Neuroscience and Pain

James Sullivan, Ph.D.

Divisional Vice President
Neuroscience Discovery
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Expanding Leadership in Neuroscience and Pain

- World's largest pharma market – growing at ~10 percent annually
  - Pain: $20 billion
  - Neurological/psychiatric: $44 billion
- Large unmet need and scientific opportunity
- Strong commercial foundation and established leadership
- Billion dollar opportunities for pain in community market
- Developing breakthrough science in pain and neurology

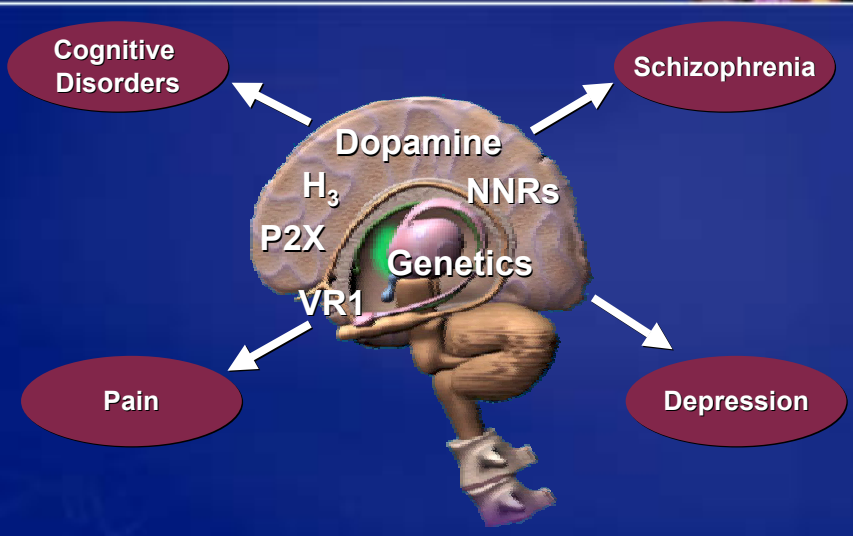
Established Leadership

STRONG FOUNDATION IN PAIN AND NEUROSCIENCE

- Major marketed products: $1.5 billion in sales
  - Depakote: #1 treatment for bipolar and #1 branded treatment for epilepsy
  - Recognized brands in pain management (Vicodin, Dilaudid, Mobic)
- Resources to develop breakthrough science
  - 350 scientists
  - Centers of Excellence (Ludwigshafen, Abbott Park)
- Strategic collaborations augment internal programs
  - NeuroSearch, Icagen, Myriad

Abbott's Leading-Edge R&D Strategy in Pain and Neuroscience

LEVERAGING INNOVATIVE TECHNOLOGY PLATFORMS AND EXISTING BRAND EQUITY



Neuroscience/Pain Pipeline

Advanced Preclinical	Phase I	Phase II	Phase III	Phase IV
COT kinase	ABT-325 (IL-18)	HUMIRA	HUMIRA	Biaxin XL
Signal transduction inhibitor	*Autoimmune disease*	*Crohn's disease*	*JRA*	Depakote ER
Cytokine inhibitor	ABT-828	*Psoriasis*	*PsA*	HUMIRA
Co-stimulation inhibitor	**ABT-202**	ABT-874 (J695)	*Ankylosing spondylitis*	Kaletra
Chemotaxis inhibitor	***Pain***	*Autoimmune disease*	Atrasentan	Meridia
Cell adhesion inhibitor	**ABT-894**	Atrasentan	*Prostate cancer*	Omnicef
ABT-769	***Pain***	*Kidney cancer*	Dilaudid CR	TriCor
VR1	**ABT-834**	*Ovarian cancer*	*Pain*	Zemplar
Na channel	***Cognition***	*Brain cancer*	ABT-773	Abbokinase
D3 antagonist	**ABT-239**	*Lung cancer*	*Infections*	Chirocaine
H3 antagonist	***Cognition***	ABT-510	r-UK	Mavik
NNR		*Cancer*	*Blood clots*	Precedex
5HT5		ABT-751	Zemplar oral	Synagis
P2X		*Cancer*	*Hyper-parathyroidism*	Tarka
D4 Agonist		Vicodin CR	Simdax	
Replication inhibitor		*Pain*	*Heart failure*	
Novel PI		ABT-089	Clivarine	
Anti-diabetes		*Cognition*	*DVT*	
Weight regulator		Iron oligosaccaride	Segard	
Next generation PPI		*Iron deficiency*	*Sepsis*	
LG122941		ABT-724	Febuxostat (TMX-67)	
		ED	*Gout*	
>70 other compounds		ABT-224	Asoprisnil (J867)	
		Constipation	*Fibroids*	
		Asoprisnil (J867)	Lupron 6 month Depot	
		Endometriosis	*Prostate Cancer*	
		J956		
		HRT		

