Supernus Pharmaceuticals

Investor Day

April 16, 2019

Introduction and Agenda

Jack Khattar
President and Chief Executive Officer

Supernus® Pharmaceuticals

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Agenda

Introduction

Corporate Overview

Product Candidates

- SPN-812 – ADHD
- SPN-810 – Impulsive Aggression
- SPN-604 – Bipolar Disorder

General Q&A and Closing Comments

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Presenters

SUPERNUS PHARMACEUTICALS

Jack Khattar
President and Chief Executive Officer

Stefan Schwabe, M.D., Ph.D.
EVP, Research and Development, Chief Medical Officer

Todd Horich, Ph.D., MBA
VP, Marketing

Taylor Raiford
VP, Sales and Market Access

Presenters

ADVISORS

Andrew J. Cutler, M.D.
EVP & Chief Medical Officer, Meridien Research
Clinical Professor of Psychiatry, SUNY Upstate Medical University

Robert Findling, M.D., MBA
Leonard Helen R. Professor of Child & Adolescent Psychiatry
Director of Child & Adolescent Psychiatry, Johns Hopkins University
VP of Psychiatric Services and Research, Kennedy Krieger Institute

Supernus® Pharmaceuticals

Strong Experience in CNS including ADHD

Ten Marketed Products Using Our Technologies

Supernus® Pharmaceuticals

Trokendi XR®
(topiramate) extended-release capsules

Oxtellar XR®
(oxcarbazepine) extended-release tablets

Shire / Takeda	Carbatrol®
	Adderall XR®
	Equetro®
	Intuniv®
	Mydayis®
GALDERMA	Oracea®
ALLERGAN	Sanctura XR®
United Therapeutics Corporation	Orenitram®

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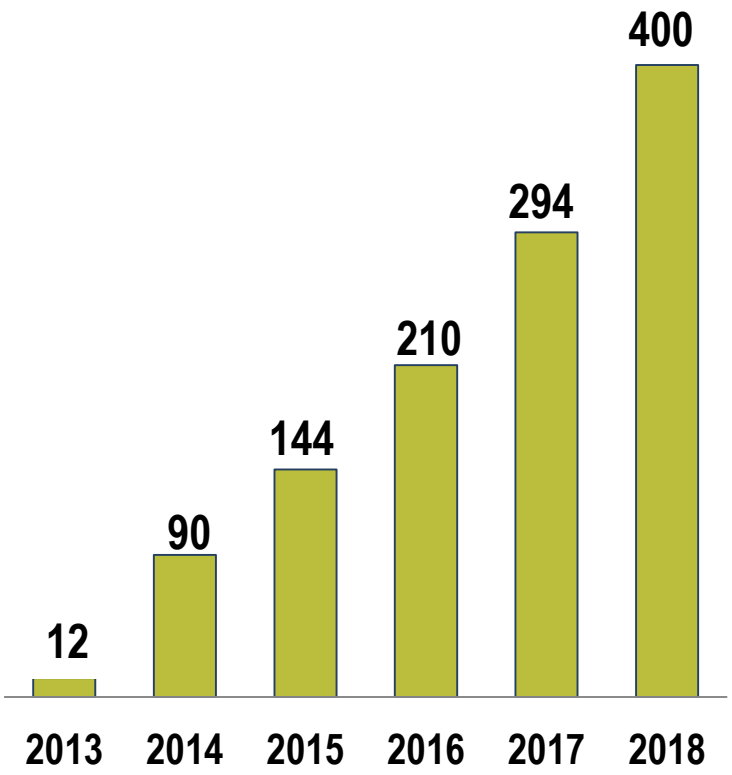
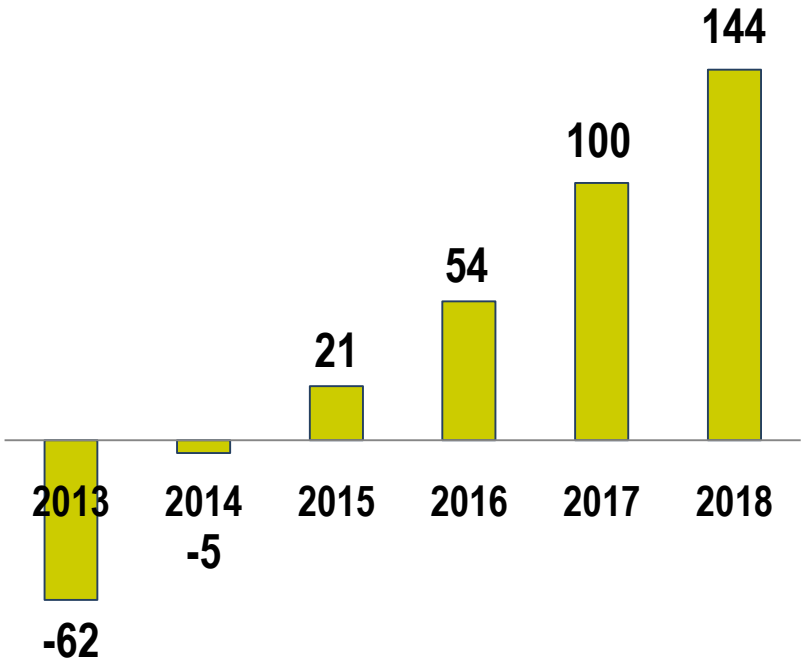
Strong Sales and Operating Earnings Growth

Total Net Product Sales ($ Millions)



Total Operating Earnings ($ Millions)



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Robust Portfolio of CNS Products

	Product	Indication	Development	NDA
Marketed	Trokendi XR® (topiramate) extended-release capsules	Epilepsy / Migraine*		
Marketed	Oxtellar XR® (oxcarbazepine) extended-release tablets	Epilepsy		
Pipeline	SPN-812	ADHD	Phase III	2H 2019
Pipeline	SPN-810	Impulsive Aggression	Phase III	2H 2020
Pipeline	SPN-604	Bipolar Disorder	Phase III (2H 2019)	
Pipeline	SPN-809	Depression	IND/Phase II Ready	
Pipeline	SPN-817	Severe Epilepsy	Phase I	

*Prophylaxis of migraine in adolescents and adults

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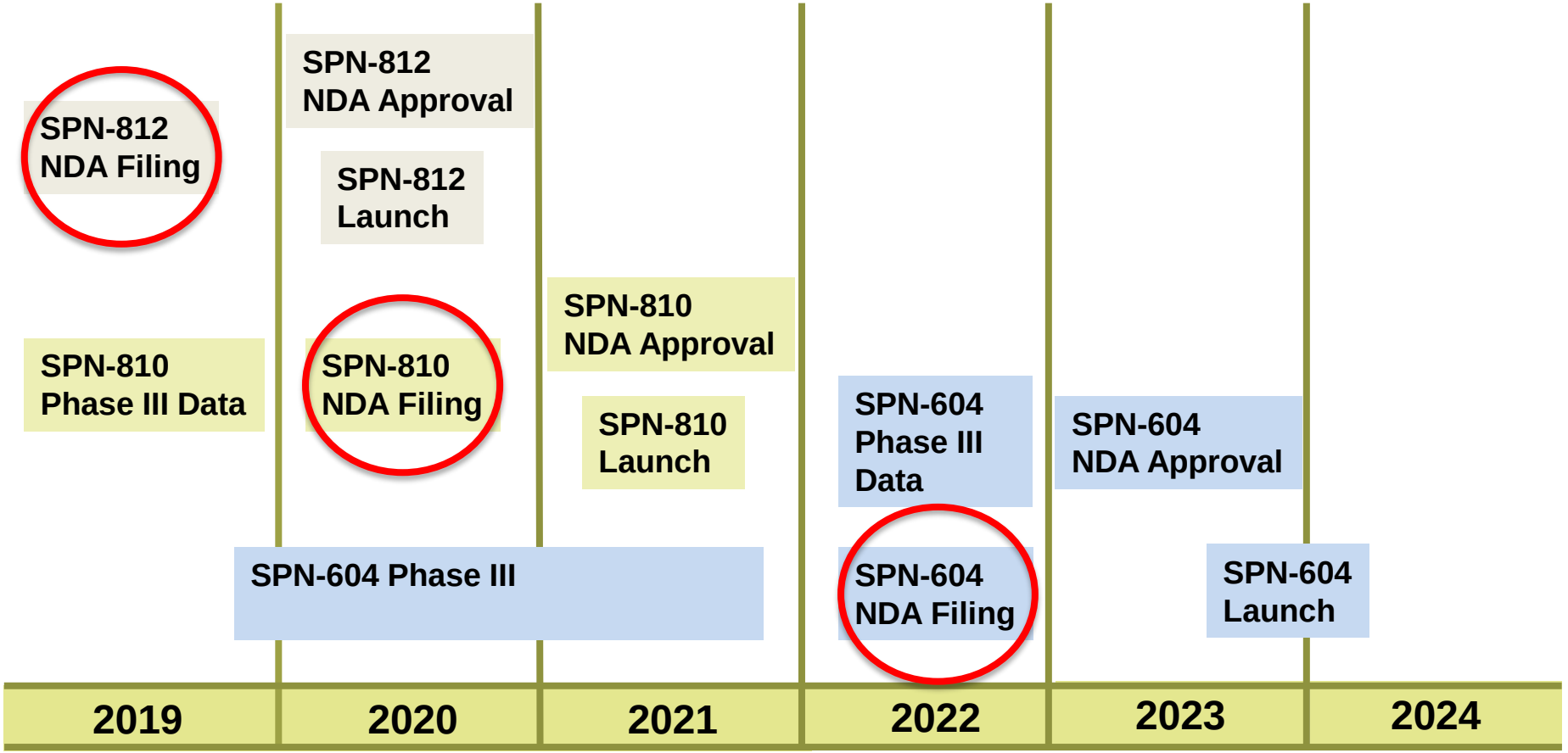
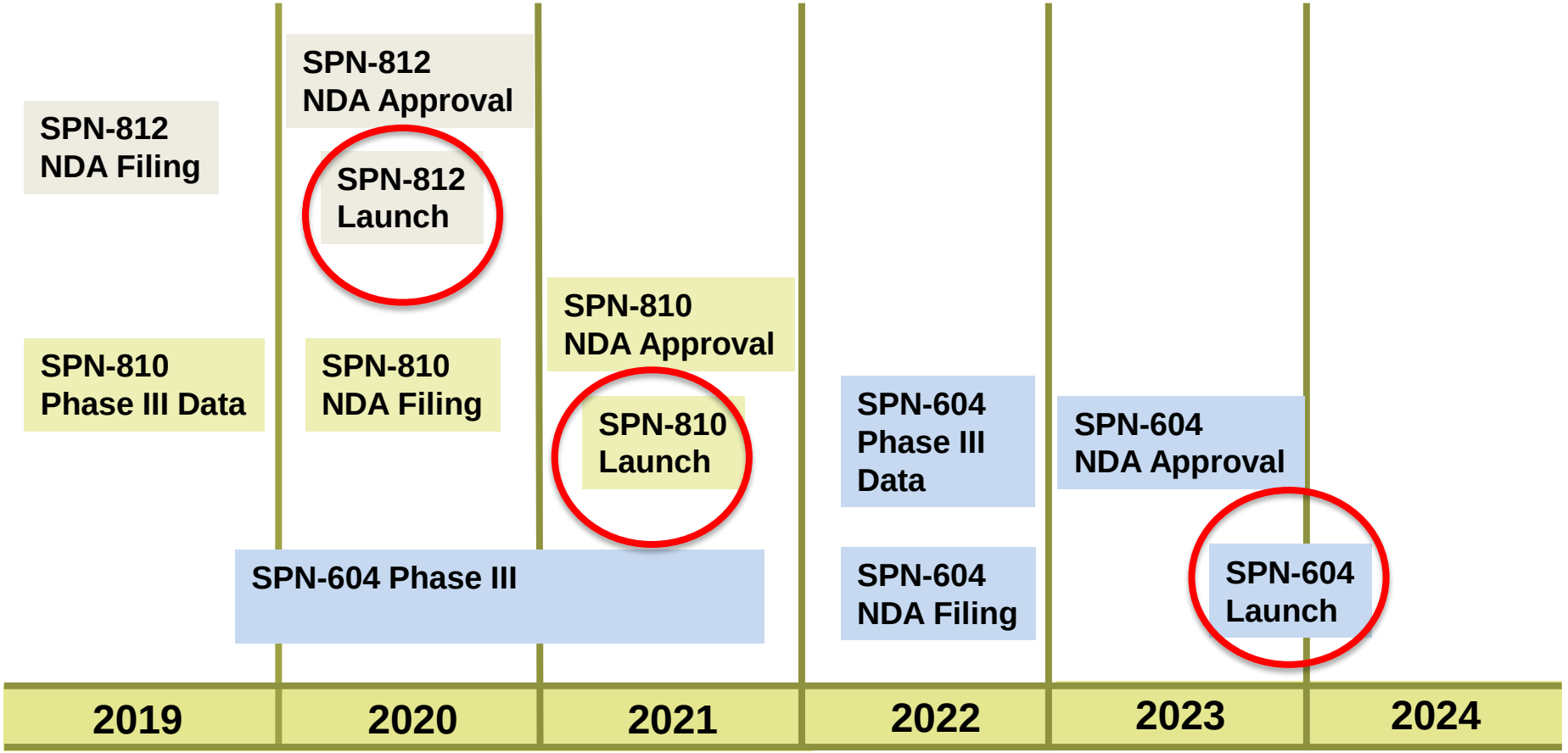
Supernus Near-Term Milestones



Above timelines represent management's estimates that are subject to several factors that are beyond our control and actual results may be significantly different from our estimates

Supernus Near-Term Milestones



Above timelines represent management's estimates that are subject to several factors that are beyond our control and actual results may be significantly different from our estimates

Positioned For Continued Strong Growth

Growth Potential for Existing Products

Potential Peak Sales for Oxtellar XR® and Trokendi XR® >$500M

Innovative Late Stage Portfolio in Psychiatry

SPN-810	**First Product to be Developed for Impulsive Aggression**
SPN-812	**Well Differentiated Novel Non-Stimulant**
SPN-604	**Novel Product for Bipolar Disorder**

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ADHD Landscape: Significant Unmet Medical Need

Andrew J. Cutler, M.D.
EVP & Chief Medical Officer, Meridien Research
Clinical Professor of Psychiatry, SUNY Upstate Medical Univ.

