

DE-RISKING DRUG DEVELOPMENT

# *Translational Comparative Medical Research (TCMR)*

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Research & External Innovation

**Elanco**

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*Lilly*

# What is TCMR?

TCMR collaborates to de-risk Lilly projects/assets by applying **proof-of-concept studies in the companion animal naturally occurring diseases** that parallel human diseases.



# What Therapeutic Areas?

- **Oncology**
  - Immuno-oncology
  - Molecular targeted therapy
  - Cytotoxic therapy
  - Radiation therapy
  - Pain management
  - Cancer cachexia
- **Endocrine & Renal**
  - Obesity
  - Diabetes
  - Chronic kidney disease
- **Pain**
  - **Osteoarthritis**
  - **Bone cancer**
- **Heart Disease**
  - Cardiomyopathy
  - Heart Failure
- **Immune-mediated Disease**
  - Inflammatory bowel disease
  - Atopic dermatitis
- **Osteoarthritis**
  - Pain management
  - Disease modification

# Osteoarthritis



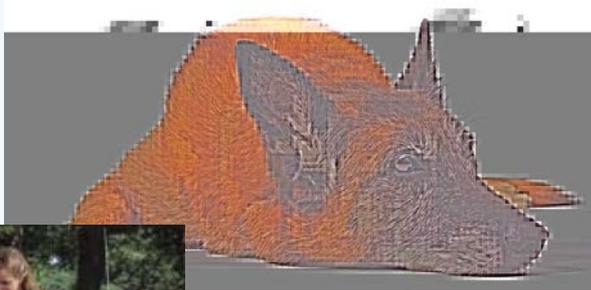
- 72 million owned dogs in the U.S.
- At least 20% have osteoarthritis
- Pathologically, physiologically, and symptomatically analogous to human osteoarthritis

## OSTEOARTHRITIS (OA)

		Humans	Dogs
<b>Pathology</b>	<b>Cartilage:</b> Proteoglycan loss, chondrocyte death, erosion	✓	✓
	<b>Subchondral Bone:</b> Increased turnover, thickening, neovascularization	✓	✓
	<b>Joint Margin:</b> Osteophytes	✓	✓
	<b>Synovium &amp; Fat Pad:</b> Inflammation, fibrosis	✓	✓
	<b>Joint Capsule:</b> Fibrosis, enthesopathy	✓	✓
	<b>Muscle:</b> Atrophy, fat infiltration	✓	✓
<b>Sources of Joint Pain</b>	<b>Direct (contains nociceptors):</b> Subchondral bone remodeling, synovitis, ± joint capsule, ± osteophytes	✓	✓
	<b>Indirect (source of inflammatory catabolites, cytokines, chemokines, neuropeptides):</b> cartilage, ligaments	✓	✓
<b>Risk Factors</b>	Obesity, age*, trauma*	✓	✓
<b>Diagnostic Modalities</b>	Radiography, computerized tomography, magnetic resonance imaging, arthroscopy, synovial fluid analysis	✓	✓
<b>Therapeutic Goals</b>	Control pain and improve function	✓	✓
	Slow progression	✓	✓
<b>Outcome Assessment in Clinical Trials</b>	Pain, mobility, stiffness, and function indices	✓	✓
	Computerized gait analysis	✓	✓
	Radiography & advanced imaging for disease modification	✓	✓



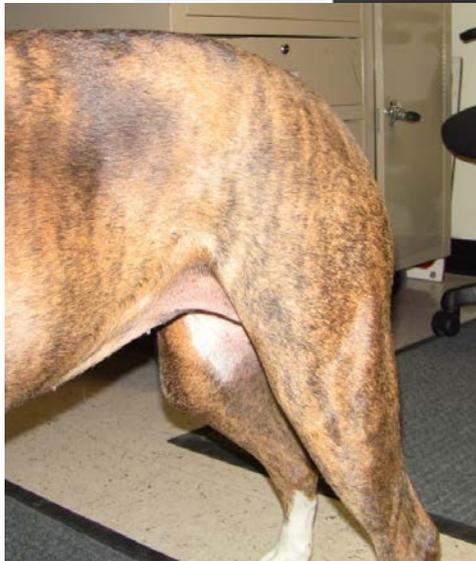
# Osteoarthritis



- Pain
- Stiffness
- Decreased range of motion
- Decreased activity
- Decreased function