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Anti-diabetes			*Sepsis*	
Weight regulator		*ED*	Febuxostat (TMX-67)	
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		HRT		

Neuroscience/Pain Pipeline – Today's Focus

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		HRT	Lupron 6 month Depot	
			Prostate Cancer	

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The Pain Market

PAIN – #1 REASON PATIENTS SEEK PHYSICIAN CARE

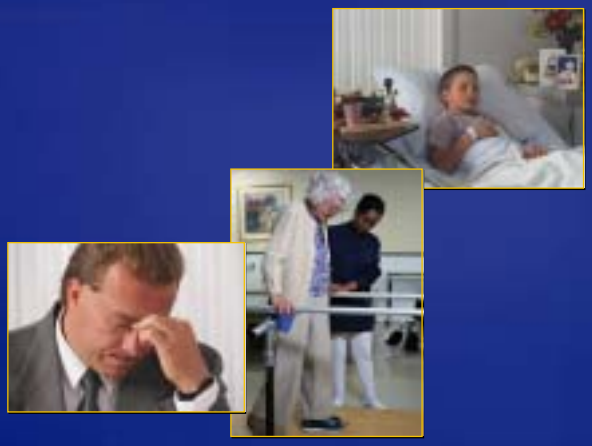
- $20 billion market worldwide – ~10 percent annual growth
- Vast, underserved patient population
- Need for more efficacious and better-tolerated drugs
  - No breakthrough classes of pain drugs in 30 years
  - Rapid advances in understanding of pain pathways have generated new molecular targets

May 19, 2003

Pain

TWO MAJOR PAIN STATES

- Inflammatory/nociceptive pain
- Neuropathic pain



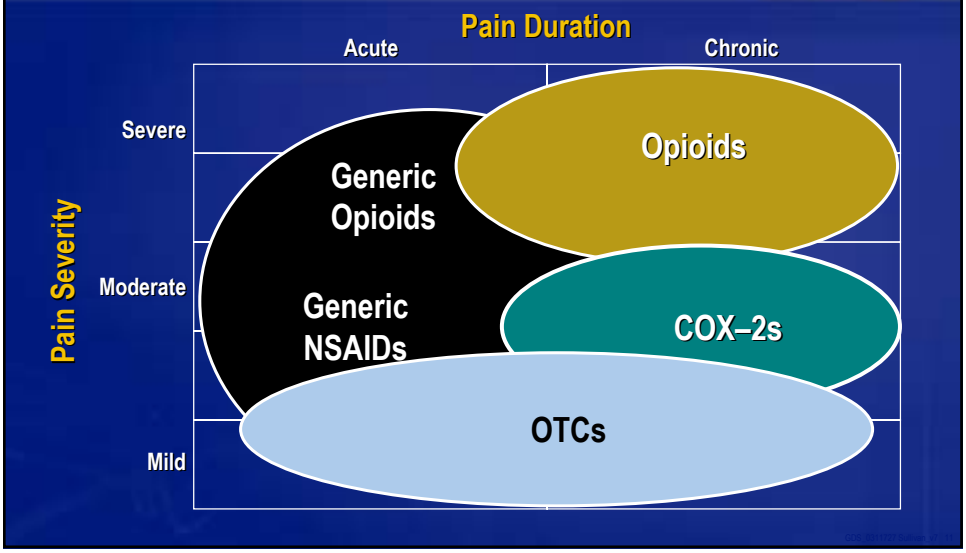
Pain

TWO MAJOR PAIN STATES

- Inflammatory/nociceptive pain
  - Acute – Post-op pain, bone fractures
  - Chronic – OA, RA, back pain, cancer pain
- Neuropathic pain