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Presentation Overview

- ADHD is heterogeneous in biology, symptoms, impairments and comorbidities
- While there are many current medications, most are stimulants
- Big unmet need for non-stimulant (non-scheduled) medication with broad spectrum/consistent efficacy and well tolerated

ADHD = Attention-Deficit/Hyperactivity Disorder

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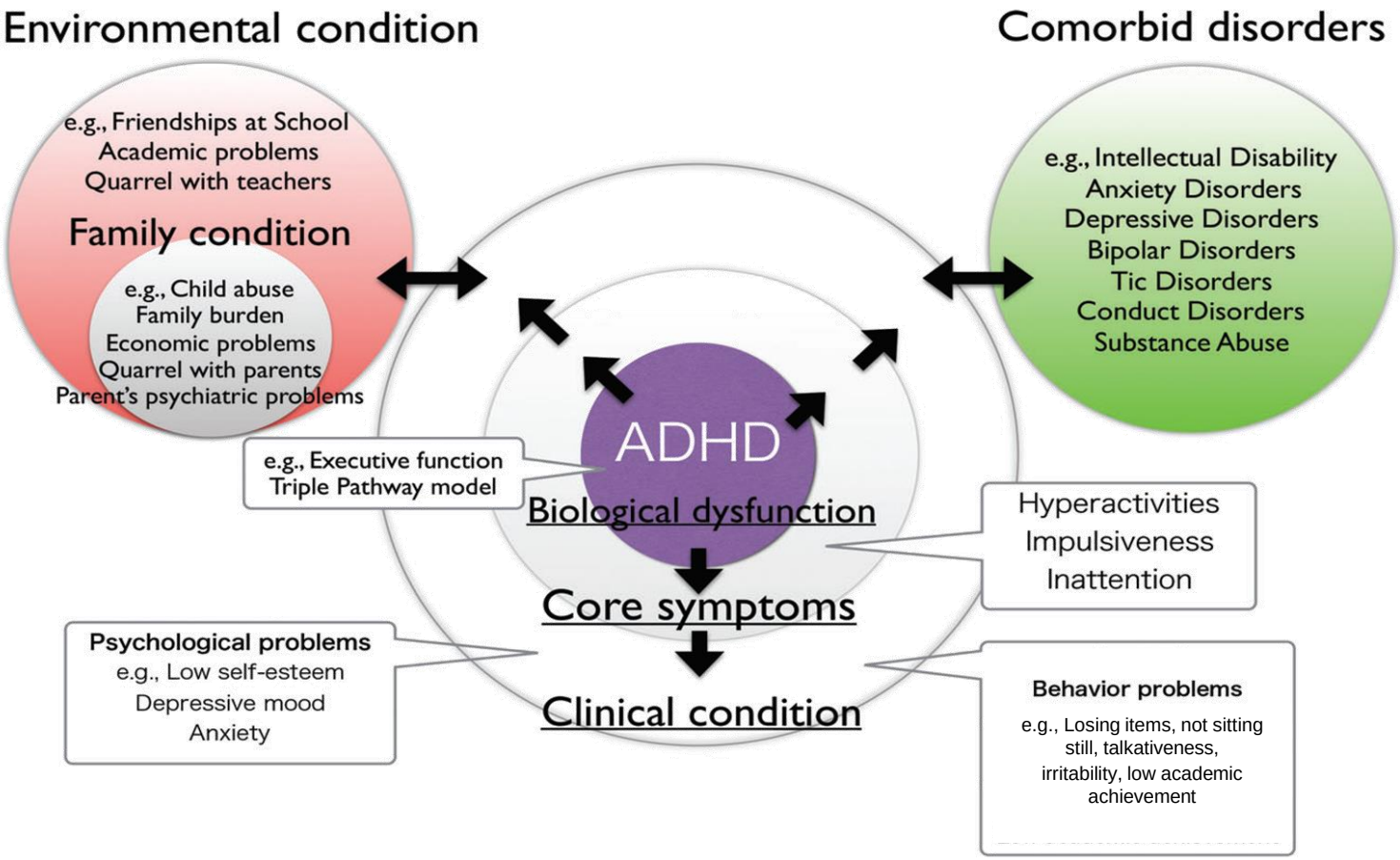
An Overview of ADHD Symptoms



Usami M et al. *PCN Front Rev*. 2016;70(8):303-317.

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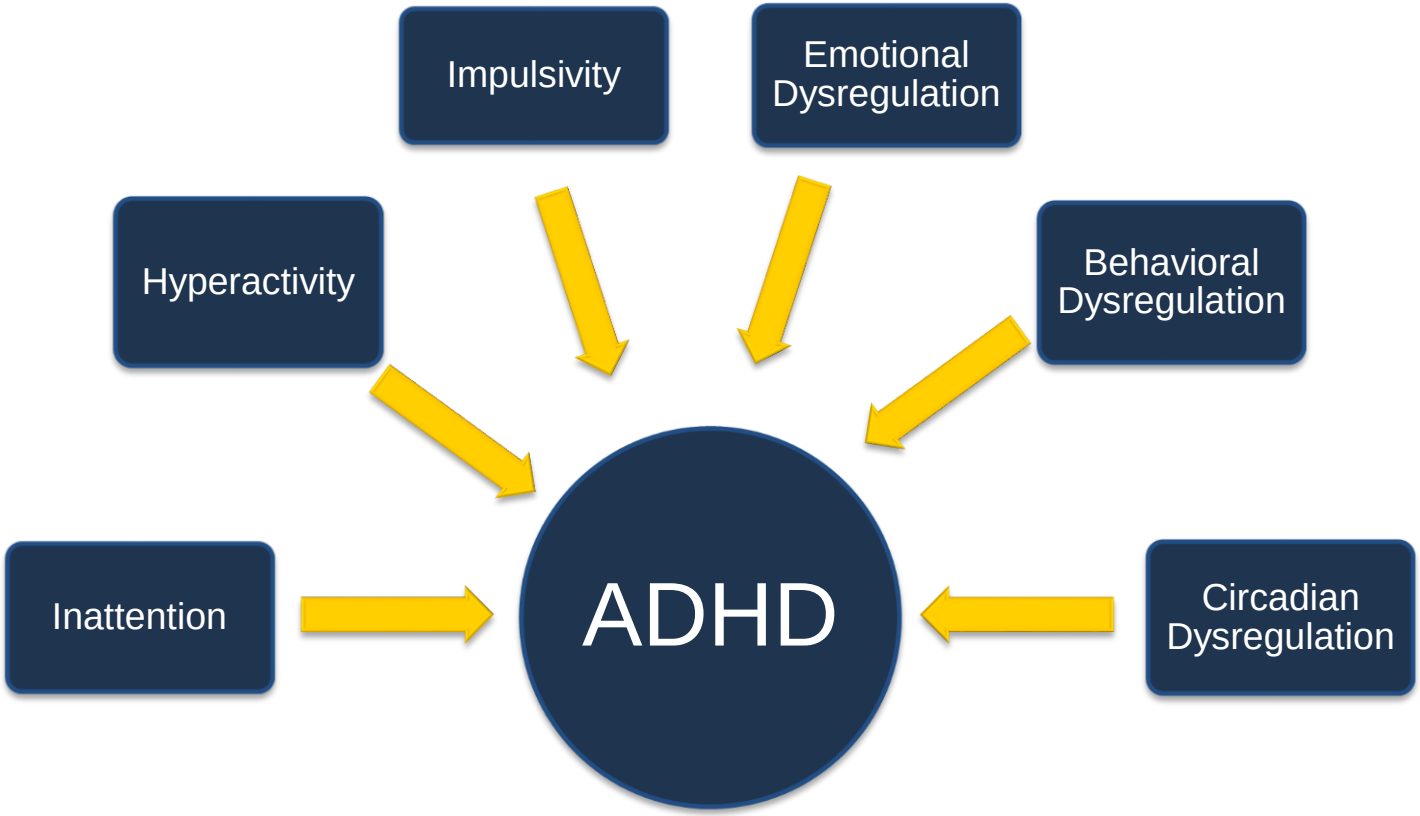
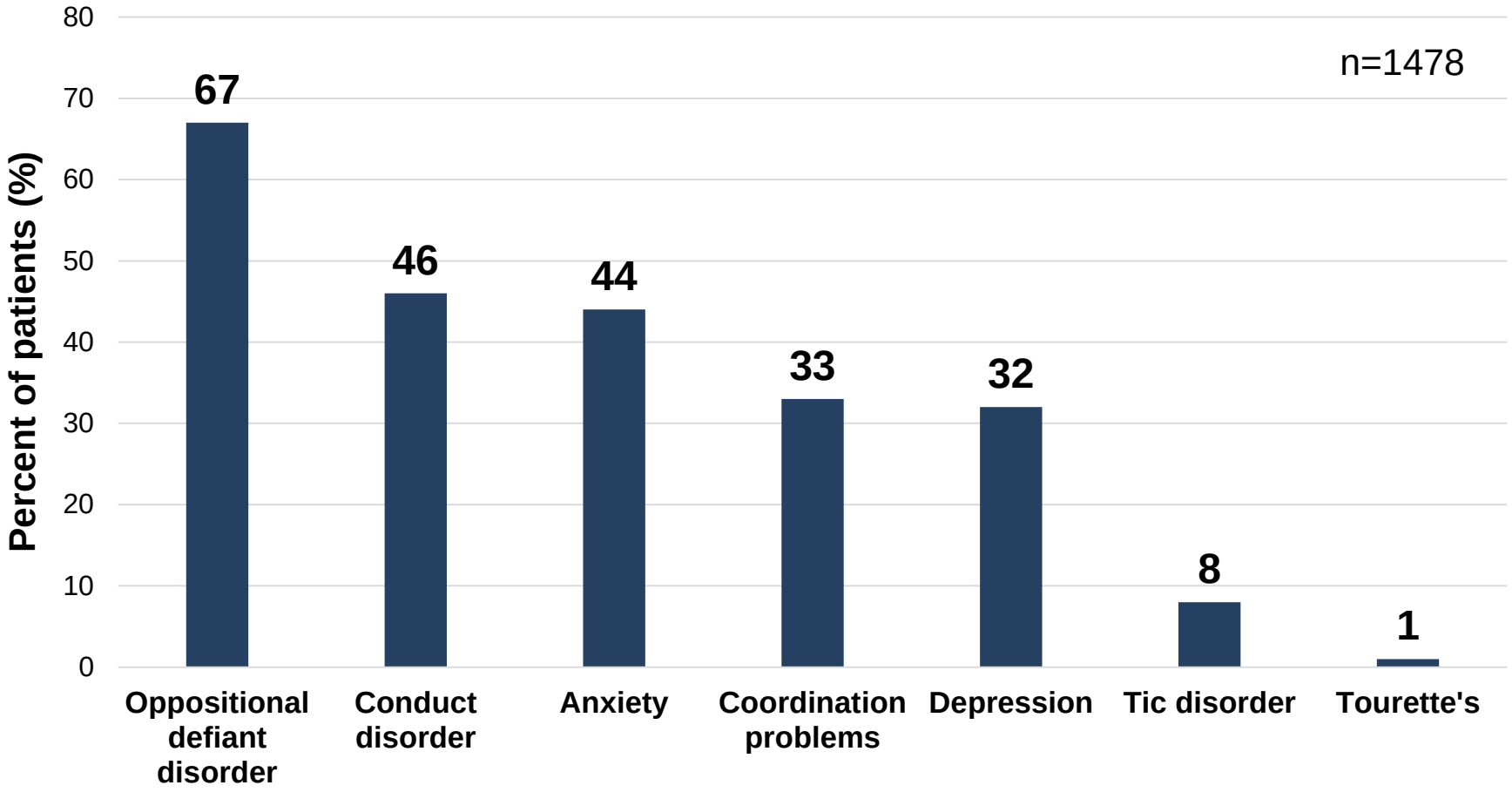
The ‘Reality’ of ADHD: A Heterogeneous Symptom Presentation Is Common



Conditions Coexistent with ADHD



Steinhausen HC, et al. *Eur Child Adolesc Psychiatry*. 2006; 15: I25-I29.

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Impairments Associated with ADHD

- Developmental delays
  - Mild delays in language, motor, or social development often co-occur with ADHD
- Impaired academic or work performance
  - Difficulty in school, poor transitions to middle school, high school, college and work
  - Poor occupational functioning (eg, completing paperwork, meeting deadlines)

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC; 2013.

Shaw M, Hodgkins P, Caci H, et al. *BMC Med*. 2012;10:99

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Impairments Associated with ADHD

- Cognitive deficits
  - Tests of attention, executive function, or memory may reveal cognitive problems
  - Not sufficiently sensitive or specific to serve as diagnostic indices
- Emotional impairments
  - Low frustration tolerance, irritability, or mood lability
  - By early adulthood, ADHD is associated with an increased risk of suicide attempt, primarily when comorbid with mood, conduct, or substance use disorders

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC; 2013.

Shaw M, Hodgkins P, Caci H, et al. *BMC Med*. 2012;10:99

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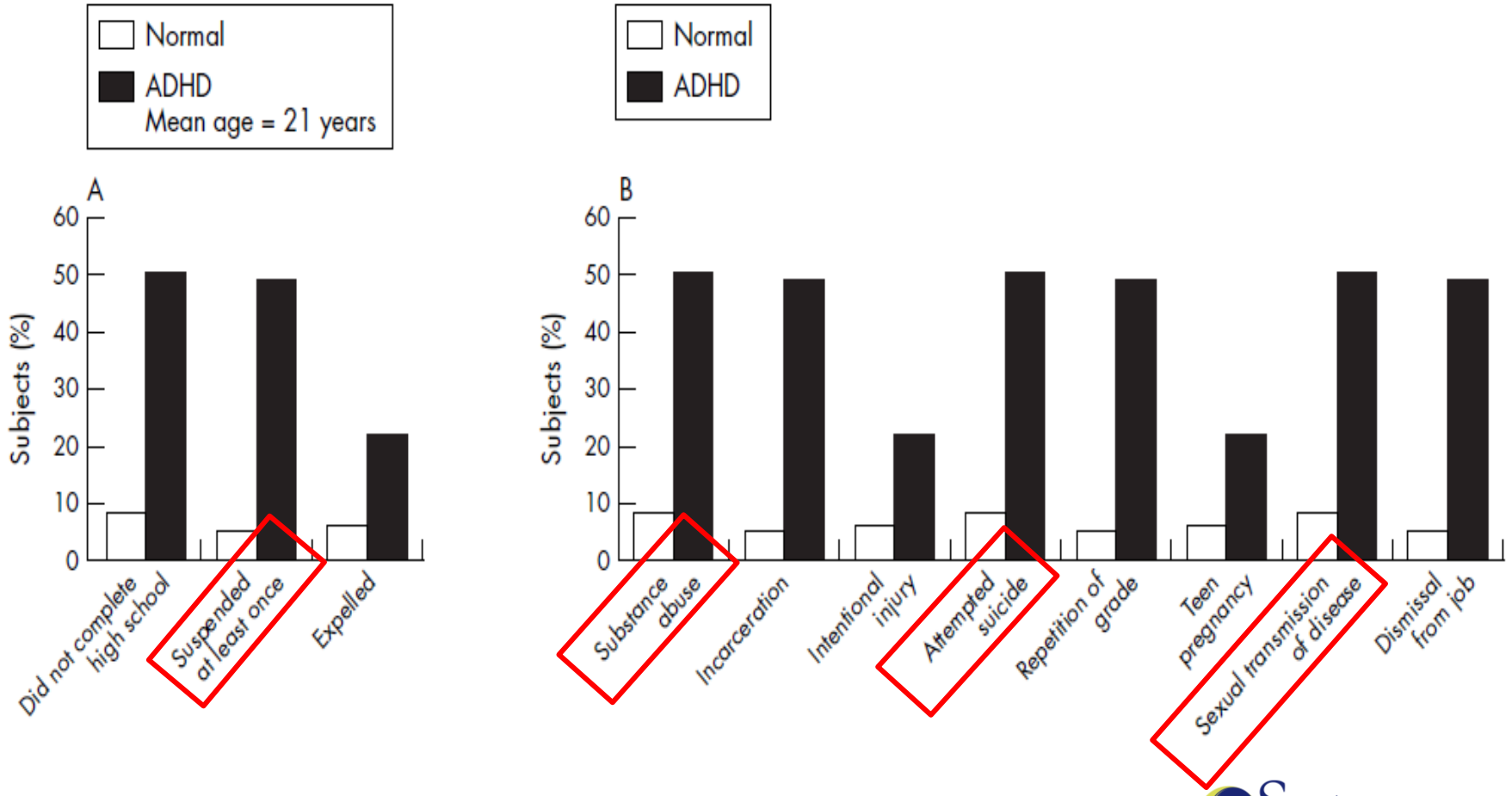
Impact of ADHD on School Attendance and Health, Social, and Psychiatric Wellbeing



Harpin VA. *Arch Dis Child* 2005;90(Suppl I):i2–i7.

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Comorbid Anxiety and Depression

- Anxiety is one of the most common comorbidities
  - Up to 50% of adults and 20-50% of children and teens with ADHD
  - Stimulants are “contraindicated” for anxiety
  - Studies of atomoxetine in children and adults show improvement in both ADHD and anxiety symptoms; higher effect size on ADHD with comorbid anxiety

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC; 2013; Masi L, Gignac M. *Clin Psychiatry.* 2015:1(1):5;1-9; Kessler RC, et al. Arch Gen Psychiatry. 2005;62(6):593-602; Orr K, Taylor D. CNS Drugs.2007;21(3):239-257; Waxmonsky JG. Essent Psychopharmacol. 2005;6(5):262-276; McIntosh D, et al. Neuropsychiatr Dis Treat. 2009;5:137-150; Biederman J, et al. Am J Psychiatry. 2010; 167: 409-417.

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Comorbid Anxiety and Depression

- Major Depression (MD) may occur before ADHD, or may develop from depressed mood/frustration and low self-esteem in response to difficulties associated with ADHD
  - Depression in patients with ADHD is high, with estimates ranging from 9%-50%
  - Antidepressants may have some efficacy for ADHD, e.g. tricyclic antidepressants (TCAs), SNRIs, bupropion
  - Atomoxetine, a norepinephrine reuptake inhibitor (NRI), failed to demonstrate antidepressant efficacy

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC; 2013; Masi L, Gignac M. *Clin Psychiatry.* 2015:1(1):5;1-9; Kessler RC, et al. Arch Gen Psychiatry. 2005;62(6):593-602; Orr K, Taylor D. CNS Drugs.2007;21(3):239-257; Waxmonsky JG. Essent Psychopharmacol. 2005;6(5):262-276; McIntosh D, et al. Neuropsychiatr Dis Treat. 2009;5:137-150; Biederman J, et al. Am J Psychiatry. 2010; 167: 409-417.