# Osteoarthritis - Recruitment & Intervention



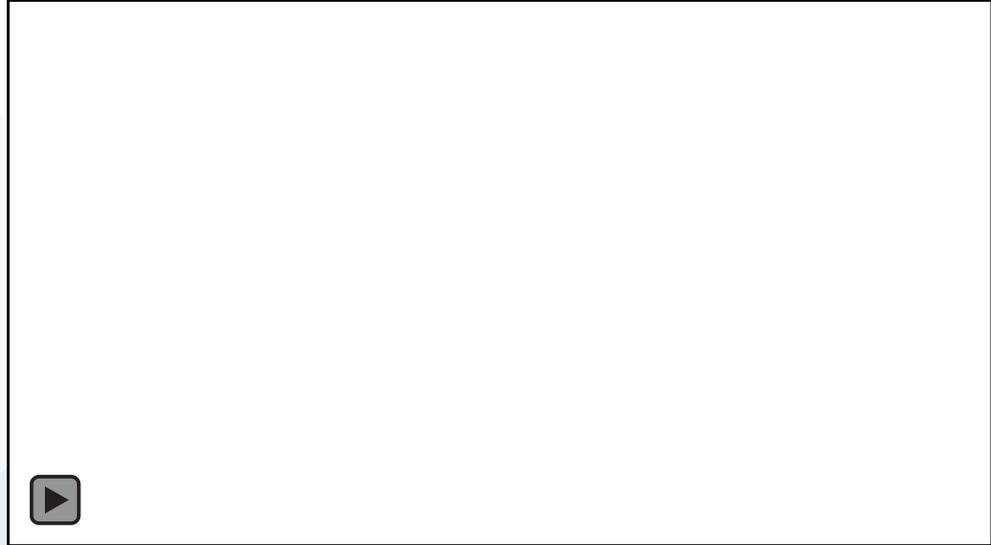
# Osteoarthritis – Outcomes: Gait Analysis



- Gold standard for lameness
- ‘Objective’
- Single point in time
- Laboratory environment



# Osteoarthritis – Outcomes: Proxy Assessment



Canine Brief Pain Inventory (CBPI)

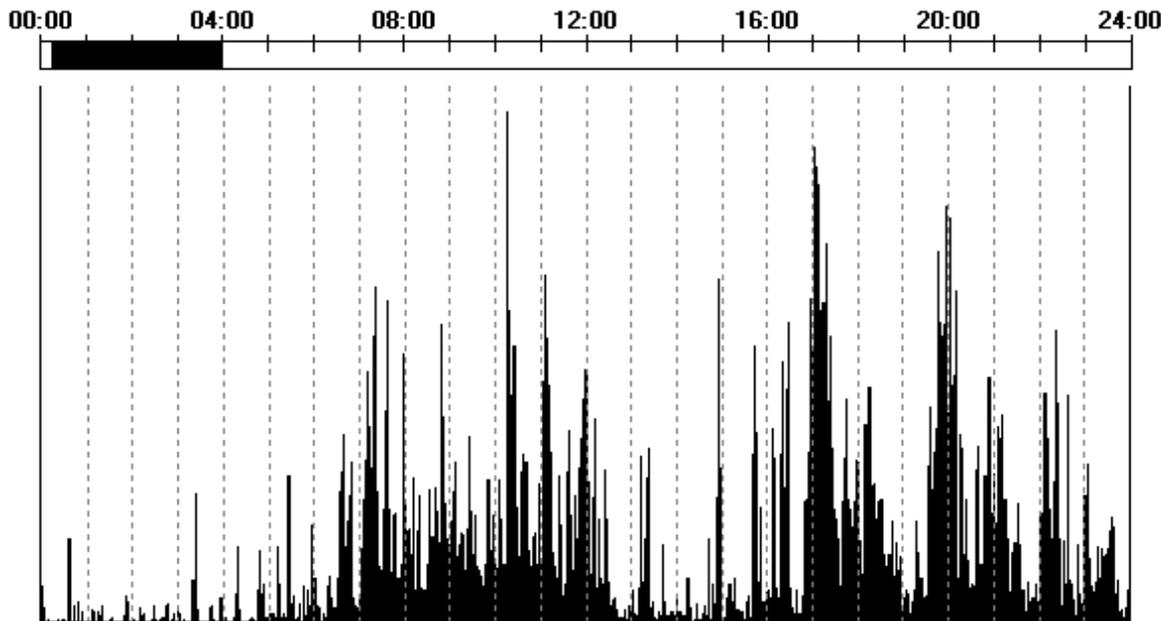
Canine Orthopedic Index (COI)