Inflammatory/Nociceptive Pain States

MODERATE TO SEVERE PAIN – 187 MILLION PRESCRIPTIONS ($5.5B);
GENERIC PRESCRIPTIONS MASK TRUE POTENTIAL OF THE MARKET



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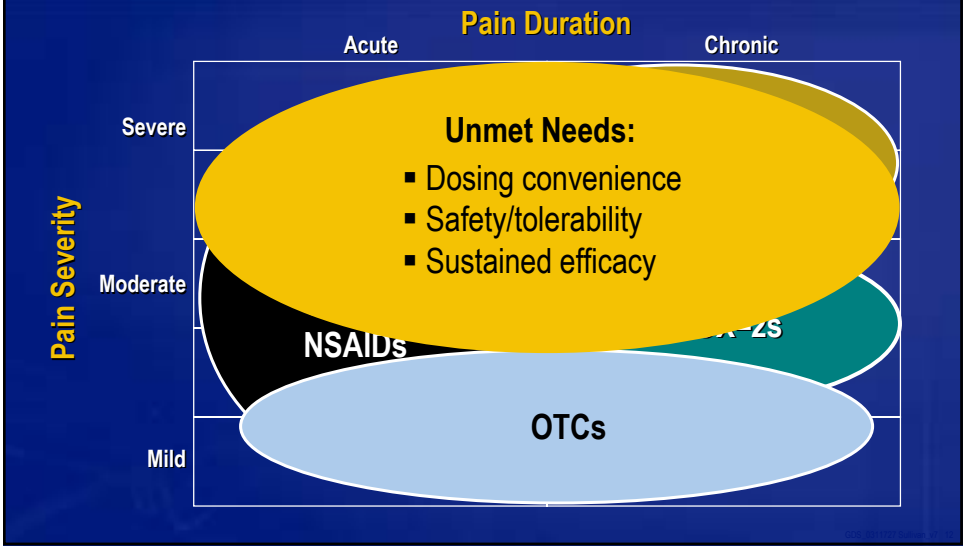
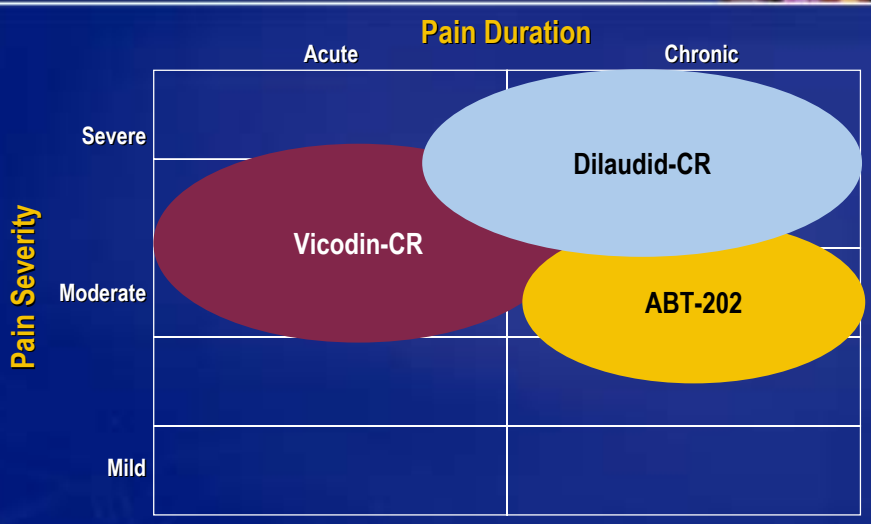