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ADHD Medication Treatments

Stimulants

Methylphenidate

- **Short Acting**
  - Ritalin
  - Focalin*
- **Intermediate**
  - Ritalin SR
  - Metadate ER
- **Long Acting**
  - Concerta
  - Metadate CD
  - Ritalin LA; Focalin XR*
  - Daytrana (patch)
  - Aptensio XR; Adhansia XR
  - Jornay PM
  - Quillivant XR (liquid); Quillichew ER; Cotempla XR-ODT

Amphetamine

- **Short Acting**
  - Dextrostat†
  - Dexedrine tabs†
- **Intermediate**
  - Dexedrine Spansule†
  - Adderall‡
  - Evekeo‡
- **Long Acting**
  - Adderall XR‡
  - Vyvanse†
  - (capsules/chewable)
  - Adzenys XR-ODT‡
  - Dyanavel XR (liquid)‡
  - Mydayis‡

Non-Stimulants

Strattera¶ **Intuniv‡‡**
Kapvay¶

*dexmethylphenidate; †dextroamphetamine sulfate/lisdexamfetamine; ‡mixed amphetamine salts; ¶atomoxetine; §tricyclic antidepressants (many brands); **modafinil, armodafinil; ††bupropion; ‡‡guanfacine ; ¶¶clonidine; §§venlafaxine

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Advantages of Stimulants

- Use in ADHD is supported by an extensive database[1]
- Available in several delivery systems[1,2]
  - Allows treatment of younger children and those who cannot swallow tablets
- Immediate-release (IR) preparations have a rapid absorption, with clinical effects within 30 minutes of absorption[1]
  - Many patients can tell when their medication has “kicked in”
- The effect size of stimulants is among the largest for any psychotropic medication[3]

1. Daughton JM, et al. *J Am Acad Child Adolesc Psychiatry*. 2009 Mar;48(3):240-248.
2. Austerrman J. *Cleve Clin J Med*. 2015;82(11 Suppl 1):S2-S7.
3. Pliszka S. *J Am Acad Child Adolesc Psychiatry*. 2007;46(7):894-921.

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Disadvantages of Stimulants: Contraindications and Side Effects Limit Their Use

- Mania and psychosis are contraindications for, and can be caused by stimulants
- Depression, tics and anxiety can worsen with stimulants
- Risk of abuse or diversion
- Common side effects
  - Anorexia/growth suppression, dry mouth, gastrointestinal effects, anxiety/agitation, headache, insomnia, jitteriness, increase in blood pressure and pulse, moodiness/irritability
- Duration of effectiveness varies (even with XR) and is usually inadequate
  - Delay in onset, withdrawal/crash/rebound, insomnia

Faraone SV et al. *Nat Rev Dis Primers.* 2015 Aug 6;1:15020; Barkley RA. Attention-Deficit Hyperactivity Disorder, 4th Ed.: A Handbook for Diagnosis and Treatment. Guilford Publications, 2014. . Post RE, et al. Am Fam Physician. 2012;85(9):890-896.

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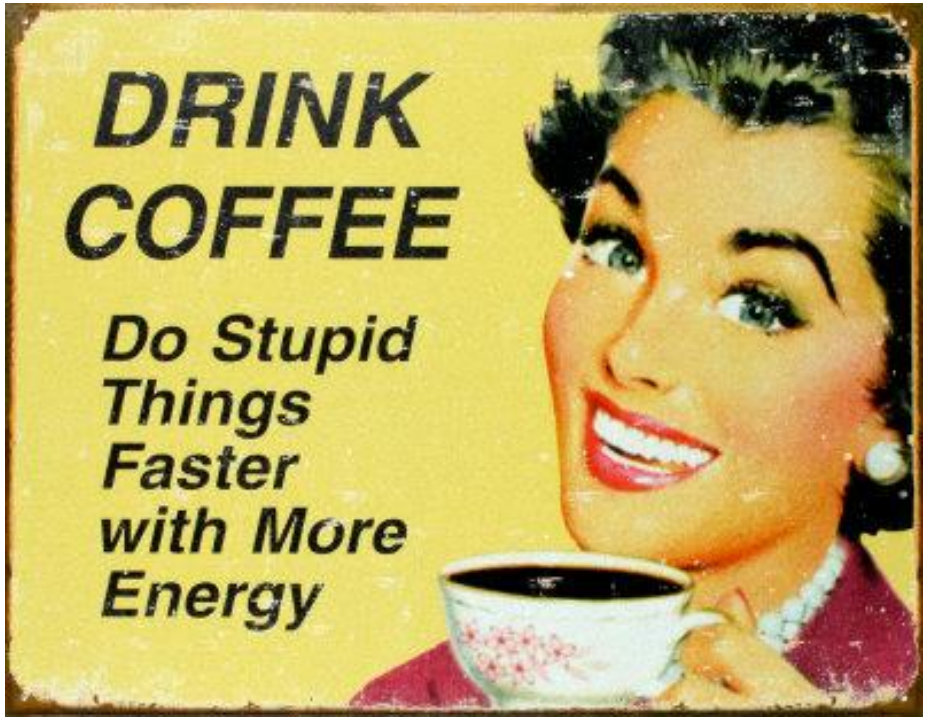
Benefits of Stimulant Treatment: Practical Implications



And…make boring tasks seem more interesting

Non-Stimulant Medications for ADHD

Drug	Brand Names	Generic Available
Atomoxetine (NRI)	Strattera	Yes
Clonidine ER (α_2-agonist)	Kapvay	Yes
Guanfacine ER (α_2-agonist)	Intuniv	Yes

- Physicians continue to seek alternatives:
  - Bupropion, modafinil, armodafinil, guanfacine IR, clonidine IR, and TCAs are also used off-label

Adapted from Briars L, et al. *J Pediatr Pharmacol Ther*. 2016;21(3):192–206.

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Advantages of Current Non-Stimulants

- Not controlled substances; lower potential for abuse
- Some (Kapvay, Intuniv) shown to be effective as primary as well as adjunctive therapy
- Do not usually exacerbate underlying tic disorders
- Can be used in children with depression, anxiety and sleep disorders
- May allow for weight-based titration (e.g., Strattera)
- Mild sedative effect may benefit patients with aggression

Daughton JM, et al. *J Am Acad Child Adolesc Psychiatry*. 2009;48(3):240-248.

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Disadvantages of Current Non-Stimulants

- Lower effect size than stimulants[1] (related to study design issues)[2]
- Slower onset relative to stimulants[1]
- Limited formulations available; multiple daily doses may be required[1]
- Medications sometimes difficult to swallow[1]
- Atomoxetine – concerns with liver injury[1]
- Clonidine and guanfacine (α_2 agonists) – significant sedation, and may cause hypotension and orthostasis[1]

1. Daughton JM, et al. *J Am Acad Child Adolesc Psychiatry*. 2009;48(3):240-248.
2. Faraone SV, et al. *J Clin Psychiatry*. 2010;71(6):754–763.

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Situations In Which Non-Stimulants May Be Used Preferentially

- Poor response/tolerability with stimulants
- Parent or patient preference
- Presence of a co-occurring condition which can be adversely affected by stimulants
  - e.g., anxiety, tics/Tourette's, sleep disorders, growth problems
- Substance abuse
- Competitive athletics
- ADHD with autism, oppositional defiant disorder, or other behavioral disorders

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Conclusions

- ADHD is heterogeneous in biology, symptoms, impairments and comorbidities
- Many currently approved medications, but most are stimulants
  - Only 3 approved non-stimulants, only 1 approved for adults
- Big unmet need for new non-stimulant (non-scheduled) medication with broad spectrum/consistent efficacy and safe/well tolerated
  - Need more options to individualize treatment, especially with comorbidity

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SPN-812: Development Program

Stefan Schwabe, M.D., Ph.D.
Executive Vice President, Research and Development,
Chief Medical Officer

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SPN-812

Novel Non-Stimulant ADHD Product Candidate

- Viloxazine hydrochloride
  - Serotonin norepinephrine modulating agent (SNMA)
  - New Chemical Entity (NCE)
  - Previously marketed outside the U.S. as an antidepressant
- Building strong IP with expirations from 2029-2033
- Clinical data point to a well-differentiated ADHD product
- Targeted NDA submission 2H 2019, and if approved, launch 2H 2020

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SPN-812

Novel Non-Stimulant ADHD Product Candidate

Mechanism of Action

- Structurally distinct, bicyclic serotonin norepinephrine modulating agent (SNMA)
  - Suggested by antidepressant effect in clinical settings
  - Differs from Strattera
  - Faster onset of drug action than Strattera
- Alteration in gene expression likely to be involved
  - Evidence for this includes different time for onset of action

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SPN-812
Completed Phase III Studies

	P301 N = 477	P303 N = 313	P302 N = 310	P304 N = 297
ADHD Patients	6-11 years	6-11 years	12-17 years	12-17 years
Daily Doses	100 mg 200 mg	200 mg 400 mg	200 mg 400 mg	400 mg 600 mg

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SPN-812 Phase III Study Design

- Randomized, double-blind, placebo-controlled, multicenter, parallel group, monotherapy for ADHD
- Primary Endpoint
  - Change from baseline on ADHD-RS-5 scale compared to placebo
- Secondary Endpoints
  - Clinical Global Impression - Improvement (CGI-I) scale
  - Conners 3rd Edition - parent, composite T-score
  - Weiss Functional Impairment Rating Scale - parent report (WFIRS-P)
- Evaluate safety and tolerability

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SPN-812 Phase III Data: Primary Endpoint

P301 (Children)	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Week 6 (EOS)	LS Mean	-10.9	-16.6	-17.7
	p-value		0.0004	<.0001
P302 (Adolescent)	**Statistics**	**Placebo (N=104)**	**200 mg (N=94)**	**400 mg (N=103)**
Week 6 (EOS)	LS Mean	-11.4	-16.0	-16.5
	p-value		0.0232	0.0091
P303 (Children)	**Statistics**	**Placebo (N=97)**	**200 mg (N=107)**	**400 mg (N=97)**
Week 8 (EOS)	LS Mean	-11.7	-17.6	-17.5
	p-value		0.0038	0.0063
P304 (Adolescent)	**Statistics**	**Placebo (N=97)**	**400 mg (N=99)**	**600 mg (N=97)**
Week 7 (EOS)	LS Mean	-13.2	-18.3	-16.7
	p-value		0.0082	0.0712

Primary Analysis of ADHD-RS-5 based on Mixed Model for Repeated Measure (MMRM) Intent to Treat (ITT Population)
EOS = End of Study

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SPN-812 Phase III Data

Significant Reduction in Hyperactivity and Inattention

Analysis in ADHD-RS-5 Inattention and Hyperactivity/Impulsivity Subscales

P301 Week 6 (EOS)	Statistics	100 mg (N=147)	200 mg (N=158)
Hyperactivity/Impulsivity	p-value	0.0026	<.0001
Inattention	p-value	0.0006	<.0001

P302 Week 6 (EOS)	Statistics	200 mg (N=94)	400 mg (N=103)
Hyperactivity/Impulsivity	p-value	0.0069	0.0005
Inattention	p-value	0.0424	0.0390

P303 Week 8 (EOS)	Statistics	200 mg (N=107)	400 mg (N=97)
Hyperactivity/Impulsivity	p-value	0.0020	0.0039
Inattention	p-value	0.0087	0.0248

P304 Week 7 (EOS)	Statistics	400 mg (N=99)	600 mg (N=97)
Hyperactivity/Impulsivity	p-value	0.0484	0.2084
Inattention	p-value	0.0042	0.1392

EOS = End of Study

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SPN-812 Phase III Data: Fast Onset of Action

Efficacy Starting in Week 1 - ADHD-RS-5 Total Score

Pooled Data – P301, P302, P303, P304					P301	
Visit	**Statistics**	Placebo (N=452)	200 mg (N=359)	400 mg (N=299)	Placebo (N=155)	100 mg (N=147)
Baseline	Mean	41.8	42.9	41.8	43.6	45.0
Week 1	p-value		0.0003	0.0016		0.0004
Week 2	p-value		<.0001	<.0001		<.0001
Week 3	p-value		<.0001	<.0001		<.0001
Week 4	p-value		<.0001	<.0001		<.0001
Week 5	p-value		<.0001	<.0001		0.0006
Week 6	LS Mean	-11.7	-17.1	-17.7	-10.9	-16.6
	p-value		<.0001	<.0001		0.0004

- Common endpoint visit for all four studies is Week 6
- Pooled Data exclude 100 mg and 600 mg that were tested in one study only
- Primary Analysis of ADHD-RS-5 in Intent to Treat Population

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SPN-812 Phase III Data: Fast Onset of Action

Efficacy Starting in Week 1 - Inattention Subscale

Pooled Data – P301, P302, P303, P304					P301	
Visit	**Statistics**	Placebo (N=452)	200 mg (N=359)	400 mg (N=299)	Placebo (N=155)	100 mg (N=147)
Baseline	Mean	22.4	22.6	22.3	22.5	22.8
Week 1	p-value		0.0086	0.0162		0.0016
Week 2	p-value		0.0001	<.0001		0.0016
Week 3	p-value		<.0001	<.0001		0.0002
Week 4	p-value		<.0001	<.0001		<0.0001
Week 5	p-value		<.0001	<.0001		0.0018
Week 6	LS Mean	-11.7	-8.9	-9.2	-5.6	-8.6
	p-value		<.0001	<.0001		0.0006

- Common endpoint visit for all four studies is Week 6
- Pooled Data exclude 100 mg and 600 mg that were tested in one study only
- Primary Analysis of ADHD-RS-5 in Intent to Treat Population

SPN-812 Phase III Data: Fast Onset of Action

Efficacy Starting in Week 1 - Hyperactivity/Impulsivity Subscale

Pooled Data – P301, P302, P303, P304					P301	
Visit	**Statistics**	Placebo (N=452)	200 mg (N=359)	400 mg (N=299)	Placebo (N=155)	100 mg (N=147)
Baseline	Mean	19.4	20.3	19.5	21.1	22.2
Week 1	p-value		<.0001	0.0010		0.0023
Week 2	p-value		<.0001	<.0001		<0.0001
Week 3	p-value		<.0001	<.0001		<0.0001
Week 4	p-value		<.0001	<.0001		0.0004
Week 5	p-value		<.0001	<.0001		0.0010
Week 6	LS Mean	-5.4	-8.2	-8.5	-5.3	-8.0
	p-value		<.0001	<.0001		0.0014

- Common endpoint visit for all four studies is Week 6
- Pooled Data exclude 100 mg and 600 mg that were tested in one study only
- Primary Analysis of ADHD-RS-5 in Intent to Treat Population

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SPN-812 Phase III Data: Secondary Endpoint

Analysis of Observed Global Improvement Score (CGI-I) at EOS

P301	Statistics	Placebo (N=155)	100 mg (N=147)	200 mg (N=158)
Week 6 (EOS)	LS Mean	3.1	2.7	2.6
	p-value		0.0020	<.0001
P302	**Statistics**	**Placebo (N=104)**	**200 mg (N=94)**	**400 mg (N=103)**
Week 6 (EOS)	LS Mean	3.0	2.5	2.4
	p-value		0.0042	0.0003
P303	**Statistics**	**Placebo (N=97)**	**200 mg (N=107)**	**400 mg (N=97)**
Week 8 (EOS)	LS Mean	3.1	2.6	2.6
	p-value		0.0028	0.0099
P304	**Statistics**	**Placebo (N=96)**	**400 mg (N=99)**	**600 mg (N=97)**
Week 7 (EOS)	LS Mean	2.9	2.4	2.6
	p-value		0.0051	0.0995