Liverpool Osteoarthritis in Dogs (LOAD)

# Osteoarthritis – Outcomes: Activity Monitoring



- Integrates the frequency and amplitude of motion and produces an electrical current that varies in magnitude
- Stores this info in the form of activity counts

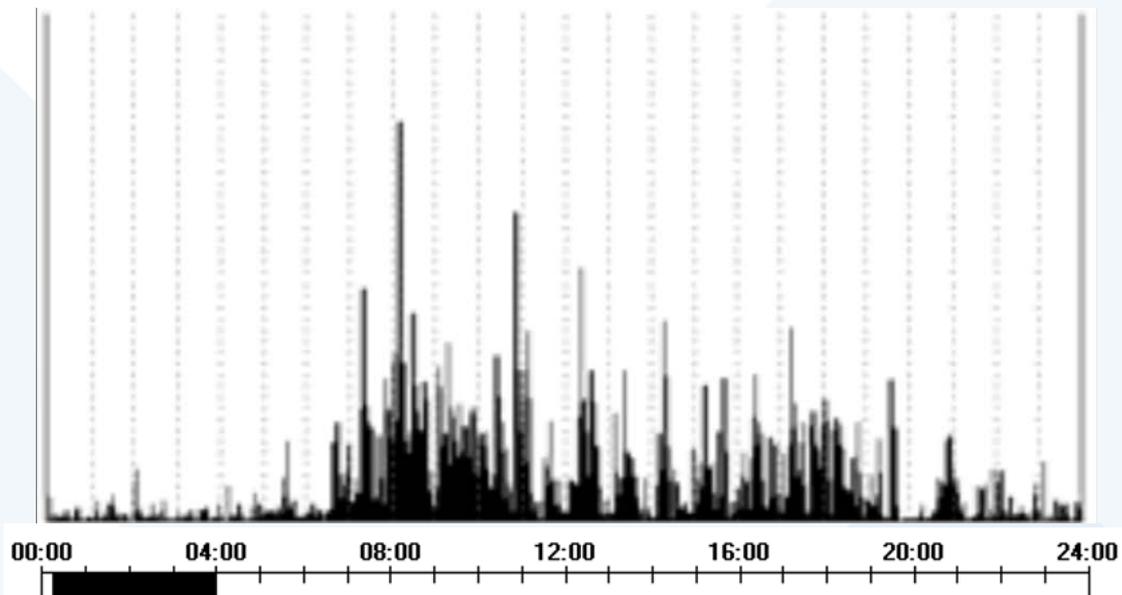


Date Stamp	Time Stamp	Activity Data
10-Jun-04	5:45:00	0
10-Jun-04	5:46:00	0
10-Jun-04	5:47:00	0
10-Jun-04	5:48:00	0
10-Jun-04	5:49:00	0
10-Jun-04	5:50:00	0
10-Jun-04	5:51:00	0
10-Jun-04	5:52:00	0
10-Jun-04	5:53:00	0
10-Jun-04	5:54:00	0
10-Jun-04	5:55:00	0
10-Jun-04	5:56:00	0
10-Jun-04	5:57:00	0
10-Jun-04	5:58:00	0
10-Jun-04	5:59:00	0
10-Jun-04	6:00:00	11
10-Jun-04	6:01:00	1355
10-Jun-04	6:02:00	249
10-Jun-04	6:03:00	316
10-Jun-04	6:04:00	569
10-Jun-04	6:05:00	665
10-Jun-04	6:06:00	1159
10-Jun-04	6:07:00	102
10-Jun-04	6:08:00	305
10-Jun-04	6:09:00	206
10-Jun-04	6:10:00	305

