

# **Entrepreneurship Bootcamp**

## ***Session 2 - Project, Product or Company***

**Mark A. Tepper, Ph.D.**  
**President & CSO**  
**Corbus Pharmaceuticals Inc.**  
**June 3, 2018**

*Developing Medicines which modulate  
the endocannabinoid system*

# JB Therapeutics: Highlights

<b>Market Focus</b>	<p>Targeted Cannabinoid Agonists and Antagonists for the treatment of:</p> <ul style="list-style-type: none"><li>• Pain: ~\$30 Billion Rx market</li><li>• Obesity: ~\$15 Billion Rx market</li><li>• CNS disorders: ~\$20 Billion market (PTSD, Anxiety, neurodegenerative diseases)</li></ul>
<b>Technology</b>	<ul style="list-style-type: none"><li>• Orally active non-psychotropic CB1/2 agonist for chronic pain</li><li>• Peripheral CB1 Antagonist for Obesity</li><li>• CB2 Agonist for Inflammatory Pain</li><li>• FAAH inhibitor for Neurodegenerative disease</li><li>• Oral Endocannabinoid mimetics</li></ul>
<b>Development Strategy</b>	<ul style="list-style-type: none"><li>• Advance programs to Phase II POC</li><li>• Partner out select programs</li><li>• Bring internal neurodegenerative disease programs to market.</li></ul>
<b>Financing Plan</b>	<ul style="list-style-type: none"><li>• Seek funding of \$5M to complete POC clinical studies with lead CB1/CB2 agonist for pain</li></ul>
<b>Leadership</b>	<ul style="list-style-type: none"><li>• Management team experienced in building biotech companies</li><li>• 60+ yrs operating experience in drug discovery and development</li></ul>