EOS = End of Study

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SPN-812 P301
Well Tolerated

Number (%) of Patients - Treatment Related AEs with ≥ 5% Incidence

	Placebo (N=159)	100 mg (N=154)	200 mg (N=161)
Somnolence	3 (1.9)	14 (9.1)	14 (8.7)
Headache	3 (1.9)	7 (4.5)	10 (6.2)
Decreased appetite	0	7 (4.5)	12 (7.5)
Discontinuation Due to AE's	**2 (1.3)**	**5 (3.2)**	**2 (1.2)**

AEs = Adverse Events

SPN-812 P302
Well Tolerated

Number (%) of Patients - Treatment Related AEs with ≥ 5% Incidence

	Placebo (N=104)	200 mg (N=99)	400 mg (N=105)
Somnolence	7 (6.7)	13 (13.1)	15 (14.3)
Decreased appetite	0	5 (5.1)	9 (8.6)
Fatigue	1 (1.0)	4 (4.0)	6 (5.7)
Headache	7 (6.7)	3 (3.0)	7 (6.7)
Nausea	3 (2.9)	5 (5.1)	5 (4.8)
Discontinuation Due to AE's	**0**	**4 (4.1)**	**2 (1.9)**

AEs = Adverse Events

Supernus® Pharmaceuticals

SPN-812 P303
Well Tolerated

Number (%) of Patients - Treatment Related AEs with ≥ 5% Incidence

	Placebo (N=103)	200 mg (N=107)	400 mg (N=100)
Somnolence	1 (1.0)	15 (14.0)	14 (14.0)
Decreased appetite	0	8 (7.5)	8 (8.0)
Fatigue	5 (4.9)	8 (7.5)	7 (7.0)
Headache	1 (1.0)	9 (8.4)	5 (5.0)
Upper abdominal pain	2 (1.9)	4 (3.7)	6 (6.0)
Discontinuation Due to AE's	**3 (2.9)**	**6 (5.6)**	**4 (4.0)**

AEs = Adverse Events

Supernus® Pharmaceuticals

SPN-812 P304
Well Tolerated

Number (%) of Patients - Treatment Related AEs with ≥ 5% Incidence

	Placebo (N=97)	400 mg (N=100)	600 mg (N=99)
Somnolence	3 (3.1)	13 (13.0)	17 (17.2)
Fatigue	4 (4.1)	11 (11.0)	10 (10.1)
Headache	3 (3.1)	9 (9.0)	7 (7.1)
Decreased appetite	2 (2.1)	6 (6.0)	6 (6.1)
Nausea	2 (2.1)	5 (5.0)	8 (8.1)
Discontinuation due to AEs	**1 (1.0)**	**4 (4.0)**	**5 (5.1)**

AEs = Adverse Events

SPN-812
Summary of Treatment Related Adverse Events

Number (%) of Patients - Treatment Related AEs with ≥ 5% Incidence
All Four Phase III Trials

	Placebo (N=463)	SPN-812 (N=925)
Somnolence	14 (3.0)	115 (12.4)
Decreased appetite	2 (0.4)	61 (6.6)
Headache	14 (3.0)	57 (6.2)
Fatigue	10 (2.2)	56 (6.1)
Discontinuation due to AEs	**6 (1.3)**	**32 (3.5)**

AEs = Adverse Events

SPN-812 Phase III Program
Executive Summary

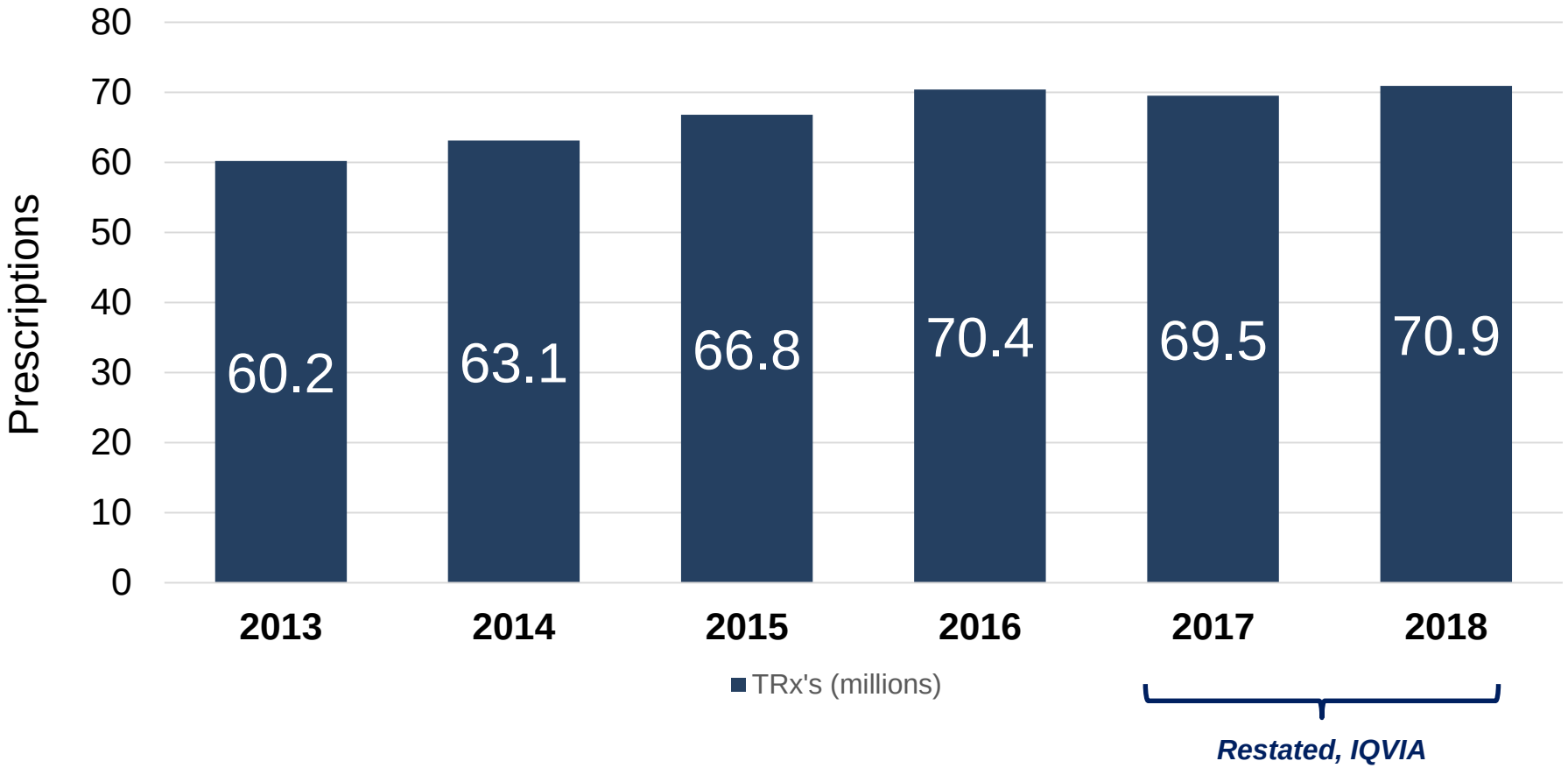
- Final Phase III data package for the NDA is robust on 100 mg, 200 mg and 400 mg doses in more than 1,000 children and adolescent patients
- P304 fourth Phase III trial
  - Consistent with and confirms results from three successful Phase III trials (P301, P302 and P303) in children and adolescents
- Clinical data point to a well-differentiated ADHD product
  - Strong efficacy with robust statistical significance
  - Efficacy on both Hyperactivity/Impulsivity and Inattention
  - Fast onset of action
  - Well tolerated
- Targeted NDA submission 2H 2019, and if approved, launch 2H 2020

SPN-812: Commercial Opportunity

Todd Horich Ph.D., MBA
Vice President, Marketing

Supernus® Pharmaceuticals

The ADHD Prescription Market Is Large



Source: IQVIA NPA including restated 2017 and 2018

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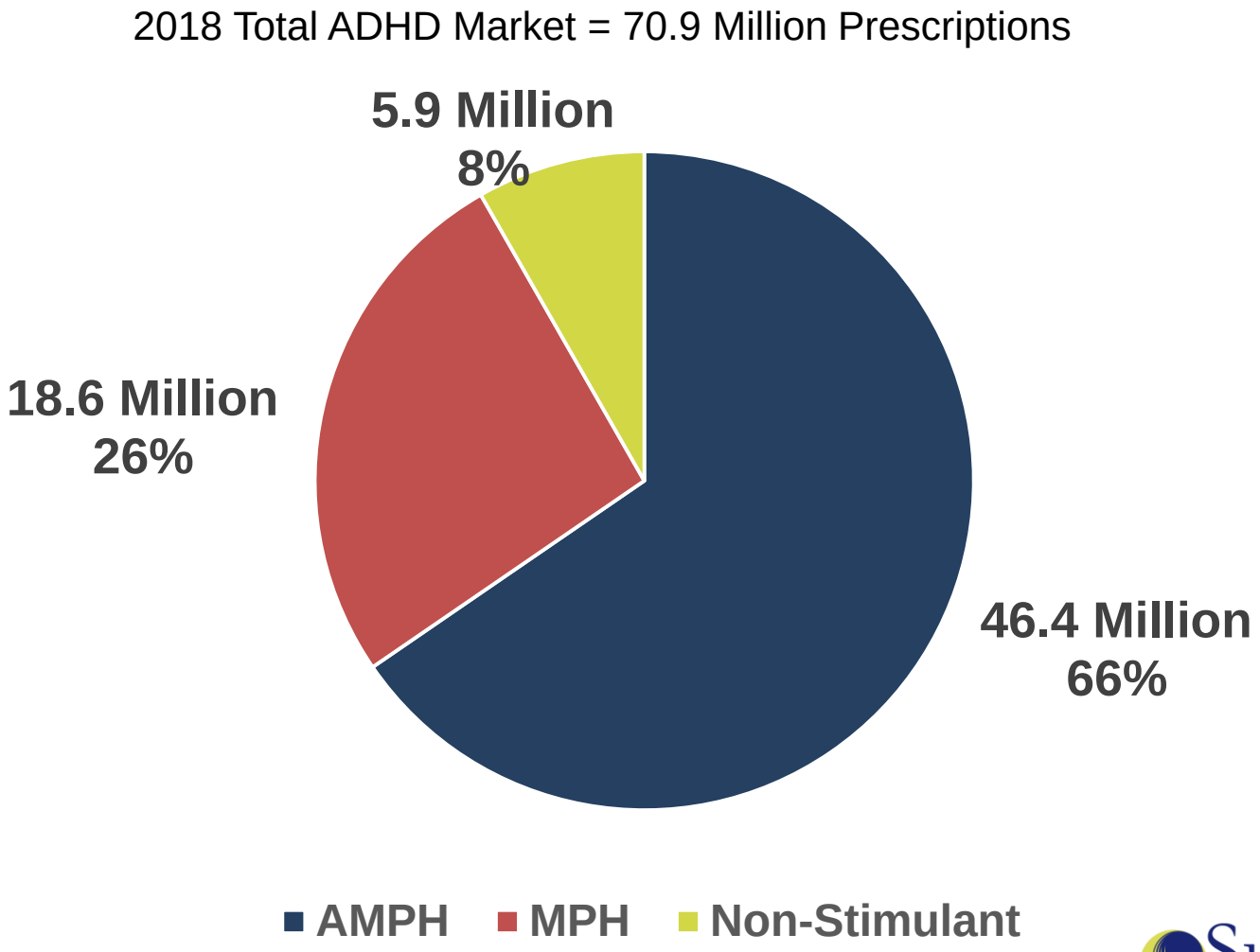
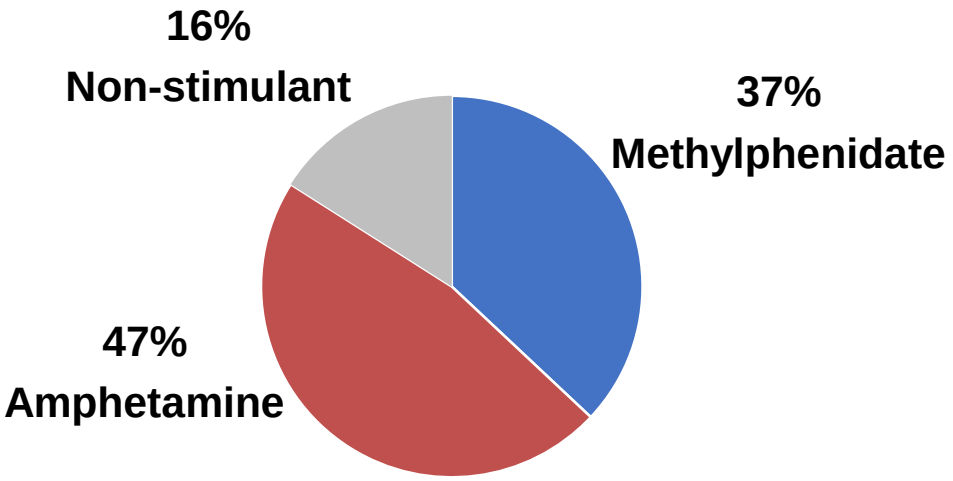
Total ADHD Prescription Market by Segment



IQVIA, 2018

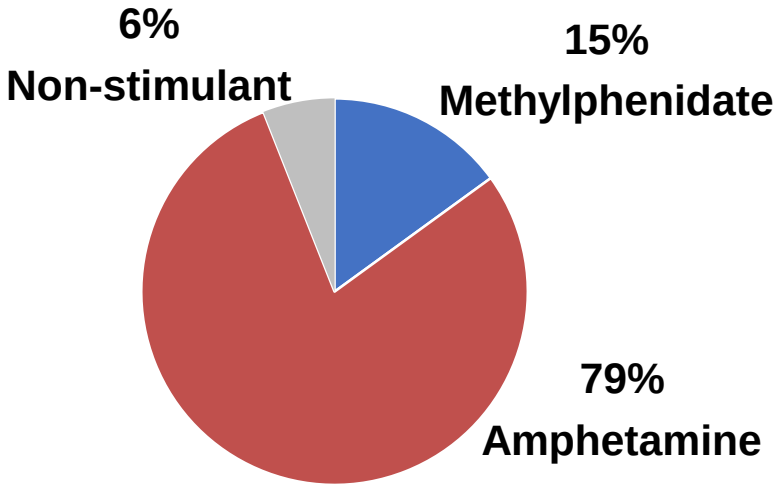
ADHD Market Split Roughly 50/50: Pediatrics/Adolescents And Adults; Product Mix Varies by Group

Children & Adolescents



49% of Prescriptions

Adults



51% of Prescriptions

IQVIA NDTI 2018

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Higher Usage of Non-Stimulants by HCPs (Decile 6-10) than by Overall Market and by Ped/Adol Treating Physicians

		Total Market	Stimulants		Non-Stimulants	
Specialty	# of HCP	TRx	TRx	% of Market	TRx	% of Market
Total Market	21,761	35.7	31.0	87%	4.8	13%
Target HCPs	**11,478 (53%)**	**18.7**	**15.3**	**82%**	**4.3**	**18%**
Child Neuro	252	0.6	0.5	76%	0.2	24%
Child Psych	2,609	5.6	4.3	77%	1.3	23%
NP,PA	3,472	5.5	4.6	84%	0.9	16%
Peds	5,145	6.9	6.0	86%	1.0	14%

98% of Non-Stimulant Prescriptions are Written by Decile 6-10 HCPs

IQVIA NPA 2018. HCP= Health Care Provider

Supernus® Pharmaceuticals

Non-Stimulants Therapy Increases Dramatically as Patients Progress Through Lines of Therapy

- **Quantitative ADHD treatment landscape market research study**
  - 125 HCPs who treat pediatric and adolescent ADHD
  - High decile prescribers of ADHD medication (Decile 6-10)
- **496 ADHD patient charts chosen at random**
  - 31% of patients on first line medication, 29% second line, and 40% third line
- **Non-stimulant use increases dramatically through therapy progression**
  - 86% of first line therapy consisted of stimulant use only
  - By second line treatment, nearly half of patients on a non-stimulant
  - By third line treatment, three-fifths of patients on a non-stimulant

Supernus ADHD Market Landscape Study, 2018

Supernus® Pharmaceuticals

Stimulants Have Disadvantages

- Prescribing challenges
- Side effects: appetite loss, abdominal pain, headaches, sleep disturbances
- Potential for diversion leading to misuse, abuse, and/or dependence
- Parent concerns
- Inadvisable to use for specific co-morbidities
  - Substance use disorder
  - Tics / Tourette's / obsessive compulsive disorder (OCD)
  - Depression and anxiety

