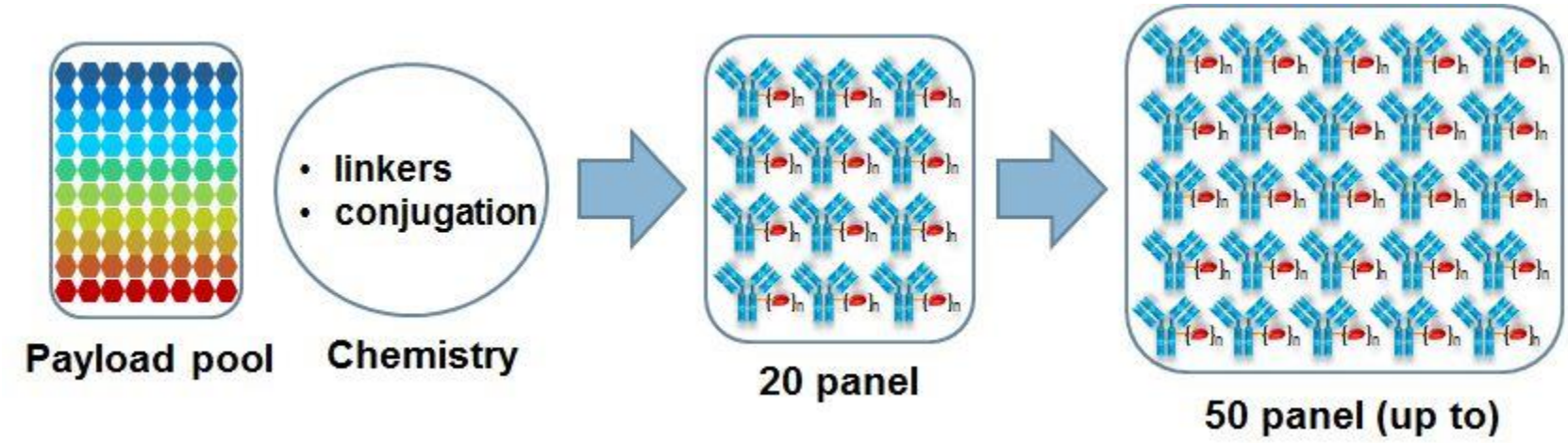
**C-lock conjugation**

Enhances ADC stability

Prolongs PK profile

Reduced off-target effects

# Proprietary ADC Screening and Optimization Panels




**Fast track to IND**

Identification of optimal combination of linker, conjugation chemistry and drug payload essential for efficient and expedited development **from target to candidates**

# Investment Highlights


**Late-Stage Cancer Drug**

Product launch expected in 1H 2016

Addresses multi-billion dollar paclitaxel market

Abbreviated regulatory pathway (“bioequivalence”) for approval


**Intractable Cancer Pain Treatment**

Ongoing Phase 1/2 study

Orphan drug status received

Three potential drug products from same API


**Targeted Cancer Immunotherapeutics**

First therapeutic antibody candidate in clinic 1H 2016

Proprietary linker/conjugation chemistry for *homogenous* ADC generation

First ADC in clinic 1H 2016

# Developing Therapeutic Solutions to Help Man's Life Companions



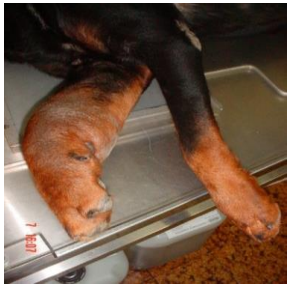

ARK

Animal Health

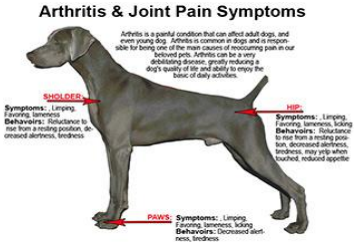
A Subsidiary of Sorrento

# Novel Products Potentially Target Unmet Needs

**Ark-001**
**(Pain assoc/ w Canine Osteosarcoma)**



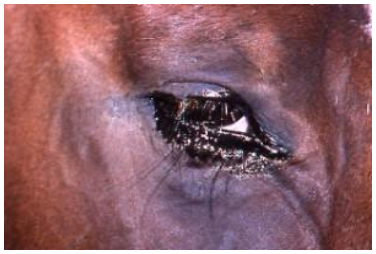
**Ark-001**
**(Pain assoc/ w Canine Osteoarthritis)**