**Mark Tepper, PhD – CEO**

- BMS, Serono
- Former CEO - NKT Therapeutics, RXi Pharmaceuticals, Arradial

**Kollol Pal, PhD – SVP R&D**

- BIPI, Mitotix, Neogenesis, Satori
- Former CEO, Rishi Pharma

**Terry Plasse, MD – Clinical Consultant**

- Former Clinical developer of Marinol

**Sumner Burstein, PhD**

- Prof. Emeritus, Biochemistry UMass Medical School
- Inventor of JBT-101

**Robert Zurier, MD**

- Prof. of Medicine, Rheumatology UMass Medical School

**Paul Goldenheim, MD**

- Former CMO, Purdue Pharm
- Analgesic Research

**Nathan Katz, MD**

- CEO Analgesic Research
- Advisor to FDA on analgesia

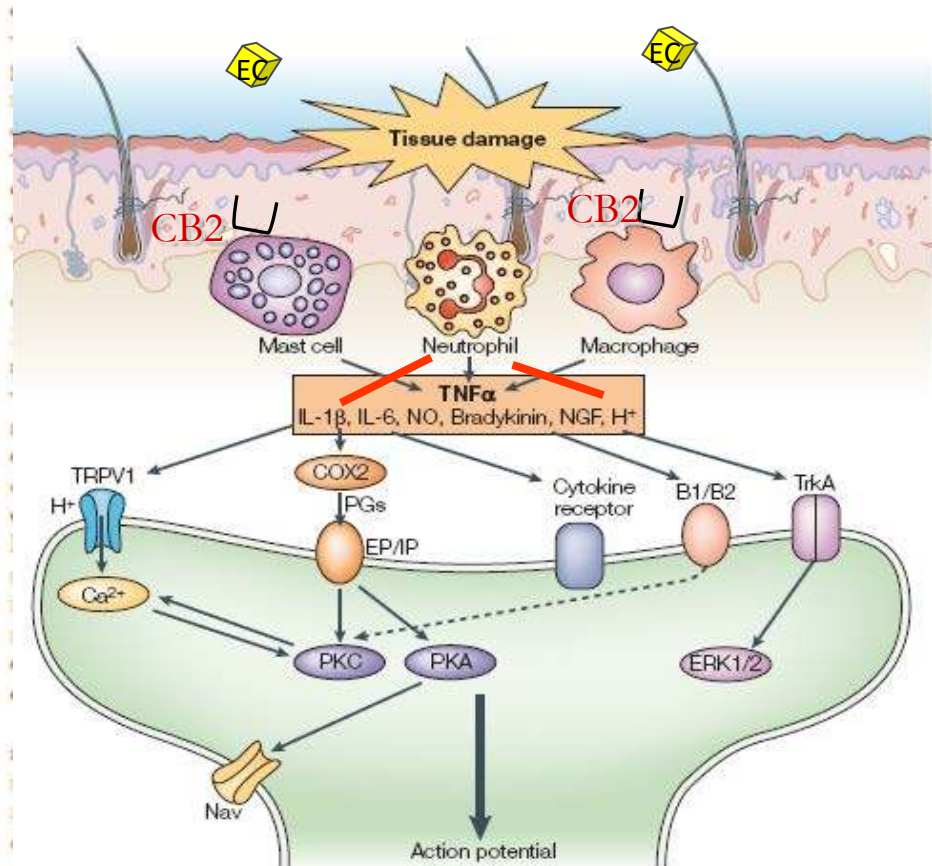
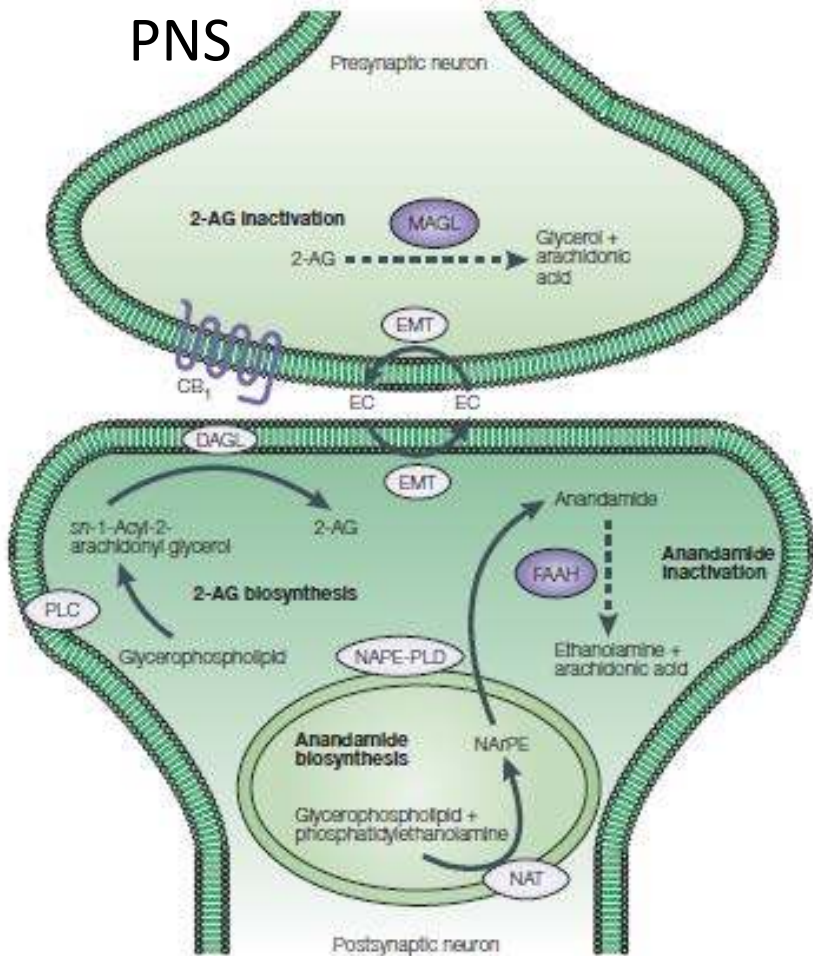
**George Kunos, MD, PhD**