Supernus® Pharmaceuticals

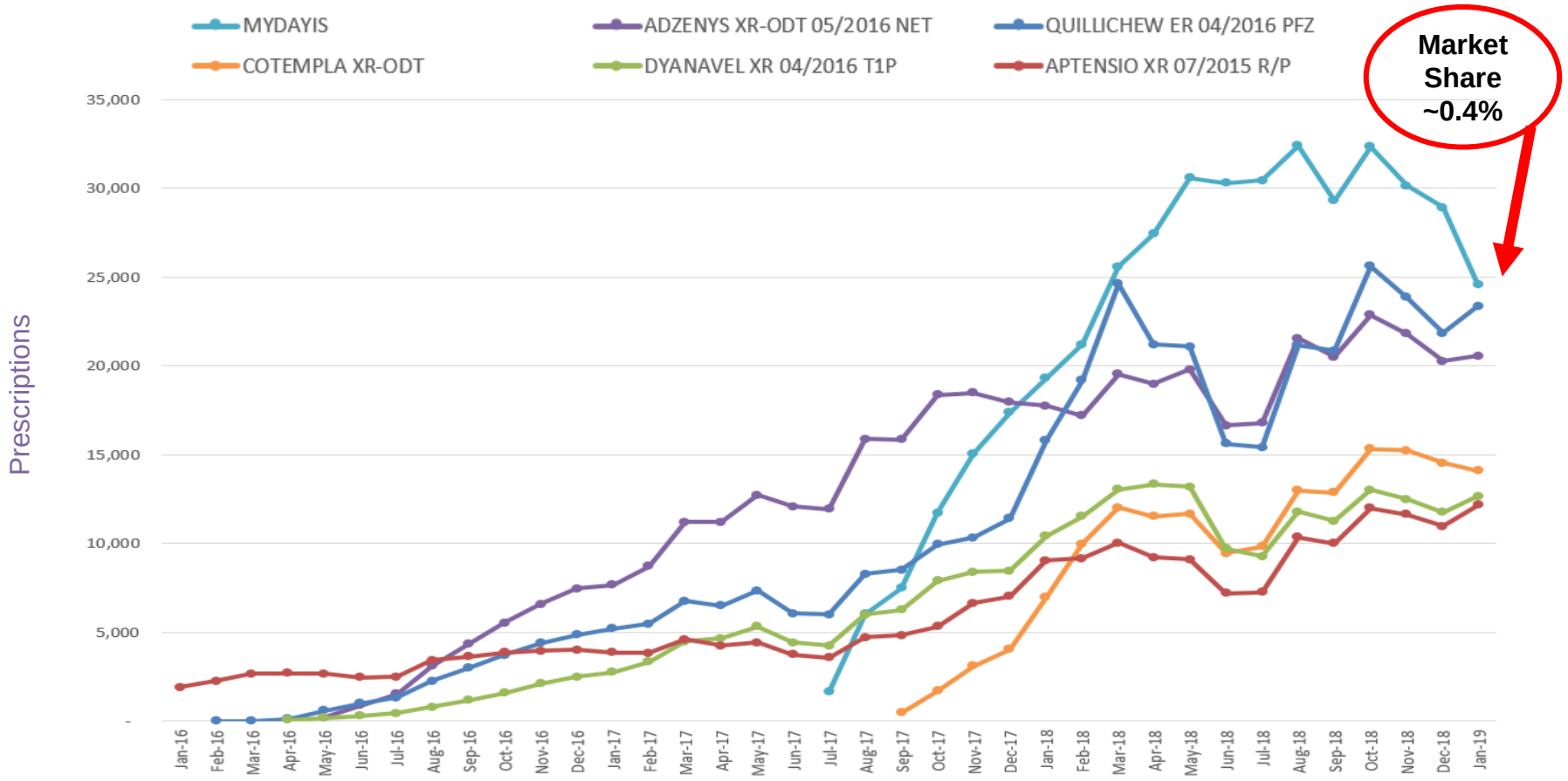
ADHD Is More Often Than Not, Associated With Other Mental Health Comorbidities

- 2007 National Survey of Children's Health conducted by American Academy of Pediatrics (AAP)
  - 61,779 children ages 6 to 17 years, including 5,028 with ADHD
- 67% of US children with ADHD had comorbid mental health conditions
  - Compared to 11% in the population without ADHD
- AAP guidelines call for assessment and management of comorbidity with ADHD
  - Comprehensive screening for conditions that occur with ADHD is necessary
  - Treatments should be tailored by comorbidity and levels of functional impairment at home and school

Larson *et al*, PEDIATRICS Volume 127, Number 3, March 2011

Supernus® Pharmaceuticals

Recent ADHD Product Launches Are Stimulant Line Extensions That Have Not Addressed the Need



IQVIA

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SPN-812 Clinical Data Point to a Well-Differentiated ADHD Product

	SPN-812 Profile
New chemical entity with distinct mechanistic properties from other non-stimulants & stimulants	✓
Strong efficacy, >1,000 children and adolescent patients Efficacy for both Impulsivity & Inattention	✓
Fast onset of action, within 1 week	✓
Consistent blood levels throughout the day	✓
Very well tolerated, low incidence of sedation, insomnia, nausea & vomiting	✓
Low to no incidence of cardiovascular AEs or liver enzyme induction	✓
QD dosing, 100mg to 400mg, ability to sprinkle	✓

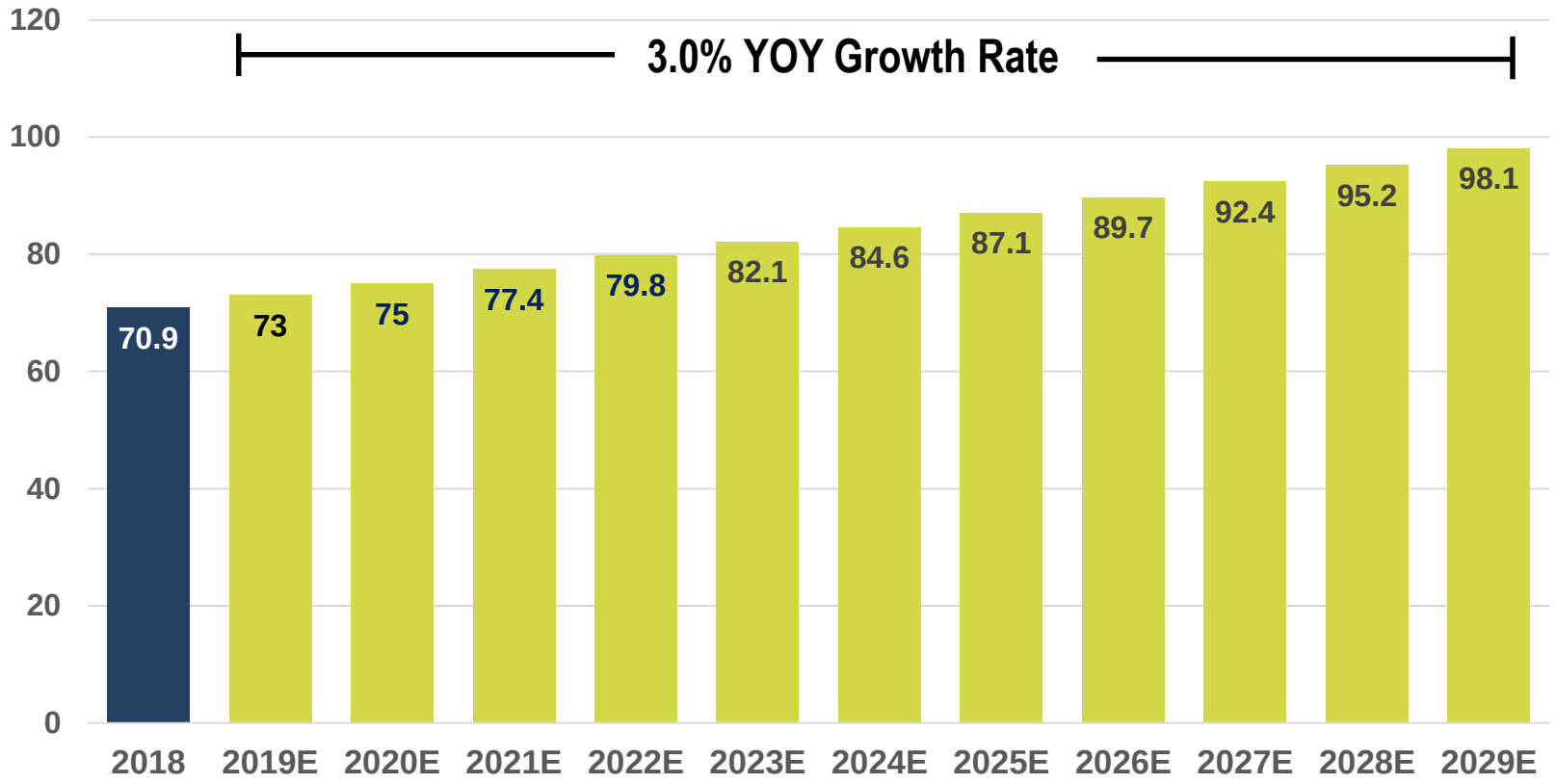
SPN-812 Launch Preparation Is Well Underway

SPN-812: Sales Force Size & Structure

Taylor Raiford
Vice President, Sales and Market Access

Supernus® Pharmaceuticals

ADHD Market Prescriptions Trending to 89 – 100M



51% of TRxs are adult; 49% are pediatric/adolescent

IQVIA

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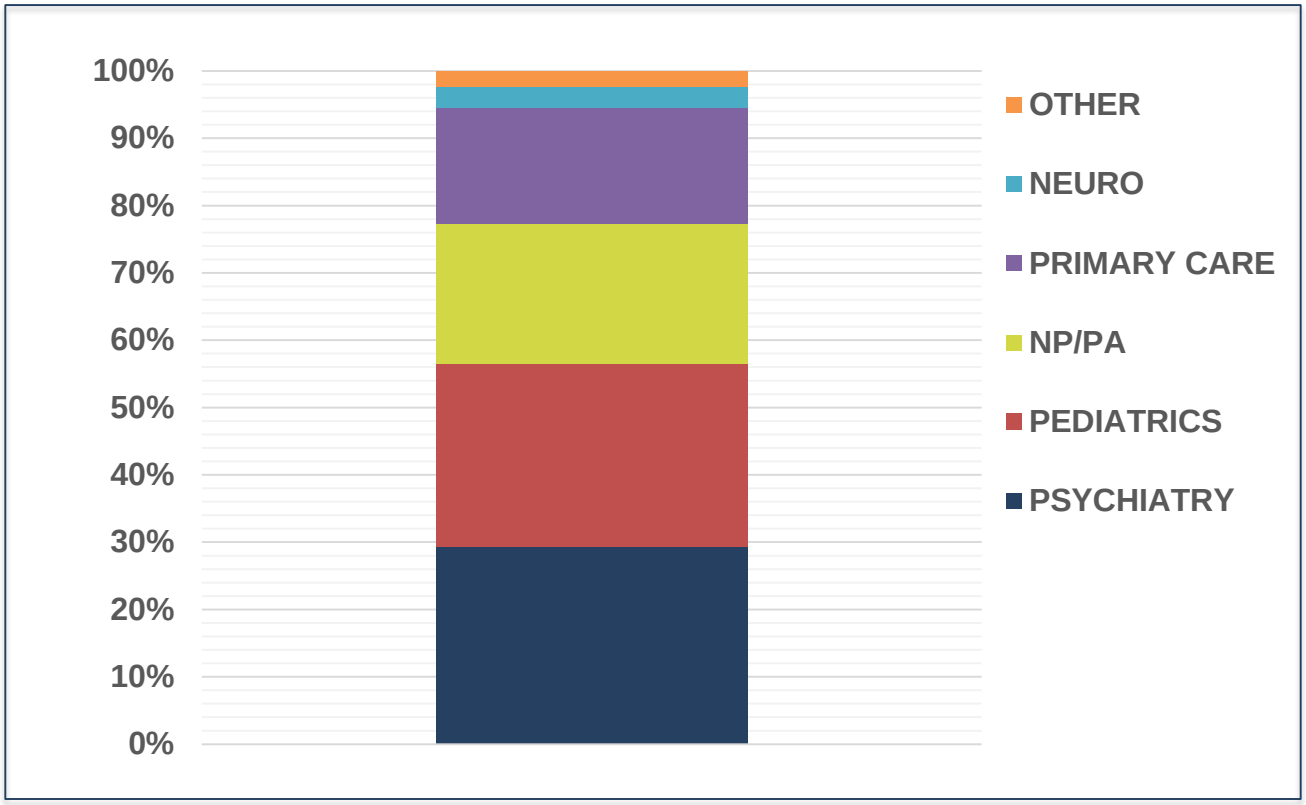
ADHD Prescriptions by Specialty for Total Market

ADHD Prescriptions by Specialty



IQVIA MAT JAN 19 based on physician prescribing for all ADHD products

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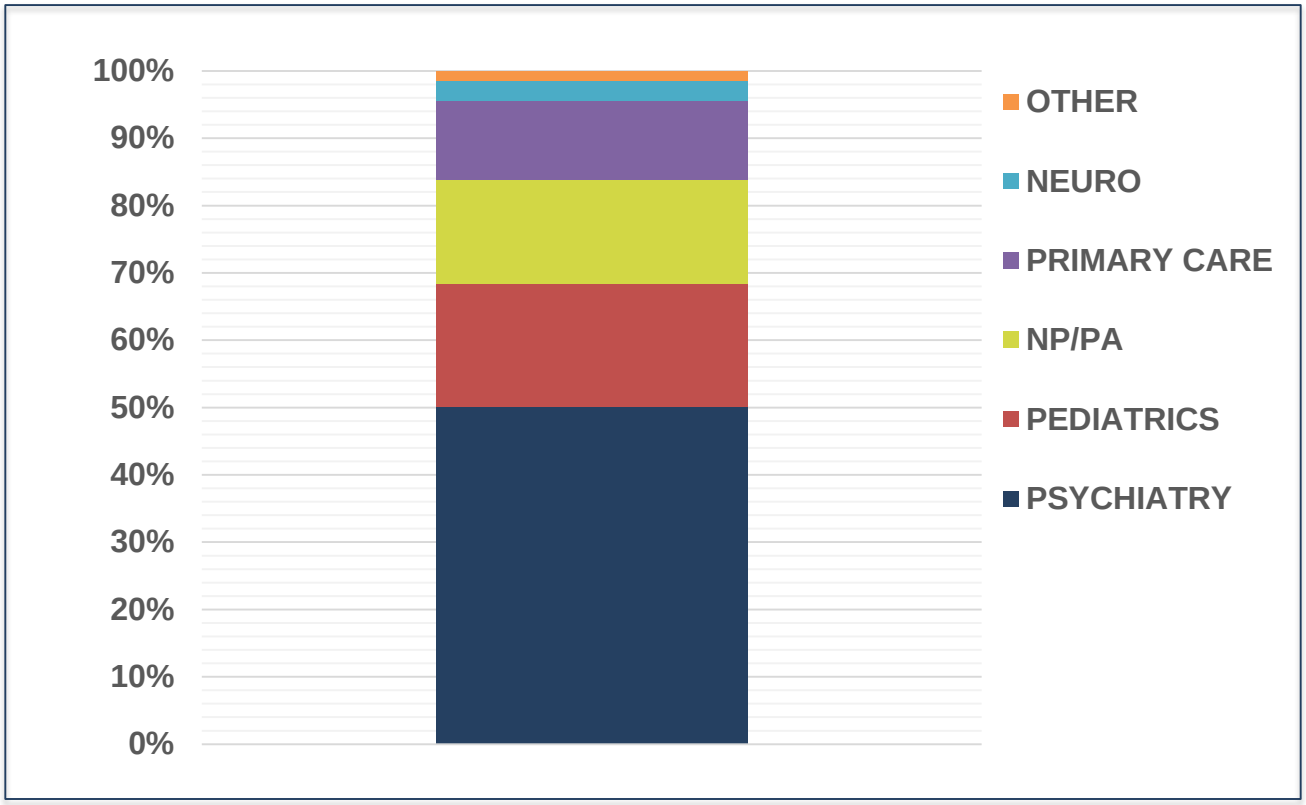
ADHD Prescriptions by Specialty for Top Deciles (7-10)