Inflammatory/Nociceptive Pain States

ABBOTT COMPOUNDS ADDRESS KEY AREAS OF UNMET NEED

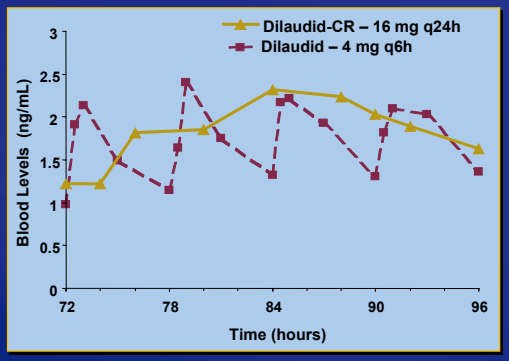


Near-Term Opportunity: Dilaudid-CR for Chronic Pain

PATIENT-FRIENDLY, ONCE-DAILY VERSION OF A WIDELY RECOGNIZED BRAND

- Addresses key unmet need of dosing convenience
- In late Phase III development
- Projected filing in 2004
- Peak-year potential of >$500 million in community market

PK Profile of Dilaudid-CR vs. Dilaudid

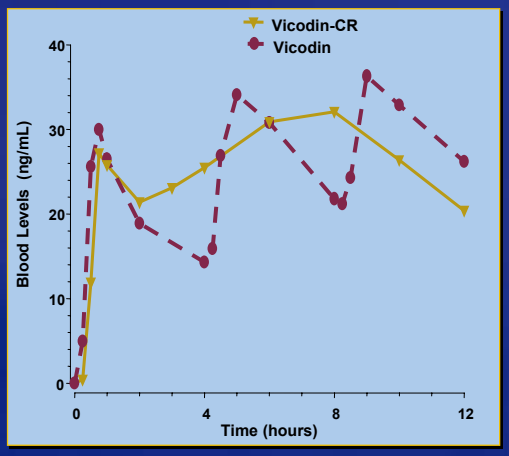


Near-Term Opportunity: Vicodin-CR for Acute Pain

MORE CONVENIENT DOSING OF A WIDELY RECOGNIZED BRAND

- 8 – 12 hour dosing (vs. 3 – 4 hour dosing with current version)
- Rapid and sustained analgesia for acute pain
- Currently in Phase II
- Projected filing in 2005
- Peak-year potential of >$500 million in community market

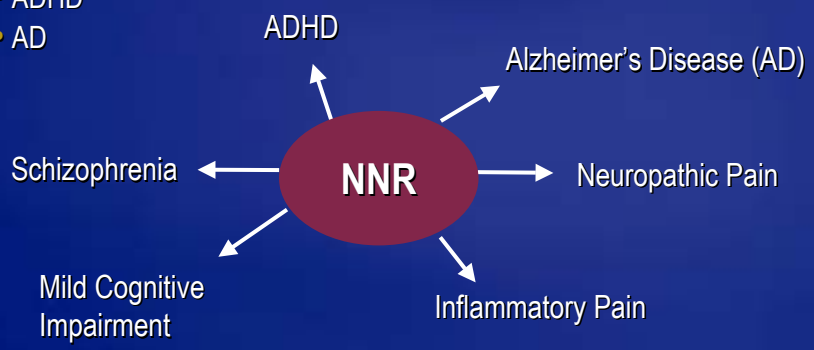
PK Profile of Vicodin-CR vs. Vicodin



Neuronal Nicotinic Acetylcholine Receptor (NNR)

BREAKTHROUGH TECHNOLOGY PLATFORM FOR PAIN / NEUROSCIENCE

- Abbott is the first company to establish efficacy of NNRs in:
  - Pain
  - ADHD
  - AD



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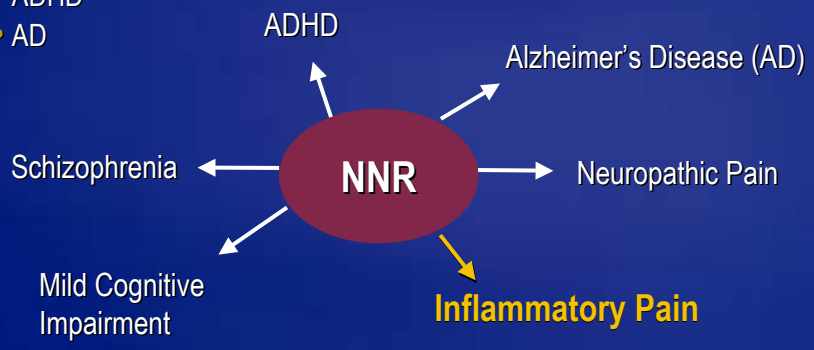