- NIH Section Head, Pain & Analgesia

**Lynn Van Campen, PhD**

- Former VP, Inhale Therapeutics, BIPI
- University of Wisconsin

# CB1 & CB2 Signaling Pathway



# Cannabinoids in Medicine

1981



1985



2005



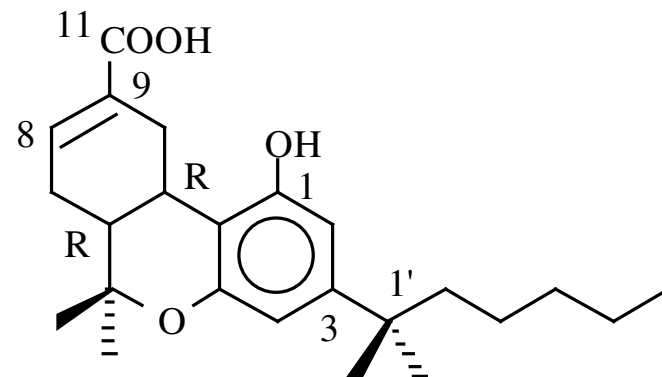
Therapeutic Validation	Cannabinoids have long history of human efficacy and safety in analgesia, emesis, MS spasticity, and neuropathic pain
High Potency	JBT-101 has $\geq$ potency to natural and synthetic cannabinoid drugs on the market
No Adverse Side-Effects	JBT-101 has reduced penetration of BBB and therefore does <b><i>not</i></b> induce psychotropic side effects like Marinol, Nabilone or Sativex
Potential Indications	Chronic Pain, Chronic inflammatory diseases, GI disorders, angiogenesis, multiple sclerosis spasticity

Ki (nM)	huCB1	huCB2
THC (Marinol)*	80.5nM	31.9nM
DMH-THC*	0.27nM	0.20nM
Nabilone (Cesamet)*	2.2nM	1.8nM
JBT-101	5.7nM	56nM

\*psychotropic

# JBT-101 (Ajulemic Acid)

- **Orally Active Non-psychotropic CB1/2 agonist**
- **Effective in 15 animal models of Pain & Inflammation**
  - Analgesic effects: 1–10 mg/kg
  - Anti-inflammatory effects: 0.1-1 mg/kg
    - Modulate inflammatory mediators: PGJ, LXA4
  - Prevents inflammatory destruction
    - Suppress IL1 $\beta$ , IL6, IL8
    - Suppress MMP1, MMP3, MMP9
- **Clinical Studies**
  - 150 patients/volunteers safely treated
  - Completed Phase I (US, Eu)
  - Completed Phase IIa in Neuropathic Pain



## JBT-101

MW = 400.55

$T_{1/2}$  = ~4 Hr

$K_i$  (CB1/2) = 5.7 nM/56 nM

EC<sub>50</sub> (CB1/2) = 11.6 nM/13.4 nM

MTD > 100mg/kg

ED<sub>50</sub> = 0.5 - 5mg/kg

Dual Analgesic & Anti-inflammatory Drug

# Unique Product Profile to Treat OA and Pain

Drug	Analgesic	Anti-Inflam	No Side Effects				No Abuse Potential
			CNS	CV	Resp	GI	
JBT-101	✓✓	✓✓	✓	✓	✓	✓	✓
Opiates	✓✓	X	X	✓	X	X	X
NSAIDs	✓	✓	✓	✓	✓	X	✓
Antidepressants Anticonvulsants	✓	X	X	✓	X	X	X
COX-2 Inhibitors	✓	✓	✓	X	✓	✓	✓

JBT-101 safer than opiates, NSAIDs and Cox-2 Inh  
with potential to treat inflammation and pain



# JBT-101 Clinical Trials Summary

## Phase I SAD

- 32 healthy volunteers
- Single ascending dose design-10mg
- Endpoints: PK, Safety, Tolerability

## Phase II Refractory Chronic NP

- 21 patients with > 6 months continuous NP pain
- 20 mg => 40 mg, po, bid, x7 days
- Endpoints: Efficacy, Safety, Tolerability