ADHD Prescriptions by Specialty



IQVIA MAT JAN 19 based on physician prescribing for all ADHD products

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SPN-812 Sales Force Optimization

Target High Volume ADHD HCPs

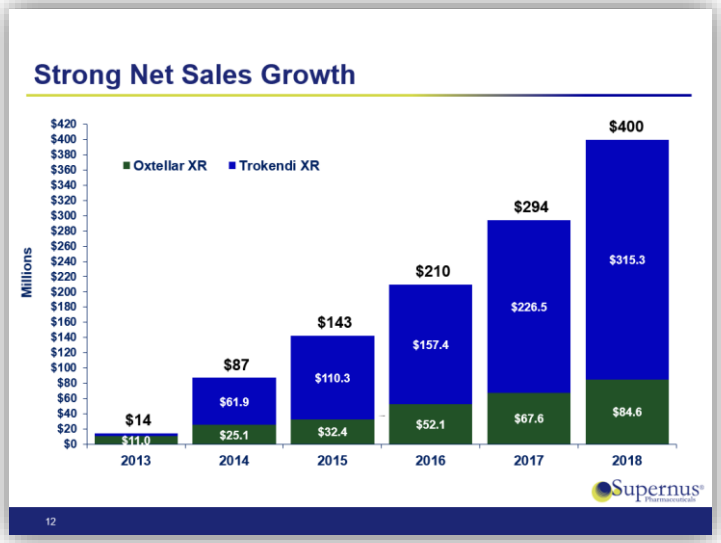
(Psychiatrists, Neurologists, Pediatricians, and NP/PAs)

Percent of ADHD Market	Number of HCPs	Percent of HCPs	Total Reps
40%	14K	3.1%	140
50%	22K	5.0%	220
60%	33K	7.6%	330
100%	440K	100%	N/A

- **Initial sales force of ~150 reps**
- **Potential to expand further as product grows**

SPN-812 Sales Force Optimization

- Build ADHD Sales Force by leveraging internal expertise
- Transfer sales reps and sales management from neurology sales force
  - Maximize the team that experienced significant success in our business model
  - Hit the ground running Day 1 of launch



- Backfill current neurology sales force with new hires

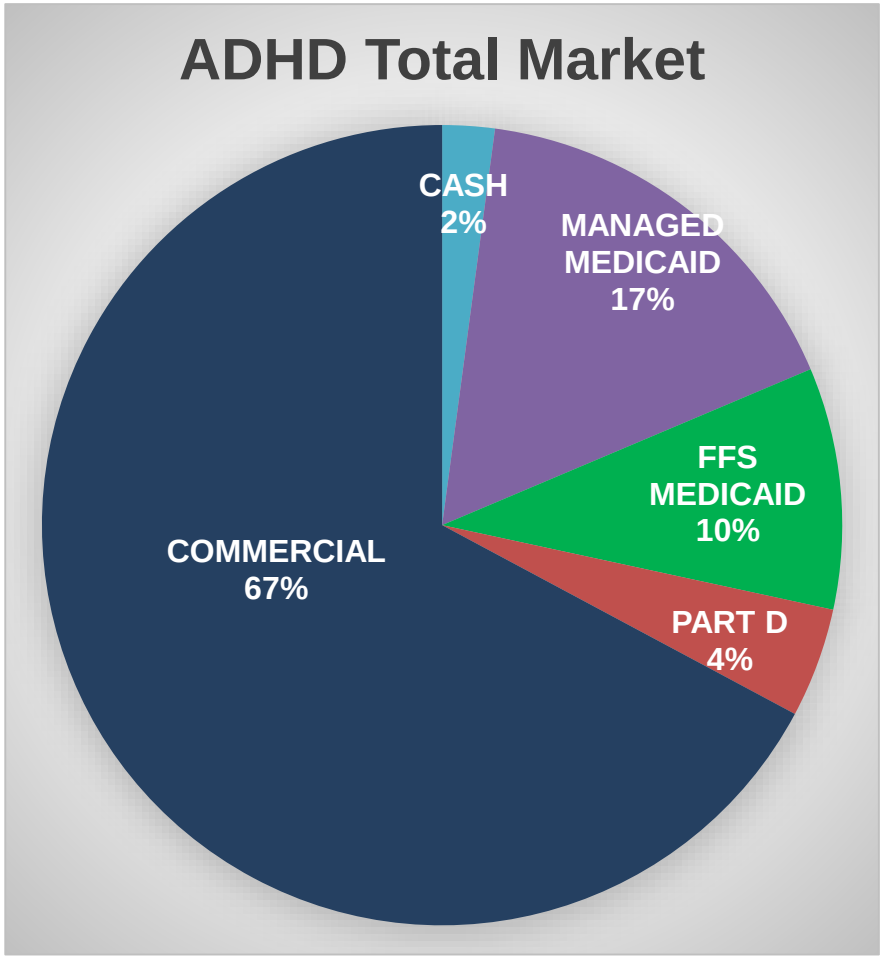
Sales Force Background in CNS/ADHD

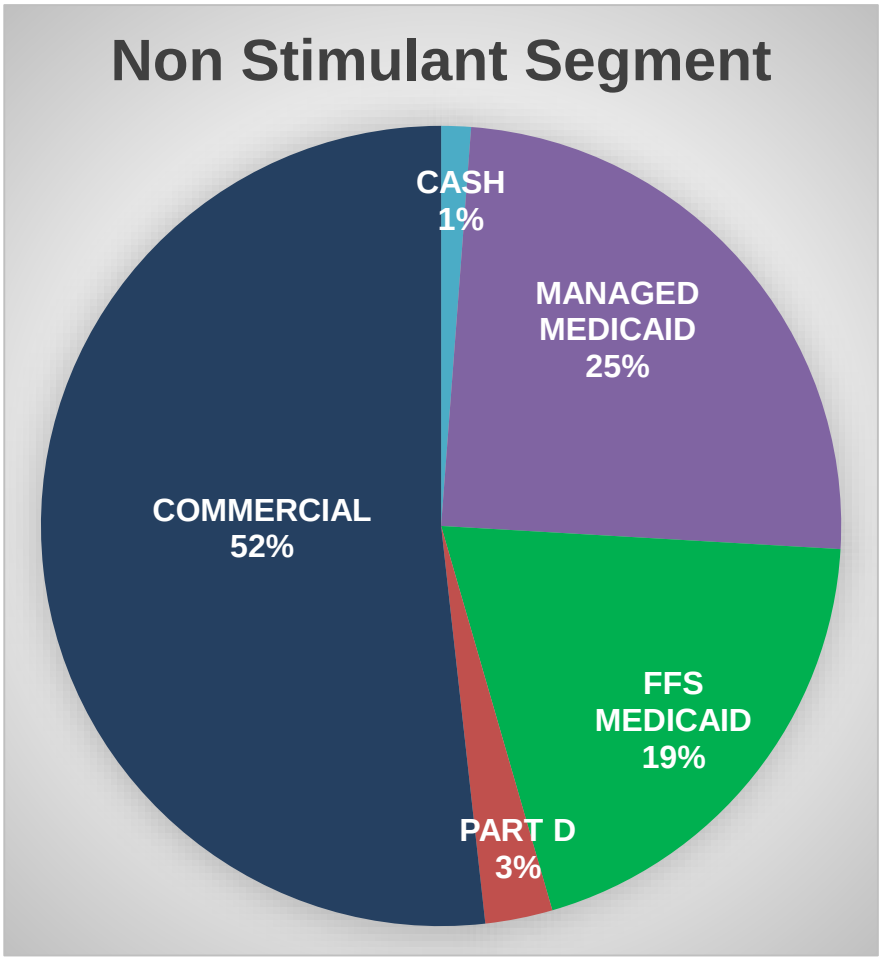
- **Vice President of Sales & National Sales Director**
  - 25 years+ pharmaceutical experience each
  - Extensive ADHD experience (Adderall, Adderall XR, Daytrana, Vyvanse, & Intuniv)
  - Extensive experience building and leading sales forces
- **Zone Directors**
  - 15 years+ pharmaceutical experience each, including ADHD experience
  - Extensive commercial backgrounds in sales, sales training, payer, and marketing
- **Regional Directors**
  - 8 RDs with previous ADHD experience
  - Remaining RDs were promoted from within after success as sales representatives
- **Sales Representatives**
  - Average tenure at Supernus is ~4 years
  - Low turnover rate (5.9% average over last 3 years)

Supernus® Pharmaceuticals

SPN-812
Payer Landscape

Payer Mix: ADHD Total Market vs. Non-Stimulant Segment





IQVIA

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U.S. Commercial And Medicaid Lives

US Commercial Rx Population / Targeted Lives	Covered Lives (Mil)	Share of US Medicaid Lives
US Commercial Rx Population	186.6	100%
Top 15 National Accounts	152.6	81.8%
Top 12 Regional Accounts	11.9	6.4%
Total Targeted SPN-812 Lives	164.5	88.2%

We will target 88% commercial Rx lives for SPN-812

US Medicaid Rx Population / Targeted Lives	Covered Lives (Mil)	Share of US Medicaid Lives
US Medicaid Rx Population	63.1	100%
Top 10 States	35.2	55.8%
11 – 30th Ranked States	24.8	39.3%
Total Targeted SPN-812 Lives	60.0	95.1%

We will target 95% Medicaid Rx lives for SPN-812

Source: Managed Markets Insight & Technology, LLC (March 2019 Data)

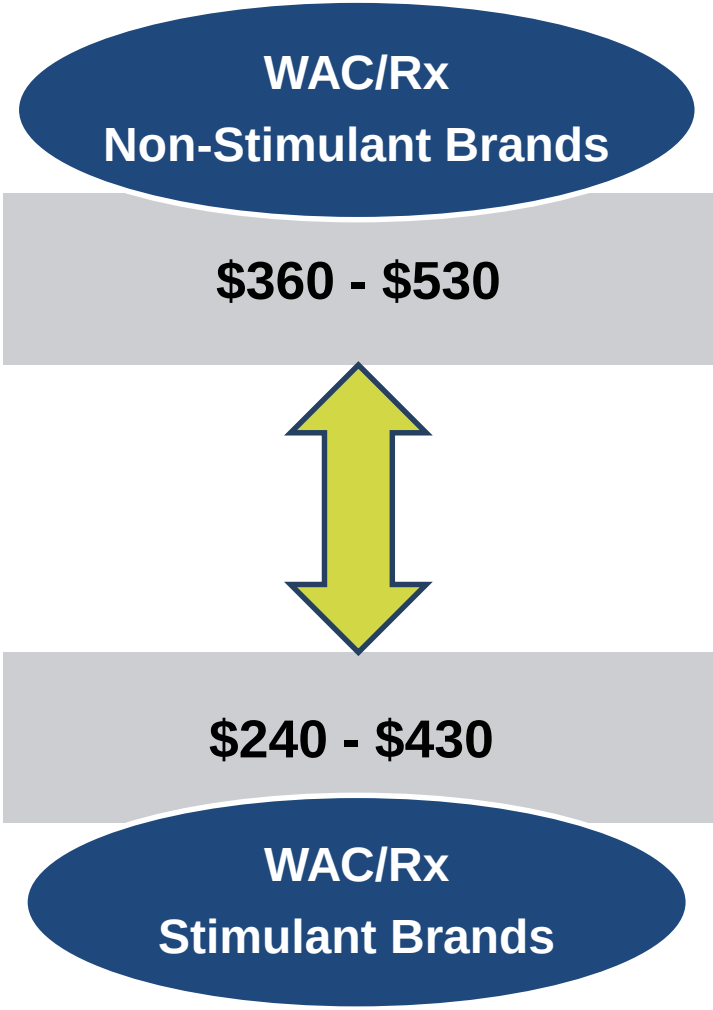
Payer Perspectives

- Payer surveys and advisory boards in 2017 and 2018 indicate that the ADHD market does not need or want another stimulant – *but there is a need for an effective alternative to stimulants*
- For SPN-812 specifically, payers are interested given that it is a New Chemical Entity and that it is a Novel Non-Stimulant
- Want to see data that supports a value proposition over existing options
- Physician and parent/patient demand, along with a responsible price, will drive market access with payers

- **Based on SPN-812 clinical profile and our past market access performance, we remain confident in our ability to create the market access needed for a successful launch**

Upcoming Market Access Initiatives

Current Pricing for ADHD Brands



*Based on Jan 2019 Average WAC/Rx for branded products

SPN-812
Significant Market Opportunity

	Percent	Estimated Prescriptions in Peak Year
ADHD Market Prescriptions		**89 – 100 Million**
	Peak Market Share	**SPN-812 Potential Prescriptions**
SPN-812 Peak Demand	**5 – 10%**	**4.5 – 10.0 Million**

Historical combined market share of Strattera/Intuniv prior to generics ~ 9%

Peak market share of Strattera in 2004 ~ 19%

Source: IQVIA NPA, Company Research and Estimates – Assumes peak at 5-7 years post launch Figures in the table above represent management's estimates that are subject to several factors that are beyond our control and actual results may be significantly different from our estimates

Supernus® Pharmaceuticals

SPN-810: Impulsive Aggression (IA)

Robert Findling, M.D.
Leonard Helen R. Professor of Child & Adolescent Psychiatry
Director of Child & Adolescent Psychiatry, Johns Hopkins University
VP of Psychiatric Services and Research, Kennedy Krieger Institute

Supernus® Pharmaceuticals

Aggression

- **Definition:** A forceful action or procedure resulting in an unprovoked attack on another or engaging in hostile, destructive, or injurious behavior. *Webster's Ninth New Collegiate Dictionary* (1989).
- Aggression as a concept is distinct from antisocial behavior, delinquency, conduct problems, disruptive behavior disorders, irritability, Oppositional Defiant Disorder, or Conduct Disorder.

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Aggression Can Be Divided into Two Groups

Adaptive Aggression

- "Appropriate"
- Serves identifiable goals
- Brain structure and / or function not impaired
- Does not require mental health research or treatment

Maladaptive Aggression

- "Excessive" or "Inappropriate"
- Does not serve identifiable goals
- Brain structure and / or function impaired
- May require psychiatric and pharmacological treatment

Connor, 2002; Wakefield, 1992

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Maladaptive Aggression Has Societal Impacts

- Occurs in 40% to 60% of all patients **referred** to child psychiatrists
- Predicts **rehospitalization** rates regardless of diagnosis in youths discharged from inpatient settings
- Associated with **staff injury** in residential care
- Associated with **polypharmacy** (multiple medications) in inpatient children and adolescents regardless of diagnosis or comorbidity
- Early onset (before age 10) predicts **poor lifetime prognosis**

Connor, 2002; Steiner & Karnik, 2003; Blader, 2004; Cunningham et al, 2003; Edelsohn et al, 2003; Connor et al. 1997; Moffitt, 1993; Scott et al, BMJ 2001; Waters et al, Health Policy, 2005

Supernus® Pharmaceuticals

Understanding Impulsive Aggression (IA)

- IA is a subtype of Maladaptive Aggression
- Impulsivity can be defined neurobiologically
  - Short fuse that causes impairment in the context of neuropsychiatric illness
  - Lack of self-control results in harm to patient with impulse control issues
- Analogous to fever as a symptom of underlying medical / surgical disease

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IA Occurs Across Multiple Disorders

- ADHD
- Autism Spectrum Disorder
- Bipolar Disorder
- Oppositional Defiant Disorder
- Conduct Disorder
- Intermittent Explosive Disorder
- Disruptive Mood Dysregulation Disorder
- Schizophrenia
- Alzheimer's Disease
- PTSD and Disorders of Traumatic Stress
- Substance Use Disorder
- Anxiety Disorders
- Psychosis
- Somatic neurological impairments
  - Traumatic Brain Injury
  - Encephalitis
  - Stroke
  - Epilepsy

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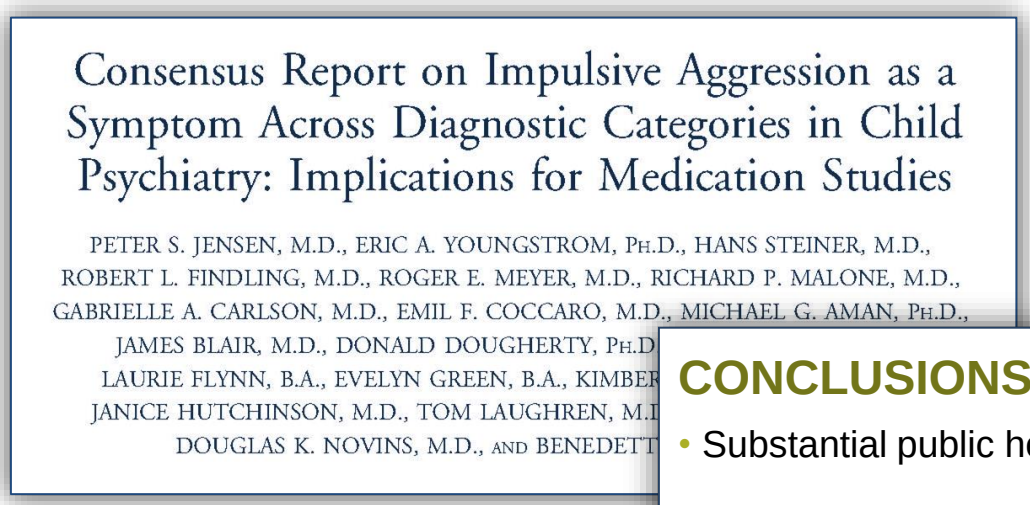
Prevalence of IA

- Survey shows IA in approximately 30% of children with ADHD
  - 1092 patient chart review
  - 120 child and adolescent psychiatrists, 32 child neurologists, and 30 developmental and behavioral pediatricians
  - Nationwide sample
- ADHD prevalence ≈ 5–7% of children worldwide

Market sizing and demand study, April 2015; Thomas R et al, Pediatrics. 2015 Apr;135(4) Epub 2015 Mar 2.