ABT-202: NNR for Chronic Inflammatory/Nociceptive Pain

EARLY-STAGE DEVELOPMENT

- Superior efficacy vs. COX-2/NSAIDs
- Efficacy comparable to opioids in inflammatory pain models
- Tolerability very favorable vs. opioids

Preclinical Efficacy – Inflammatory/Nociceptive Pain

	Mild-Moderate	Moderate-Severe
ABT-202	>75%	>75%
COX-2	>75%	<30%
Opioids	>75%	>75%

Pain

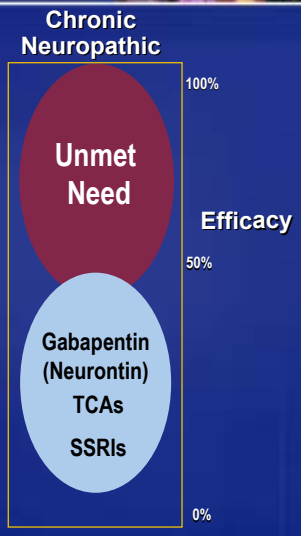
TWO MAJOR PAIN STATES

- Inflammatory/nociceptive pain
- Neuropathic pain – encompasses a wide range of pain syndromes
  - Diabetic neuropathy
  - Cancer neuropathy
  - HIV pain
  - Postherpetic neuralgia

Neuropathic Pain

GROWING MARKET WITH SIGNIFICANT UNMET MEDICAL NEEDS

- 10 million patients worldwide
- Current market leaders only offer modest efficacy
- Key needs:
  - Greater efficacy
  - Faster onset of action



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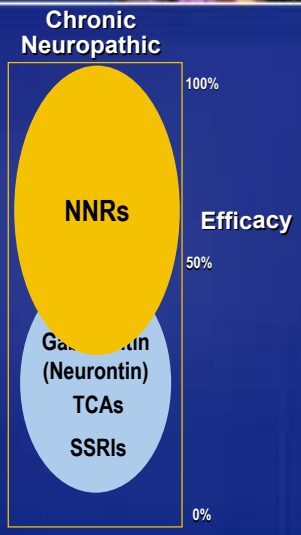
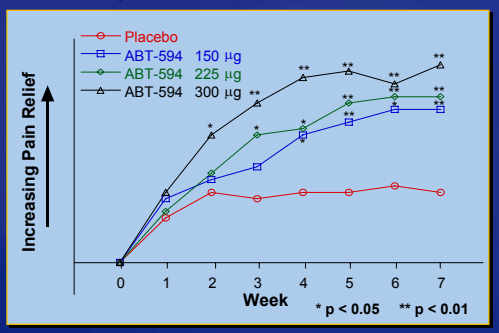


ABT-594: First-Generation NNR

EFFICACY IN MULTIPLE CLINICAL MODELS

- Efficacy comparable to market leader in neuropathic pain
- Limited tolerability
  - Key Issue: nausea and GI side effects
- Discovery goal: Identify compound with 30-fold improvement in therapeutic index

Efficacy in Neuropathic Pain Patients



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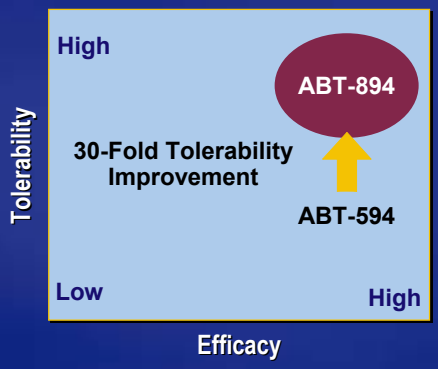
EFFICACY IN MULTIPLE CLINICAL MODELS

- Efficacy comparable to market leader in neuropathic pain
- Limited tolerability
  - Key Issue: nausea and GI side effects
- Discovery goal: Identify compound with 30-fold improvement in therapeutic index
- Next-generation compound: ABT-894