## Phase I SAD/MAD

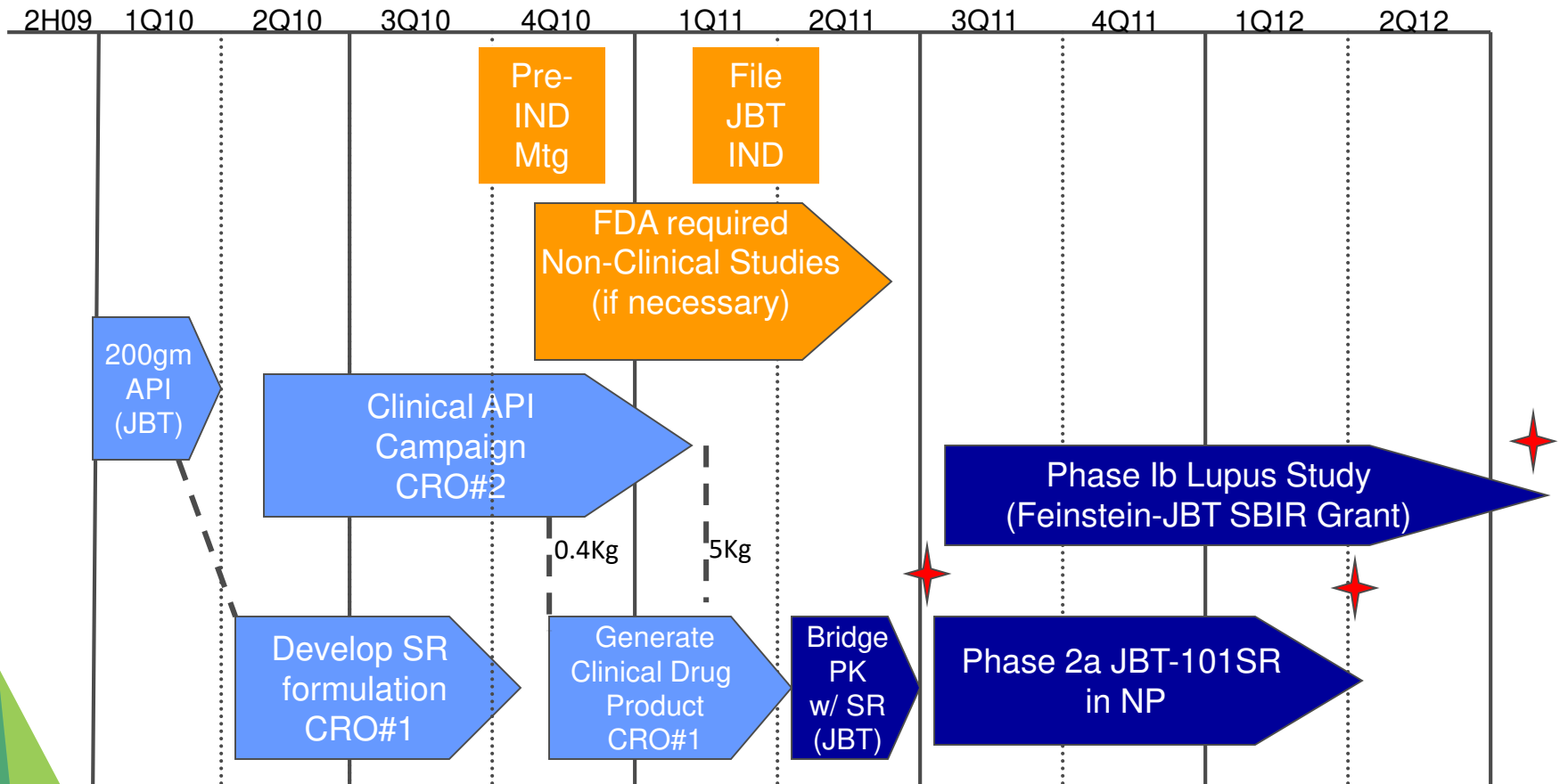
- 104 healthy volunteers
  - Single dose: 10, 20, 40, 80, 120, 150, 180, or 280mg
  - Multiple doses : 20, 40 & 80mg, tid
  - Endpoints: PK, AEs, Safety, MTD