Supernus® Pharmaceuticals

2007 Benchmark Paper Defines Substantial Clinical and Public Health Concerns in IA



Consensus Report on Impulsive Aggression as a Symptom Across Diagnostic Categories in Child Psychiatry: Implications for Medication Studies

PETER S. JENSEN, M.D., ERIC A. YOUNGSTROM, PH.D., HANS STEINER, M.D., ROBERT L. FINDLING, M.D., ROGER E. MEYER, M.D., RICHARD P. MALONE, M.D., GABRIELLE A. CARLSON, M.D., EMIL F. COCCARO, M.D., MICHAEL G. AMAN, PH.D., JAMES BLAIR, M.D., DONALD DOUGHERTY, PH.D., LAURIE FLYNN, B.A., EVELYN GREEN, B.A., KIMBER JANICE HUTCHINSON, M.D., TOM LAUGHREN, M.D., DOUGLAS K. NOVINS, M.D., AND BENEDETT

CONCLUSIONS:

- Substantial public health concern
- Substantial clinical concern
- Identifiable and constitutes a key therapeutic target across multiple disorders
- Can be measured with sufficient precision that pharmacological studies are warranted
- Should be studied within well-defined clinical disorders such as ADHD, autism, bipolar disorder

JAACAP, 2007:46(3):309-322.

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IA is a Significant Health Concern Requiring Pharmacological Intervention

- Clear distinction between IA and other forms of aggression
  - Occurs outside of expected social context or preceding event
  - Disproportionate to causes in frequency, intensity, duration, and / or severity
  - Prolonged and does not terminate readily
- Associated with substantial daily impairment in functioning with implications in public health
- Substantial need to develop specific tools and treatments for IA

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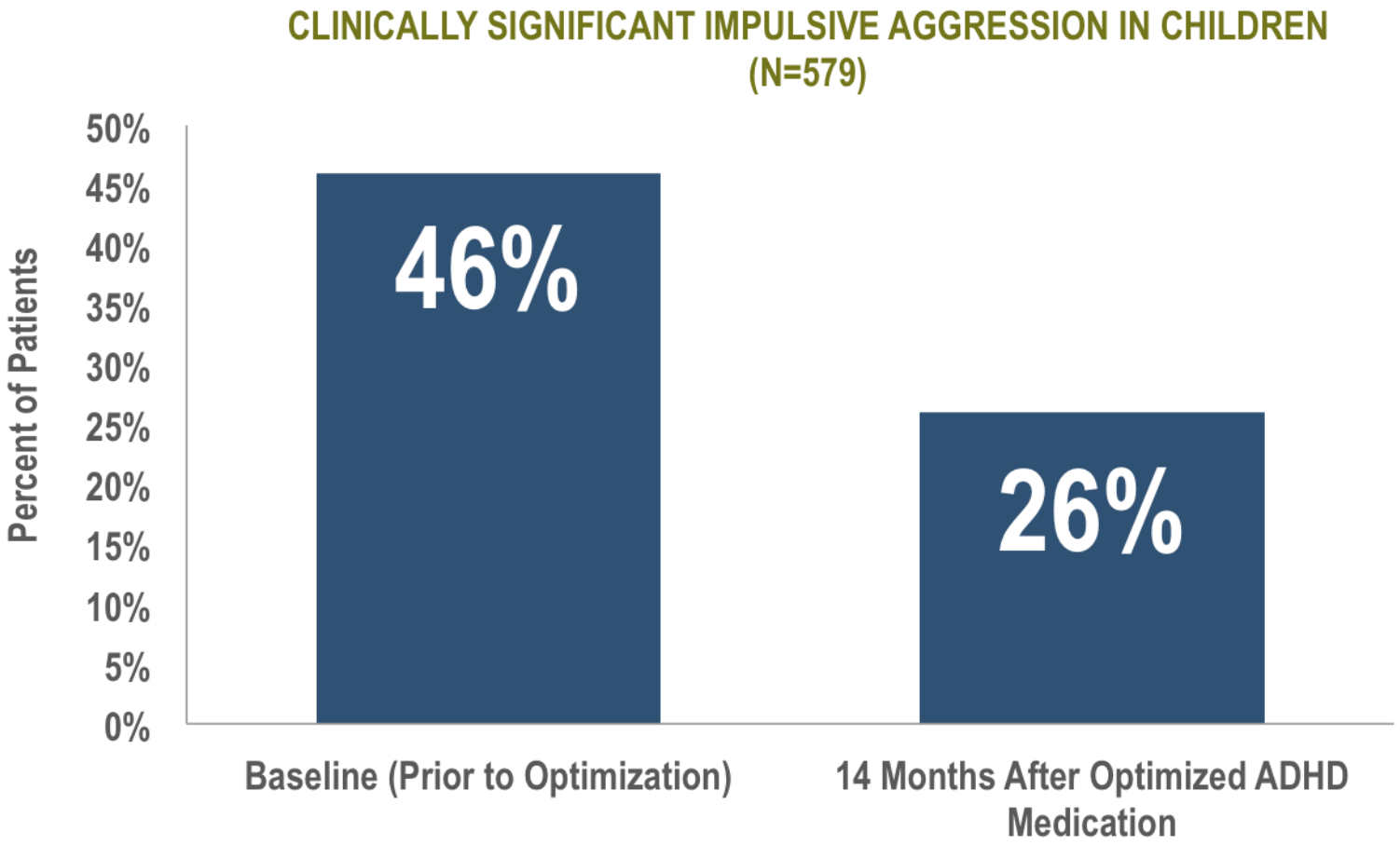
Stimulant Optimization is First Step in Managing IA in ADHD

- No FDA approved treatments for IA

Optimize ADHD Stimulant

Supernus® Pharmaceuticals

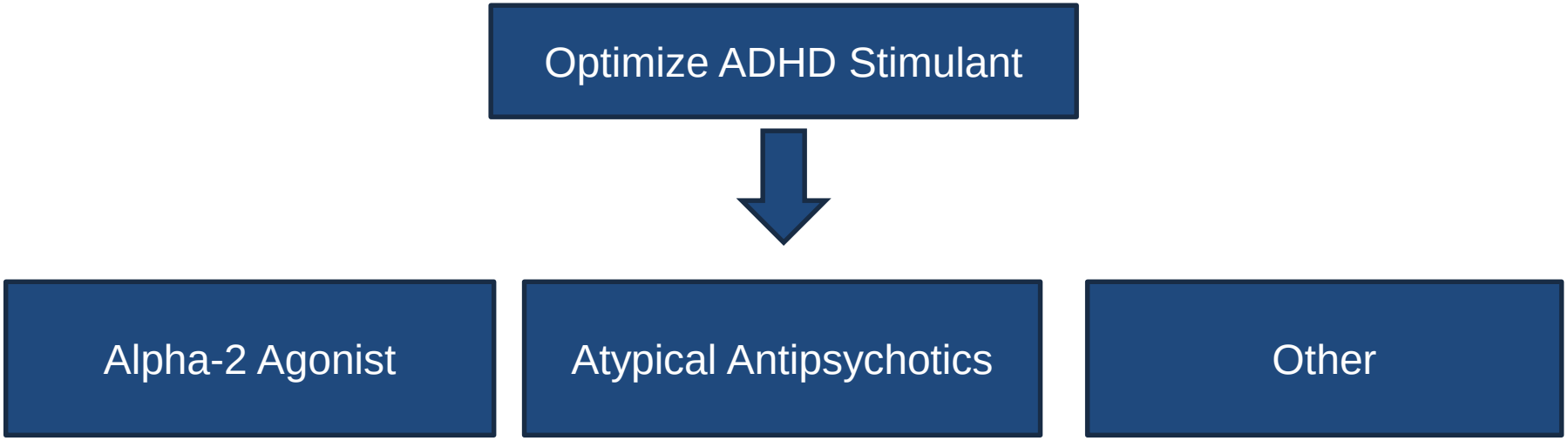
IA Symptoms Still Present After Optimized ADHD Treatment



MTA Cooperative Group, Arch Gen Psychiatry, 1999; 56:1073–1086.; Jensen et al, JAACP, 46:3, March 2007

Following Stimulant Optimization, Off-Label Agents are Used for Remaining Aggression

- No FDA approved treatments for IA



- Intuniv (extended release guanfacine)
- Kapvay (extended release clonidine)

- Risperdal (risperidone)
- Abilify (aripiprazole)
- Zyprexa (olanzapine)
- Geodon (ziprasidone)
- Seroquel (quetiapine)

- Depakote (valproic acid)
- Lithium

Supernus® Pharmaceuticals

Unmet Needs Exist for Treatments Specific for IA

- No FDA approved treatments for IA

Alpha-2 Agonist

- Limited data in impulsive aggression
- Relatively benign safety profile: mild to moderate somnolence, headache, sedation

Atypical Antipsychotics

- Effective for aggression
- Significant side effects include elevated prolactin levels, increased weight gain, extrapyramidal symptoms, metabolic changes, sedation

Other

- Limited data in aggressive population

CNS Drugs. 2010 Sep;24(9):755-68; Can J Psychiatry. 2015 Feb 1;60(2):52-61

Supernus® Pharmaceuticals

SPN-810: Promising Candidate for IA Treatment

- Originally marketed by Endo Pharmaceuticals as Moban® for the treatment of schizophrenia in 1974[1]
  - Marketing discontinued for commercial reasons in 2010
- Moban® dosing as high as 225 mg/day
- SPN-810 to be dosed ≤ 36 mg/day

[1]Federal Register. https://www.federalregister.gov/articles/2013/11/06/2013-26550/determination-that-moban-molindone-hydrochloride-tablets-5-milligrams-10-milligrams-25-milligrams-50. Accessed November 3, 2014;

Supernus® Pharmaceuticals

SPN-810: Promising Candidate for IA Treatment

- Extended Release Molindone Hydrochloride
  - Potent D2 antagonist (efficacy)
  - Low H1 binding (tolerability; e.g. weight gain)
  - Low 5-HT2C (tolerability; e.g. weight gain)
- Anticipated to be first FDA approved product for Impulsive Aggression in children/adolescents with ADHD
- Potential differentiation includes less impact on:
  - Weight gain
  - Sedation rates
  - Prolactin levels
  - Extrapyramidal symptoms (EPS)

Neuropsychopharmacology (2003) 28, 519-526.

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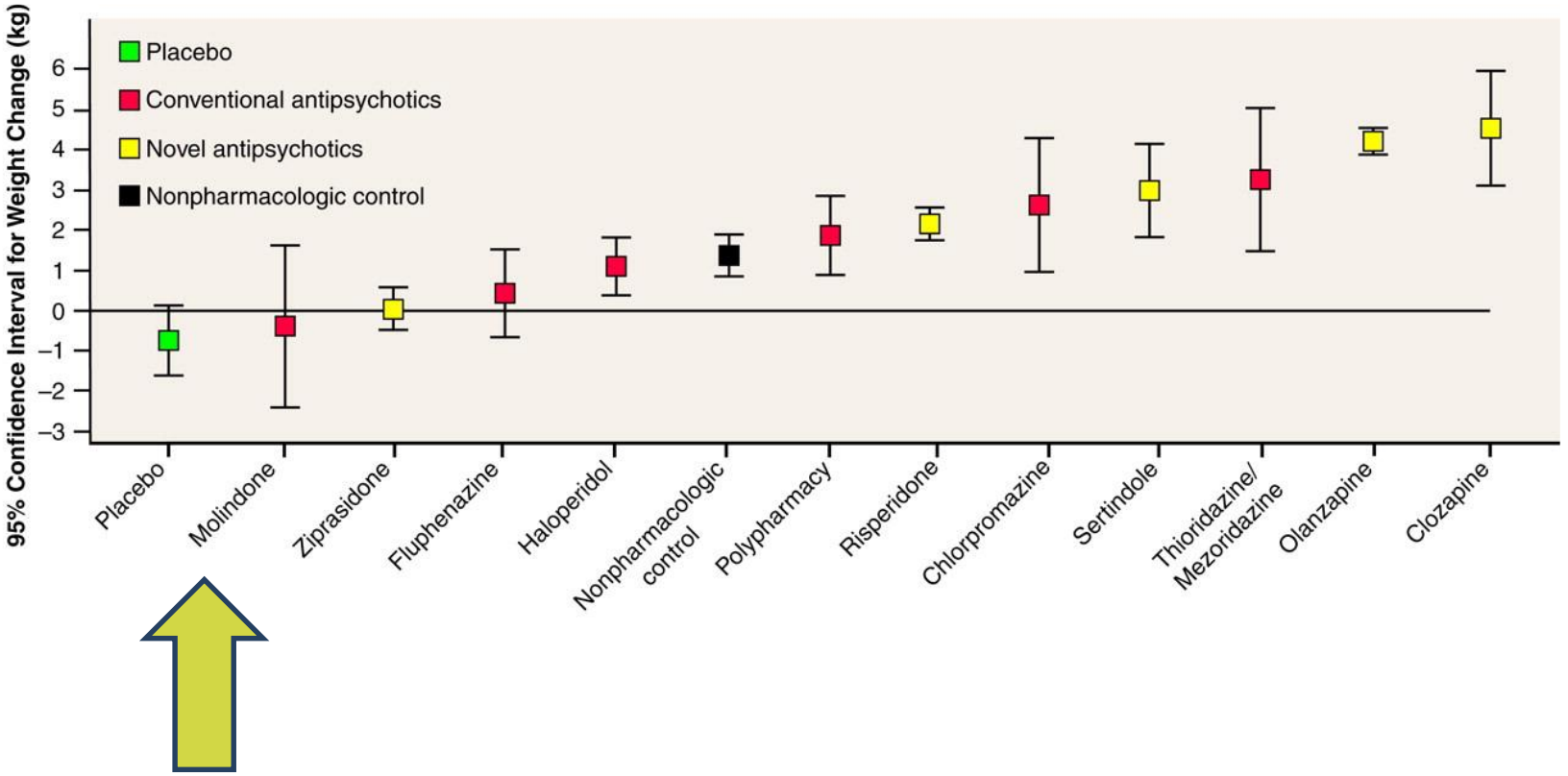
Molindone Exhibited Least Weight Gain Compared to Other Antipsychotics



Allison DB, et al. *Am J Psychiatry*. 1999;156(11):1686-1696.