ABT-894: Next-Generation NNR

EARLY-STAGE DEVELOPMENT FOR NEUROPATHIC PAIN

- Full efficacy in multiple preclinical models of neuropathic pain

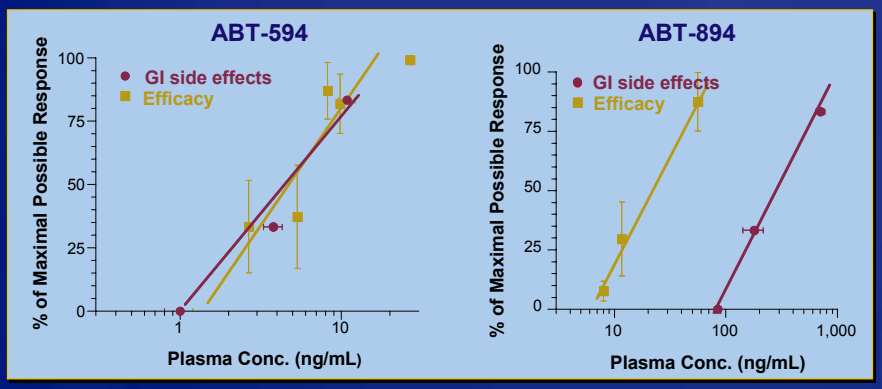
Preclinical Efficacy – Neuropathic Pain

	Sciatic Nerve Injury	Chemotherapy
ABT-894	>75%	>75%
COX-2	<30%	<30%
Gabapentin (Neurontin)	>75%	50%

ABT-894: Next-Generation NNR

FULL EFFICACY WITHOUT GI SIDE EFFECTS

- Exhibits marked improvement vs. ABT-594 in models of neuropathic pain



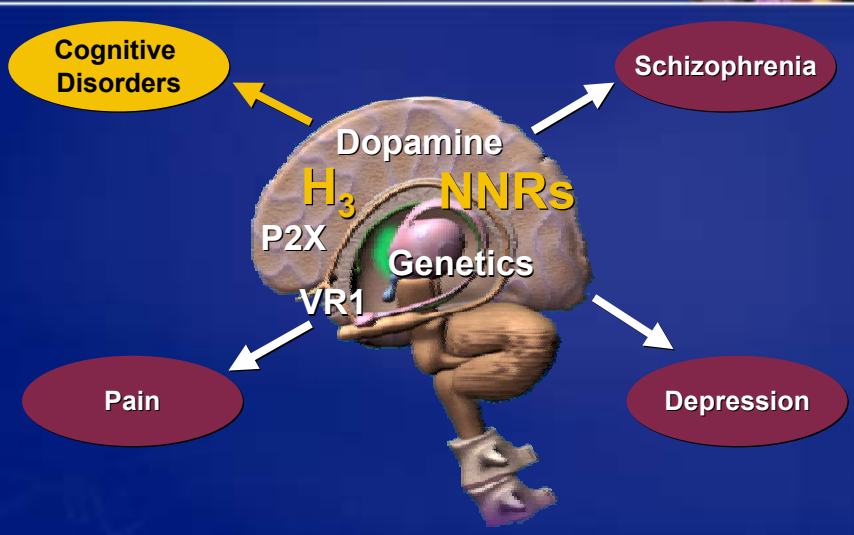
Abbott Is Poised to Expand Its Presence in Pain

SIGNIFICANT NEAR-TERM AND LONG-TERM OPPORTUNITY

- Today
  - Widely recognized brand names in pain (Vicodin, Dilaudid, Mobic)
- Future
  - Potential for combined sales of >$1 billion in community market
    - Dilaudid-CR: projected 2004 filing
    - Vicodin-CR: projected 2005 filing
  - Long-term potential to revolutionize pain treatment
    - 2008 – 2010: ABT-202 and ABT-894

Abbott's Leading-Edge R&D Strategy in Neuroscience

LEVERAGING INNOVATIVE TECHNOLOGY PLATFORMS AND EXISTING BRAND EQUITY



Cognitive Disorders

- ADHD, mild cognitive impairment, schizophrenia, and Alzheimer's disease affect greater than 35 million worldwide
- Current therapies
  - Weak efficacy in Alzheimer's disease
  - No treatments available for cognitive aspects of schizophrenia
  - Stimulants used to treat ADHD