JBT-101 dosed orally in 150 patients/volunteers

	<b>Cohort 1 Active vs Placebo</b>	<b>Cohort 2 Active vs Placebo</b>
<b>Primary Endpoint:</b> VAS Reduction	31% vs 2%*	18% vs 5%*
<b>Secondary Endpoint:</b> Responders (>30% pain reduction) VRS Reduction Allodynia Pressure Test	67% vs 10% 20% vs 4%** Variable	20% vs 10% 16% vs 1%** Variable
<b>Global Impression Score (CGI)</b> Clear improvement	<b>Cohort 1 &amp; 2 combined</b> 11 patients	
<b>NIDA Addiction Research Center Inventory- Marijuana (ARCI-M)</b>	No $\Delta$ between active and placebo groups	
<b>Safety &amp; Adverse Events</b>	No safety issues No $\Delta$ in AEs between active, placebo and baseline	

- $p \leq 0.032$ ; \*\* $p \leq 0.052$
- N=21 patients

# Timeline



Milestones: 2 Clinical trails + SR formulation

# JBT-101 Patent Estate

1992                      2008                      2009                      2010                                      2015                                      2020                                      2030                                      2031



US 5,338,753 – JBT101 Comp of matter



- NCE data exclusivity & Orphan Drug

2010– Composition, Dose & Sustained-release

2011– Method of Use – JBT101 Fibrotic Disease

2011– Improved Pharmaceutical Composition & Method of Synthesis

IP Counsel  
Landro & Anastasi  
Clark & Elbing

JBT-101 Franchise Covered Through ~ 2031



# Market Opportunity- Franchise in a product

JBT-101	Indication	Market
Extended release Capsules	<b>Chronic Pain:</b> Neuropathic pain, Cancer pain, Phantom limb pain, back pain, osteoarthritis, Fibromyalgia, Gout, Arthritis pain	\$30 billion
	<b>Autoimmune/Inflammatory Diseases:</b> MS, Scleroderma, Systemic Lupus, RA, Uveitis, Asthma, endometriosis, IBD	\$10 billion
Topical/Patch	<b>Local Pain &amp; Inflammation:</b> Neuropathic pain, Cancer pain, back pain, osteoarthritis, RA, Fibromyalgia, Gout, poison ivy, eczema, allergic dermatitis	\$5 billion
Sterile Solution-urinary, ophthalmic	<b>Bladder Pain:</b> Interstitial cystitis, overactive bladder, neurogenic detrusor overactivity	\$3 billion
	<b>Eye Disease:</b> Glaucoma, Uveitis	\$2 billion
Combo with Pain Rx (Opiates, NSAIDs, others)	<b>Chronic Pain-</b> Cancer pain, Neuropathic pain, Arthritis, etc.	\$10 billion