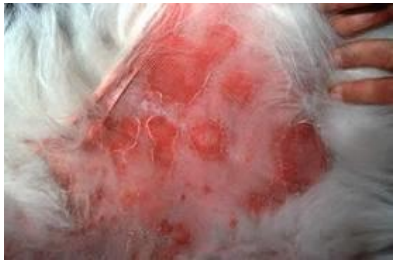

**Ark-002**
**(Neuropathic Pain- Navicular Syndrome/Laminitis)**

**Ark-003**
**(Idiopathic Cystitis in cats)**

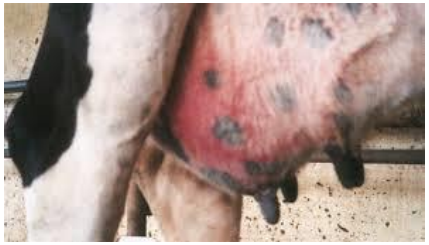
**Ark-004**
**(Inflammation and Pain Ocular Abrasion)**



**Ark-005**
**(Staph Infections in dogs Dermatitis)**



**Ark-006**
**(Mastitis in cows)**



**Ark-007**
**(Post Surgical Pain In dogs)**

Potential in license

Ark 001, 002, 003 & 004 are RTX-based formulations.
Ark 005 & 006 are AIP vaccines (staph).

# Disease-Specific Market Factors
## *Small Animals*

| Disease/Drug | Unmet Need | Competition | Prevalence | Level of Differentiation |
|---|---|---|---|---|
| Ark-001 (Dogs)<br>Osteosarcoma/Pain | High | Opiates rare use<br><br>Amputation<br><br>Alternative interventions unsatisfactory | *83 M Pet dogs<br>1 in 3 have tumors<br>5% of all tumors= Osteosarcoma<br>Approximately 1.35 M | Transformative |
| Ark-001 (Dogs)<br>Osteoarthritis/Pain | Moderate to High | NSAIDs<br>May result in hepatic and GI toxicity | 4 M dogs in active NSAID treatment | Transformative<br>Intrathecal inj may allow for coverage of all joints |
| Ark-005 (Dogs)<br>Recurring dermatitis/infections | Moderate to High | Antibiotics<br><br>Corticosteroids | **MRSA 1.5-2 % of dogs in community and Vet hospitals | Moderate to significant |
| Ark-003 (Cats)<br>Interstitial Cystitis | High | Castration/Spaying<br><br>Anti-anxiety drugs<br>Pheromones | Unknown | TBD<br>May reduce bladder hyperactivity |

*APPA 2012 and Canine Cancer.com
**Veterinary Medicine, Dec 1, 2012

# Disease-Specific Market Factors
## *Large Animals*

| Disease/Drug | Unmet Need | Competition | Prevalence | Level of Differentiation |
|---|---|---|---|---|
| Ark-006 (Cows)<br>Mastitis | High | Antibiotics<br><br>Mastitis prevention programs | Approximately 9.2M cows and 1/3 infected with mastitis annually | TBD:<br>Vaccine delivery may offer high differentiation potential |
| Ark-004 (Horses)<br>Ocular Pain/Ocular abrasions | High | Eye drops<br><br>Antibacterial opthalmic ointments<br><br>Lidocaine | High<br>No reliable estimates | Moderate to High:<br>Desensitization of nerves may facilitate abrasion healing |
| Ark-002 (Horses)<br>Laminitis | Moderate to High | Pain Killers including NSAIDs<br><br>Peripheral vasodilators | *9.2 M horses in US<br>** 15% will suffer from laminitis in lifetime | Potentially high based on limited results to date |

* Making sense of laminitis; Michelle Andersen, Feb 1 2013
** US Horse Industry Statistics- The equestrian channel 2013

# Market Valuation of Competitor Companies

| | Products on Market | Products in development | Disease Area Focus | Time to market | Market Valuation |
|---|---|---|---|---|---|
| **ARATANA (PETX)** | None | >15 | Pain<br>Appetite Stimulants etc | Near Term | $529 M |
| **KINDRED (KIN)** | None | 10 | Pain<br>Cancer<br>GI, Allergy<br>Inflammation<br>Autoimmune | Near Term | $295 M |
| **ARK ANIMAL THERAPEUTICS** | **None** | **>10** | **Pain<br>Osteoarthritis<br>Infections<br>Interstitial Cystitis<br>Mastitis<br>Ocular Pain<br>Laminitis** | **Near Term** | **IPO TBD** |


# Next-Generation Cancer Therapeutics

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