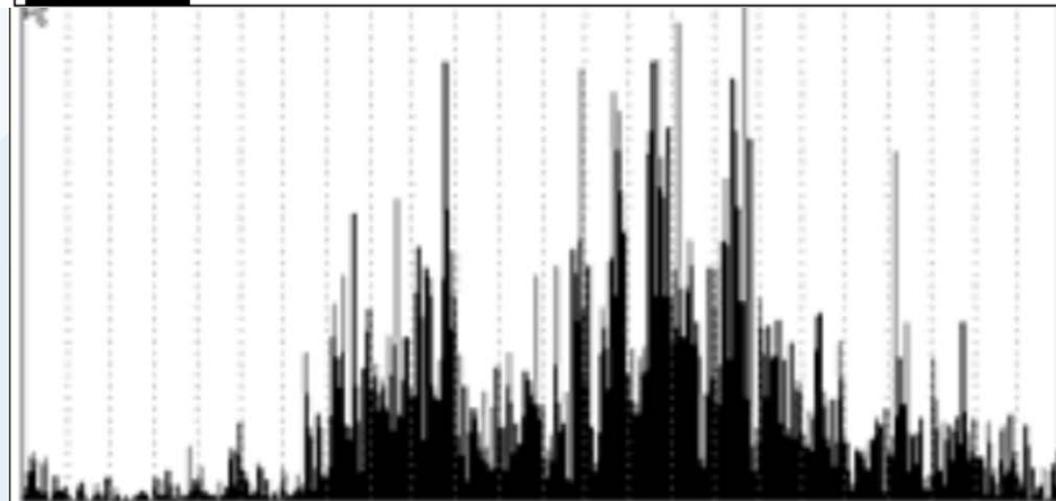
# Osteoarthritis – Outcomes: Activity Monitoring



Pre-NSAID



Post-NSAID





# A Novel Approach to Treating Pain

Our pipeline consists of new and emerging, non-opioid pain therapies aimed at selectively interrupting pain transmission pathways to more effectively treat moderate to severe chronic pain without risks of dependence or abuse.

PRODUCT CANDIDATE	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
<b>CNTX-4975</b>	Human Osteoarthritis Pain			
<b>CNTX-4975</b>	Canine Osteoarthritis Pain 			
<b>CNTX-4975</b>	Morton's Neuroma Pain			
<b>CNTX-0290</b>	Neuropathic, Inflammatory and Mixed Pain			
<b>CNTX-6970</b>	Inflammatory Pain			

# Bone Cancer Pain

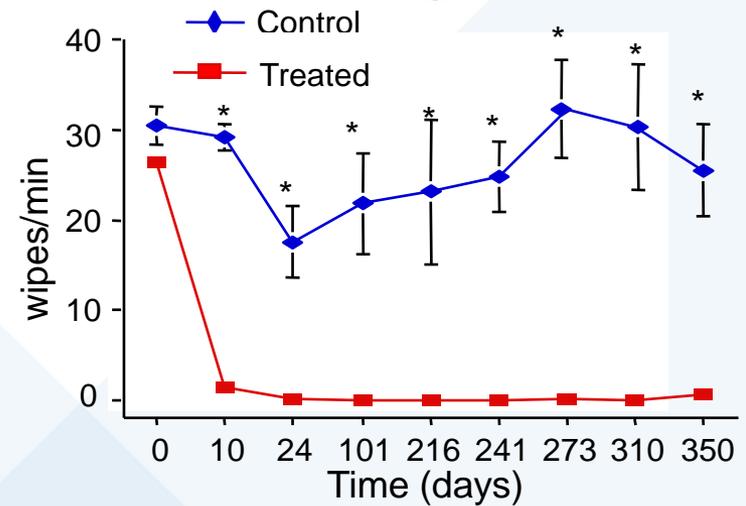
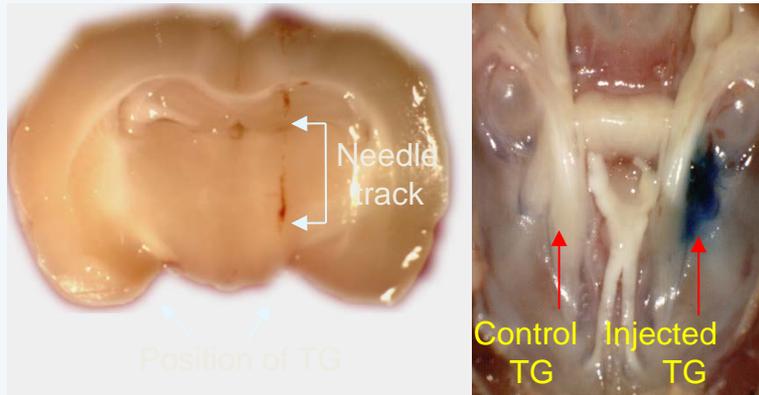