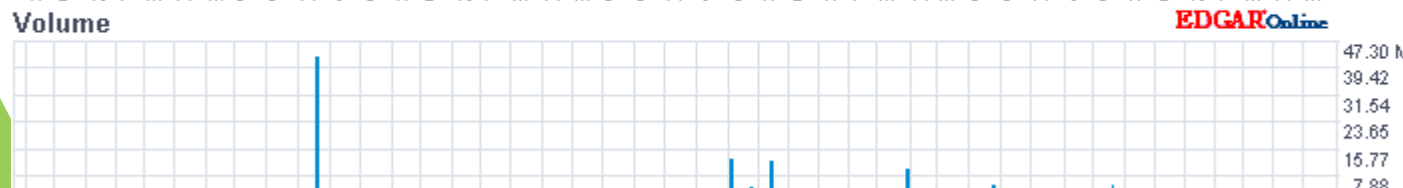
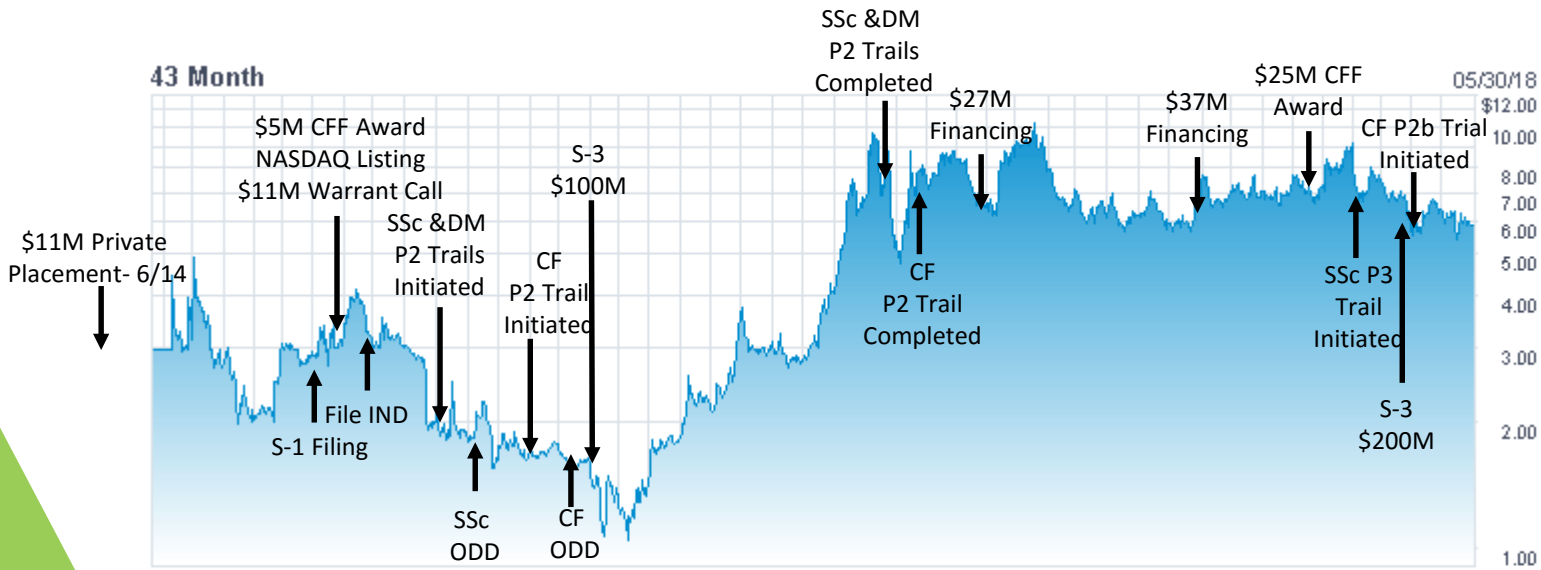
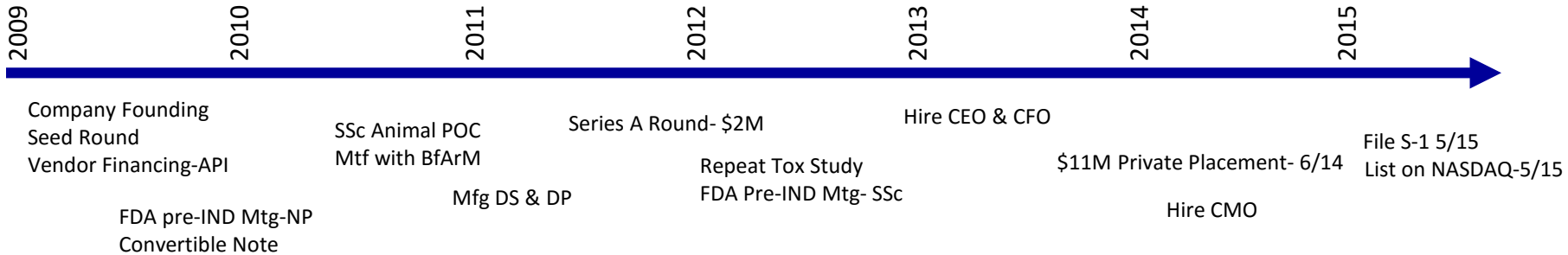
<b>Product</b>	<ul style="list-style-type: none"> <li>• First non-psychotropic CB1/CB2 Agonist for treating pain and inflammation</li> <li>• <b>POC</b> established in refractory neuropathic pain patients</li> </ul>
<b>Pipeline</b>	<ul style="list-style-type: none"> <li>• 1 Phase 2, 1 Preclinical and 2 lead optimization programs targeting endocannabinoid system</li> <li>• Multiple formats – sustained release, topical, patch</li> <li>• Multiple indications &amp; combinations with NSAIDs, opioids</li> </ul>
<b>Market</b>	<ul style="list-style-type: none"> <li>• Large unmet medical need-</li> <li>• Pain, Obesity, Neurodegenerative Disease- All \$ billion markets</li> </ul>
<b>Investor Opportunity</b>	<ul style="list-style-type: none"> <li>• Seeking Funding of \$5 Million to complete Phase 2 POC studies with SR formulation</li> <li>• Advance preclinical pipeline</li> </ul>