Neuroscience Pipeline – Today's Focus

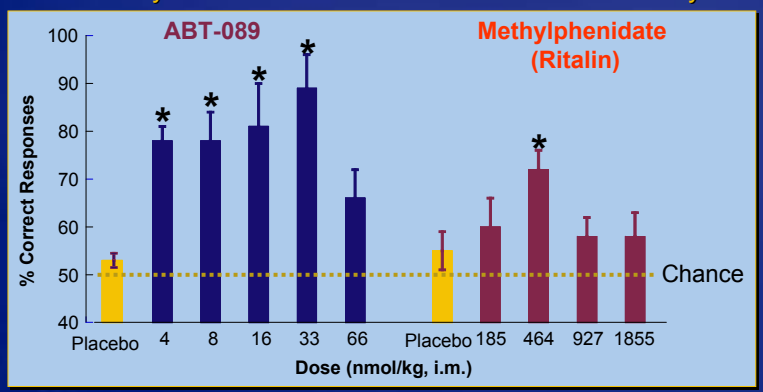
Advanced Preclinical	Phase I	Phase II	Phase III	Phase IV
COT kinase Signal transduction inhibitor Cytokine inhibitor Co-stimulation inhibitor Chemotaxis inhibitor Cell adhesion inhibitor **ABT-769** **VR1** **Na channel** **D3 antagonist** **H3 antagonist** **NNR** **5HT5** **P2X** **D4 Agonist** Replication inhibitor Novel PI Anti-diabetes Weight regulator Next generation PPI LG122941 *>70 other compounds*	ABT-325 (IL-18) *Autoimmune disease* ABT-828 **ABT-202** ***Pain*** **ABT-894** ***Pain*** **ABT-834** ***Cognition*** **ABT-239** ***Cognition***	HUMIRA *Crohn's disease* *Psoriasis* ABT-874 (J695) *Autoimmune disease* Atrasentan *Kidney cancer* *Ovarian cancer* *Brain cancer* *Lung cancer* ABT-510 *Cancer* ABT-751 **Vicodin-CR** ***Pain*** **ABT-089** ***Cognition*** *ED* ABT-224 *Constipation* Asoprisnil (J867) *Endometriosis* J956 *HRT*	HUMIRA *JRA* *PsA* *Ankylosing spondylitis* Atrasentan **Dilaudid-CR** ***Pain*** *Infections* r-UK *Blood clots* Zemplar oral *Hyper-parathyroidism* Simdax *Heart failure* Clivarine *DVT* Segard *Sepsis* Febuxostat (TMX-67) *Gout* Asoprisnil (J867) *Fibroids* Lupron 6 month Depot *Prostate Cancer*	**Depakote-ER** Meridia Omnicef TriCor Zemplar Abbokinase Chirocaine Mavik Precedex Synagis Tarka

ABT-089: NNR for Cognitive Disorders

STRONG EFFICACY WITHOUT STIMULANT-LIKE SIDE EFFECTS

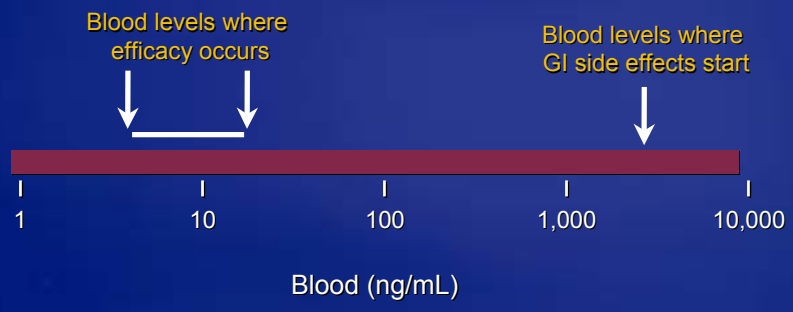
- Preclinical profile suggests utility in cognitive deficits in ADHD, AD and schizophrenia