- ~10,000 osteosarcoma cases diagnosed each year
- Large and giant breeds
- 85% of canine bone tumors are osteosarcoma

# Bone Cancer Pain



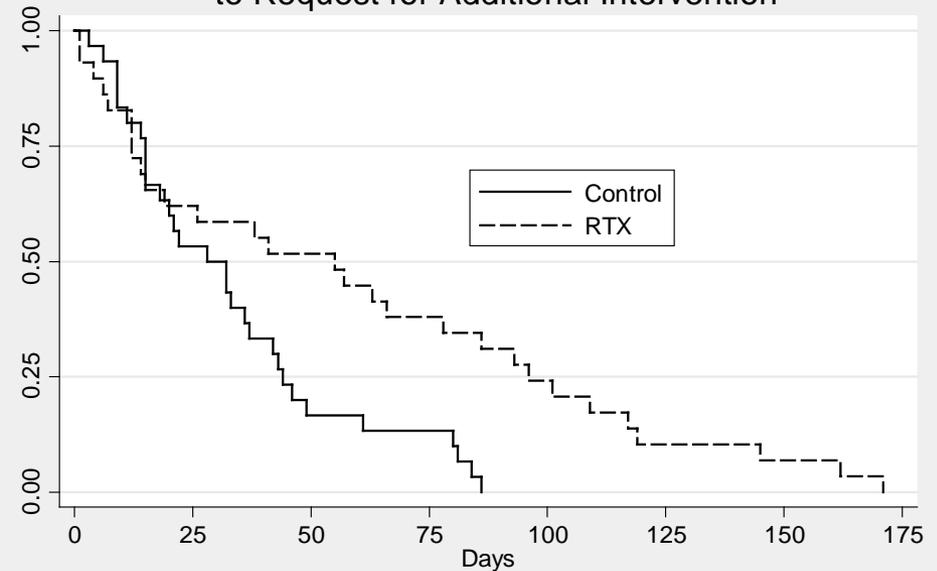
# Bone Cancer Pain: Central TRPV1 Agonist



# Bone Cancer Pain: Central TRPV1 Agonist



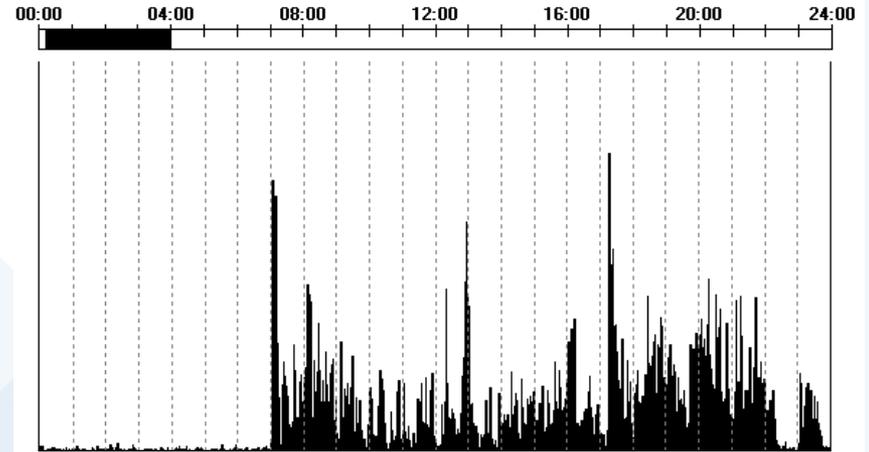
Time From Randomization/Injection to Request for Additional Intervention