# Corbus Pivots

Risks	Original	Current
<b>Product</b>	Single Asset, 1 large indication	Single asset multiple indications
<b>IP</b>	Limited IP life with 5 yr NCE protection	Issued IP to 2033 + ODD
<b>Team</b>	2FTEs Mgmt + consultants	4 FTEs Mgmt w 120 yr experience -62 total FTEs
<b>Regulatory</b>	Repeat Tox study File new IND	Phase 3 with multiple FDA/EMA mtgs with agreement on endpoints
<b>Market</b>	Large Market	Niche/Orphan
<b>Financial</b>	Private/Angels	Public- 45% institutions
<b>Competition</b>	Opiates, NSAIDs	SSc, CF, DM, SLE (novel MOA)



# Corbus Funding History





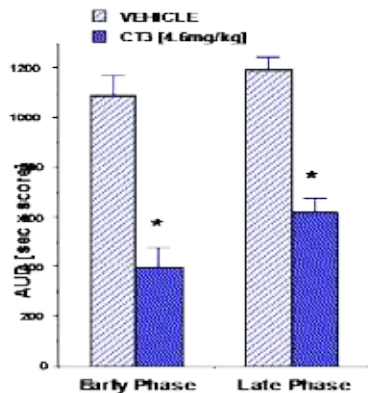
# Thank You!