Efficacy in Preclinical Model of Attention/Distractibility



ABT-089: NNR for Cognitive Disorders

- Excellent safety profile in preclinical models
  - >100-fold separation between efficacy and GI side effects

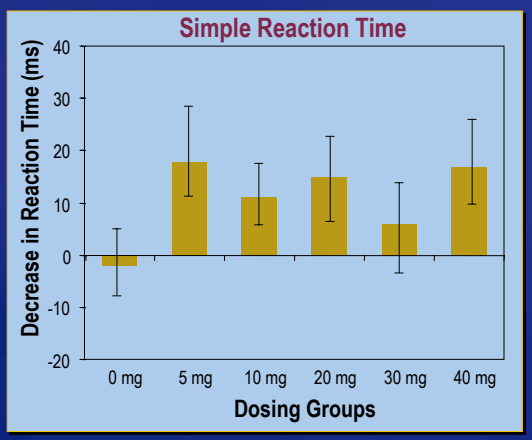


ABT-089: Next-Generation NNR

PHASE I DATA SUPPORTS PRECLINICAL PROFILE

- Phase I completed
  - Efficacy signal
  - Very well-tolerated
- Phase II underway
  - Efficacy studies
    - AD
    - ADHD
    - Schizophrenia

Improvement in Measure of Attention in Humans



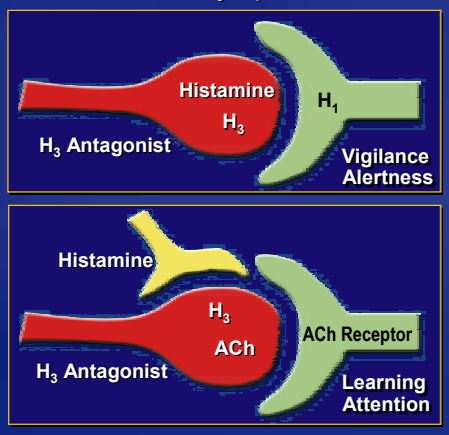
Histamine H_3 Receptors

NEW MOLECULAR APPROACH TO ATTENTIONAL/COGNITIVE DISORDERS

Histamine modulates vigilance and alertness

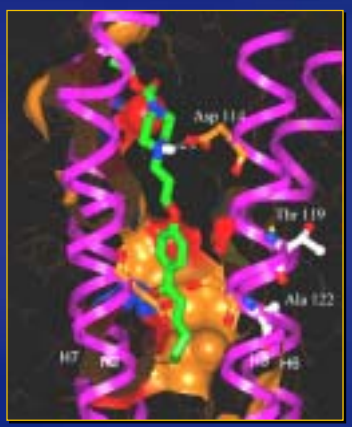
Acetylcholine (ACh) is important for learning and attention

Brain Synapse



Novel H_3 Receptor Antagonists Identified

- Designed by molecular modeling (structural biology)
- Potent and selective antagonists identified
- Lead compounds active in preclinical models of attention/cognition



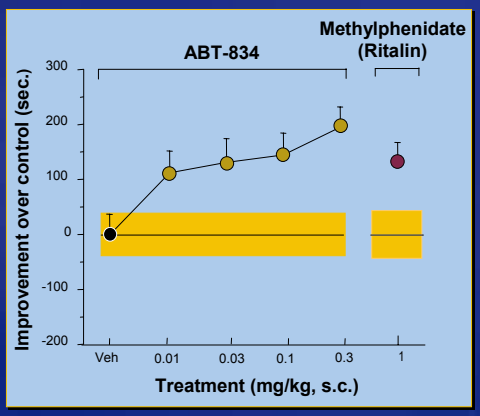
Interaction of Abbott Compound With Human H_3 Receptors

H_3 Antagonists for Cognitive Disorders

ABT-834 – EARLY CLINICAL DEVELOPMENT

- Potent and selective H_3 antagonist
- Efficacy in attention/ cognition models
- Excellent safety and tolerability
  - No stimulant liability unlike stimulants
- Very favorable PK
  - No drug-drug interactions unlike atomoxetine (Strattera)

Rodent Model of Attention/Impulsivity



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