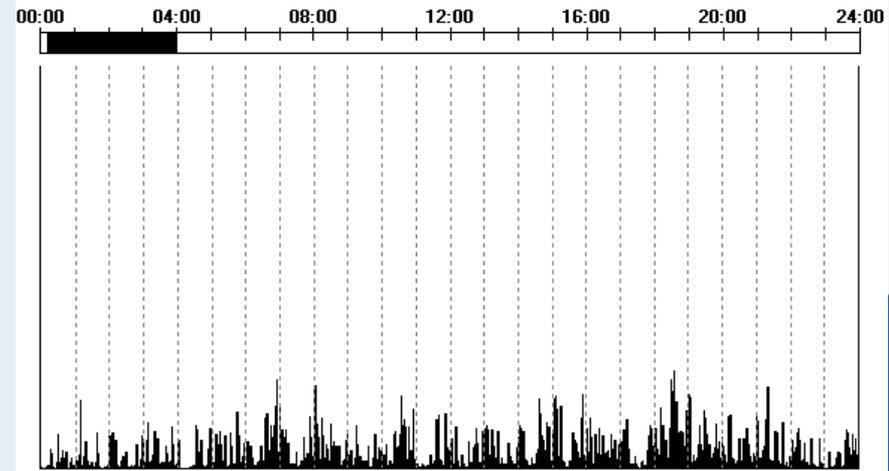
# Bone Cancer – Outcomes



Normal Dog



Dog w/Bone Cancer



## Sorrento Announces Presentation of Data from Clinical Study of Resiniferatoxin for Intractable Cancer Pain at ASRA Meeting

- Clinically meaningful improvement in quality of life with single injection of resiniferatoxin
- Improvement in pain intensity by 20%, as measured by numerical rating scale, with most patients experiencing increased activity levels
- Resiniferatoxin appears well-tolerated with no opioid-like toxicities





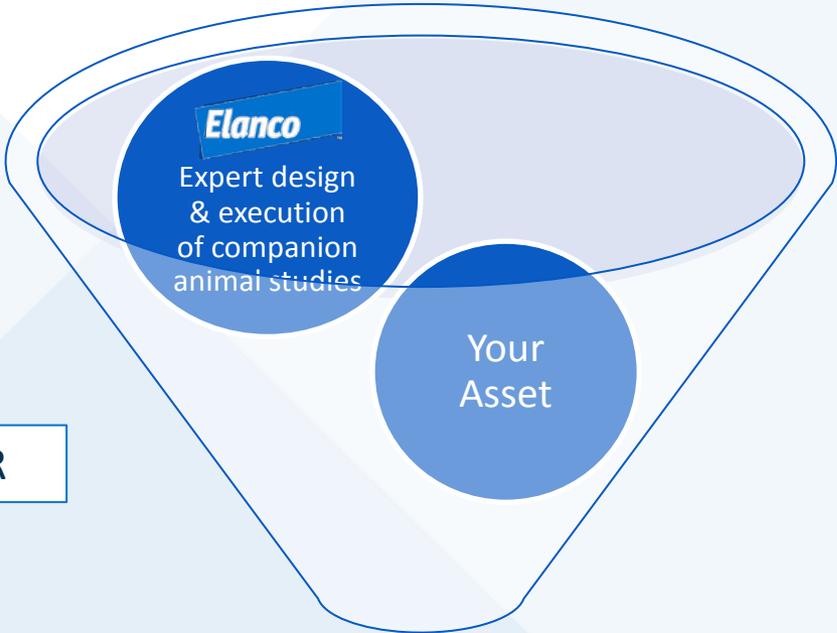
Clinical



# External Facing TCMR



OR



Robust & Informative  
Proof-of-Concept Data Package

Robust & Informative  
Proof-of-Concept Data Package

# Why Lilly & Elanco Invest in TCMR

- Science & Business wins
  - Understanding projects/assets
  - Understanding biology/disease
- Patients win
  - Safer clinical trials
  - Increased probability of technical success
- Owners/Pets win
  - Access to care
  - Access to approved products
  - Investment in the future