# Back Up Slides

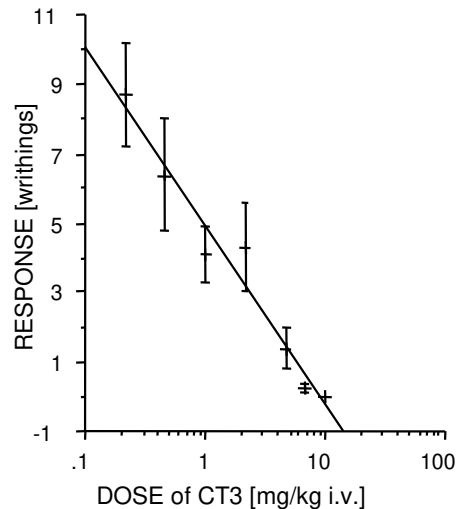
# JBT-101: Analgesic Activity

## Formalin Test



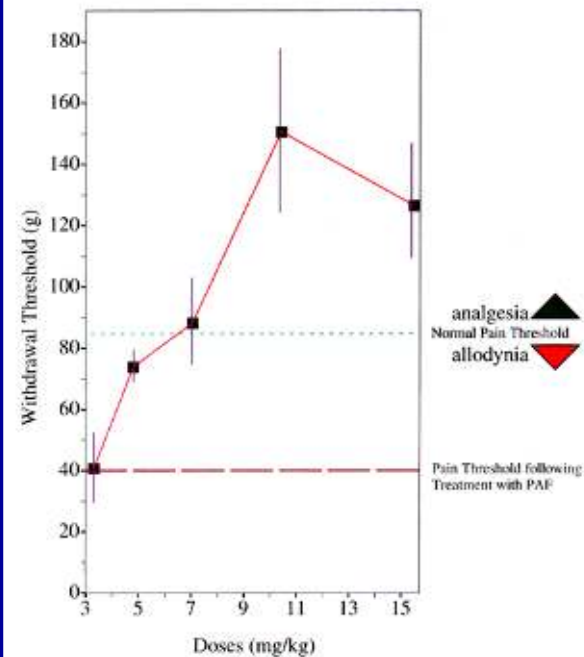
4.6 mg/kg JBT-101  
5% formalin sc in hindpaw  
Early phase: 0-15 min  
Late phase: 15-30 min

## Writhing Model



JBT-101 iv in 10% Cremophor  
0.02% phenylquinone

## Analgesia Model



JBT-101 reversed PAF induced  
Allodynia, improved analgesia

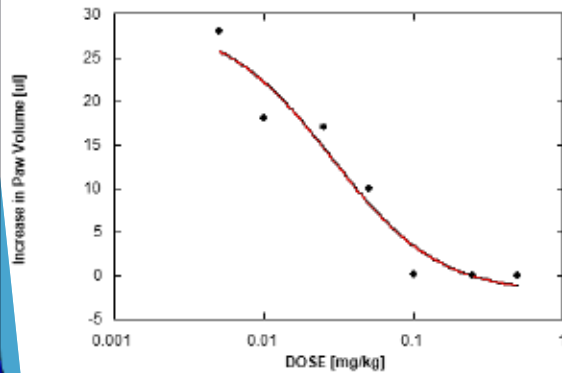
Life Sci, 1998

Neurosci, 2000

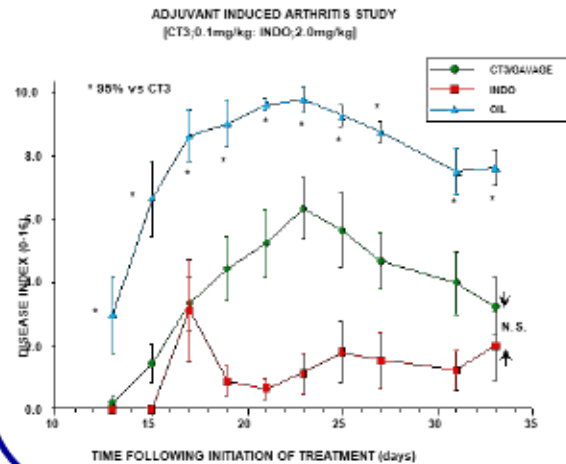
Reduces Pain in Animal Models

# JBT-101: Anti-inflammatory Activity

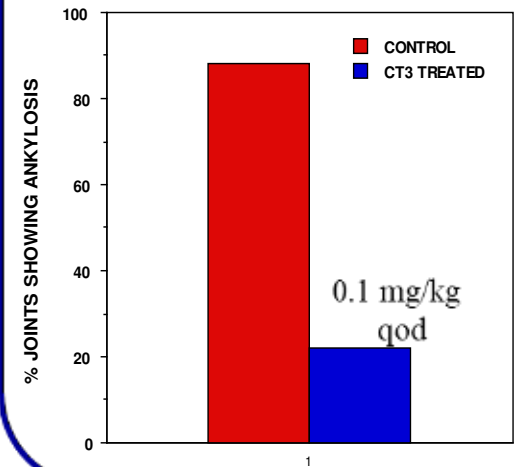
## AA-induced Paw Edema



## Adjuvant Arthritis Model



## Joint Damage Model



Life Science, 2004

Arthritis & Rheum, 1998

Reduces Inflammation & Joint Damage in Arthritis Model