Supernus® Pharmaceuticals

TEOSS Study Demonstrated Molindone Safety Profile in Pediatric Population

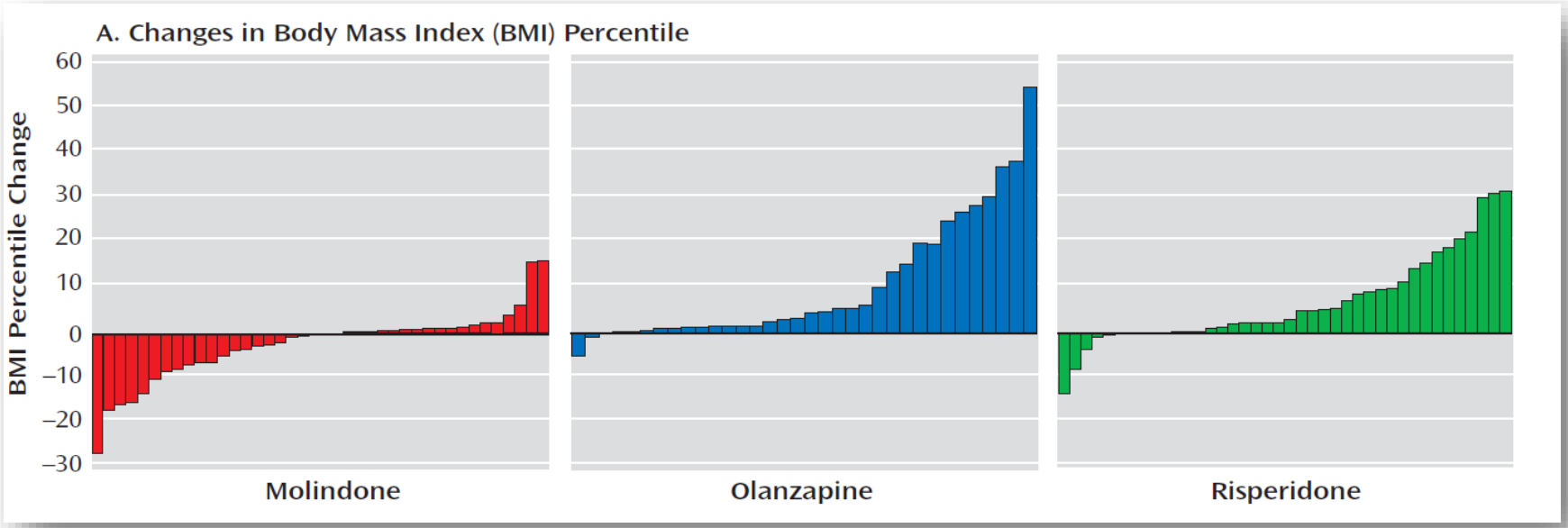
- Evaluated 119 children (early onset schizophrenia and schizoaffective disorder)

Product	Dose Range (mg/day)	Mean Dose (mg/day)
Olanzapine	2.5 – 20	11
Risperidone	0.5 – 6	3
Molindone	10 – 140	60

Am J Psychiatry. 2008 Nov;165(11):1420-31.

Supernus® Pharmaceuticals

Molindone Exhibited Less Weight Gain



Am J Psychiatry. 2008 Nov;165(11):1420-31.

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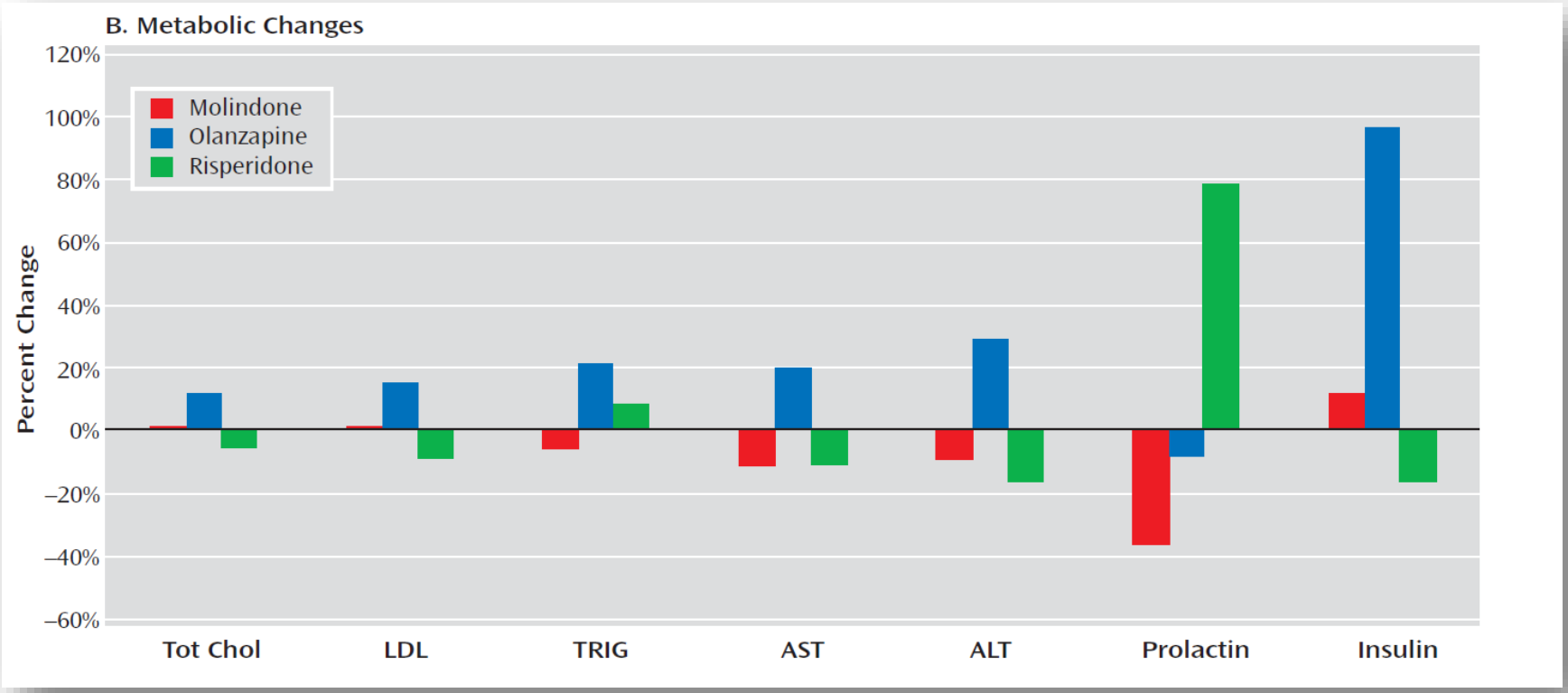
Molindone Showed Significantly Less Effect on Metabolism

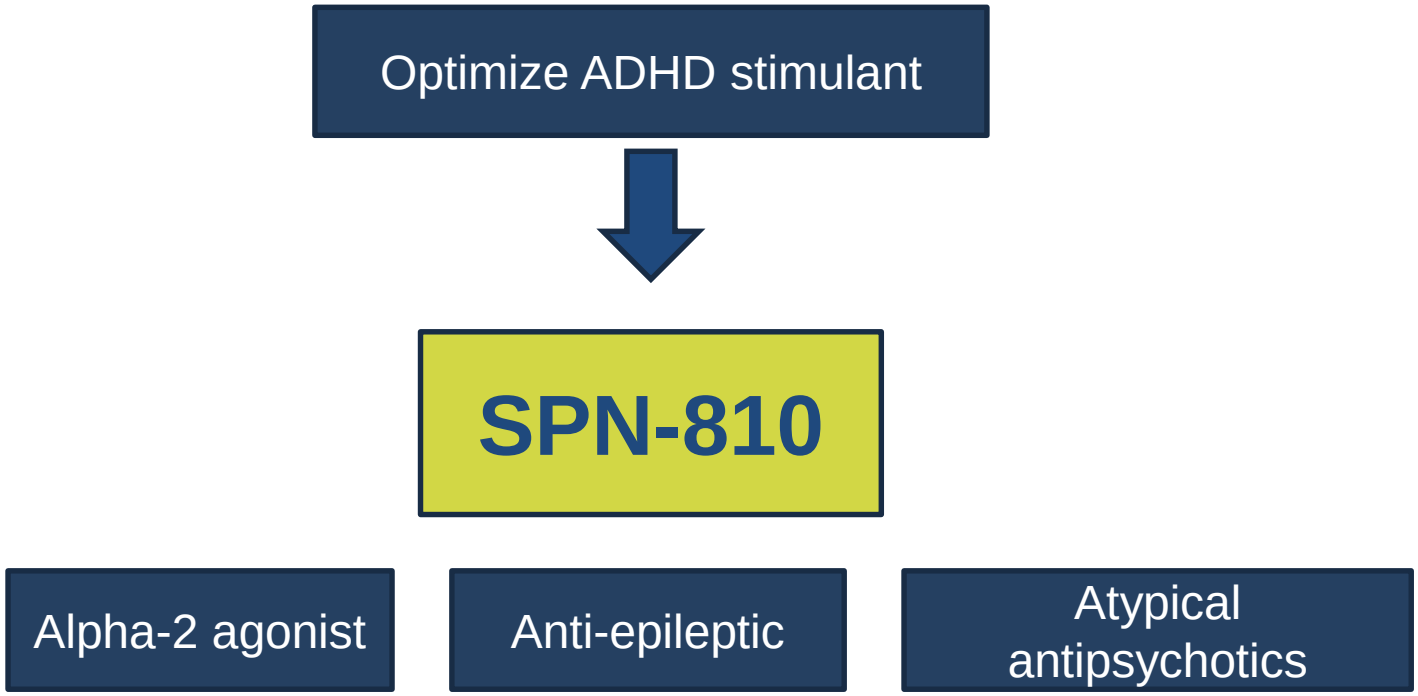


Measures of Liver Function - AST: aspartate aminotransferase; ALT: alanine transaminase

Am J Psychiatry. 2008 Nov;165(11):1420-31.

Supernus® Pharmaceuticals

SPN-810: Promising Candidate for IA Treatment



SPN-810: Development Program

Stefan Schwabe, M.D., Ph.D.
Executive Vice President, Research and Development,
Chief Medical Officer

Supernus® Pharmaceuticals

SPN-810: Mechanism of Action for IA Treatment

- Extended Release Molindone Hydrochloride
- Potent D2 antagonist (efficacy)
  - But less potent than most antipsychotics
  - Infrequent extrapyramidal symptoms
  - Moderate prolactin elevation (shown in clinical trials)
- 5-HT2B antagonist
- No potency for 5-HT2A
  - Differs from atypical antipsychotics
- Lack of binding affinity to H1 and 5-HT2C
  - Less weight gain

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IA Indication

- Granted Fast Track designation
  - Unmet medical need was affirmed
- Collaborated with FDA to develop indication statement
- Worked closely with the FDA to:
  - Develop the IA Diary to measure the primary endpoint
  - Develop the pivotal Phase III efficacy and safety studies

Supernus® Pharmaceuticals

SPN-810 Phase III Studies

Study	Population	Primary Objective	Dose	No. of Subjects	Data Expected
P301	Pediatric (6-12 years)	Efficacy	Placebo 36mg	300+	**2H 2019**
P302	Pediatric (6-12 years)	Efficacy	Placebo 36mg	300	**2H 2019**
P503	Adolescents (12–17 years)	Efficacy	Placebo 36mg 54mg	300	**2020**
P304	Pediatric and Adolescents (6-17 years)	Safety	Flexible dose (OLE)	900	**1H 2020**

*Primary Endpoint: Change in IA behavior frequency, OLE = Open Label Extension

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SPN-810 CHIME 301 and 302 Study Endpoints

Primary Efficacy Endpoint

Percentage change in frequency of IA behaviors per 7 days in the treatment period (titration + maintenance) relative to the baseline period

Key Secondary Efficacy Endpoints

- Clinical Global Impression-Improvement Scale (CGI-I)
- Clinical Global Impression-Severity Scale (CGI-S)

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SPN-810 Adolescent Study (P503) Endpoints

Primary Efficacy Endpoint

Percent change in the frequency of IA behaviors per 7 days in the treatment period (titration + maintenance) relative to the Baseline period.

Key Secondary Efficacy Endpoints

- CGI-S scale
- R-MOAS* rating scale

* Retrospective Modified Overt Aggression Scale;

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SPN-810 P304 Open Label Extension Safety Study

Patients Enrolled	#6 months	#12 months
431	234	142

- Average duration on study is 42.1 weeks (about 10.5 months)
- Achieved the goal of 100 subjects treated for 12 months
- Starting dose at 18 mg with majority of patients trending up to 36 mg
- Good retention and low discontinuations for adverse events (5%)

OLE = Open Label Extension

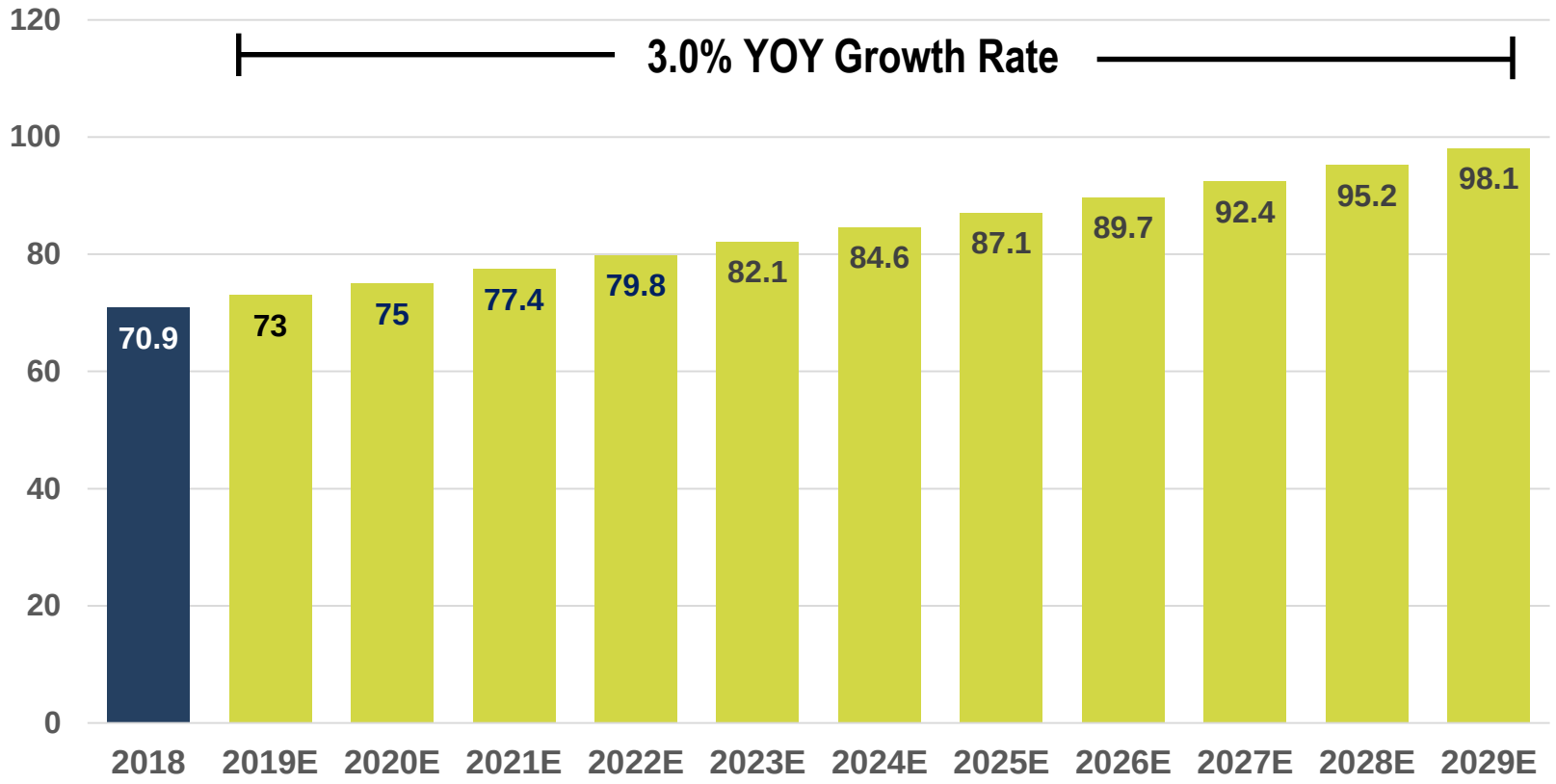
Supernus® Pharmaceuticals

SPN-810: Commercial Opportunity

Todd Horich Ph.D., MBA
Vice President, Marketing

Supernus® Pharmaceuticals

ADHD Market Prescriptions Trending to 89 – 100M



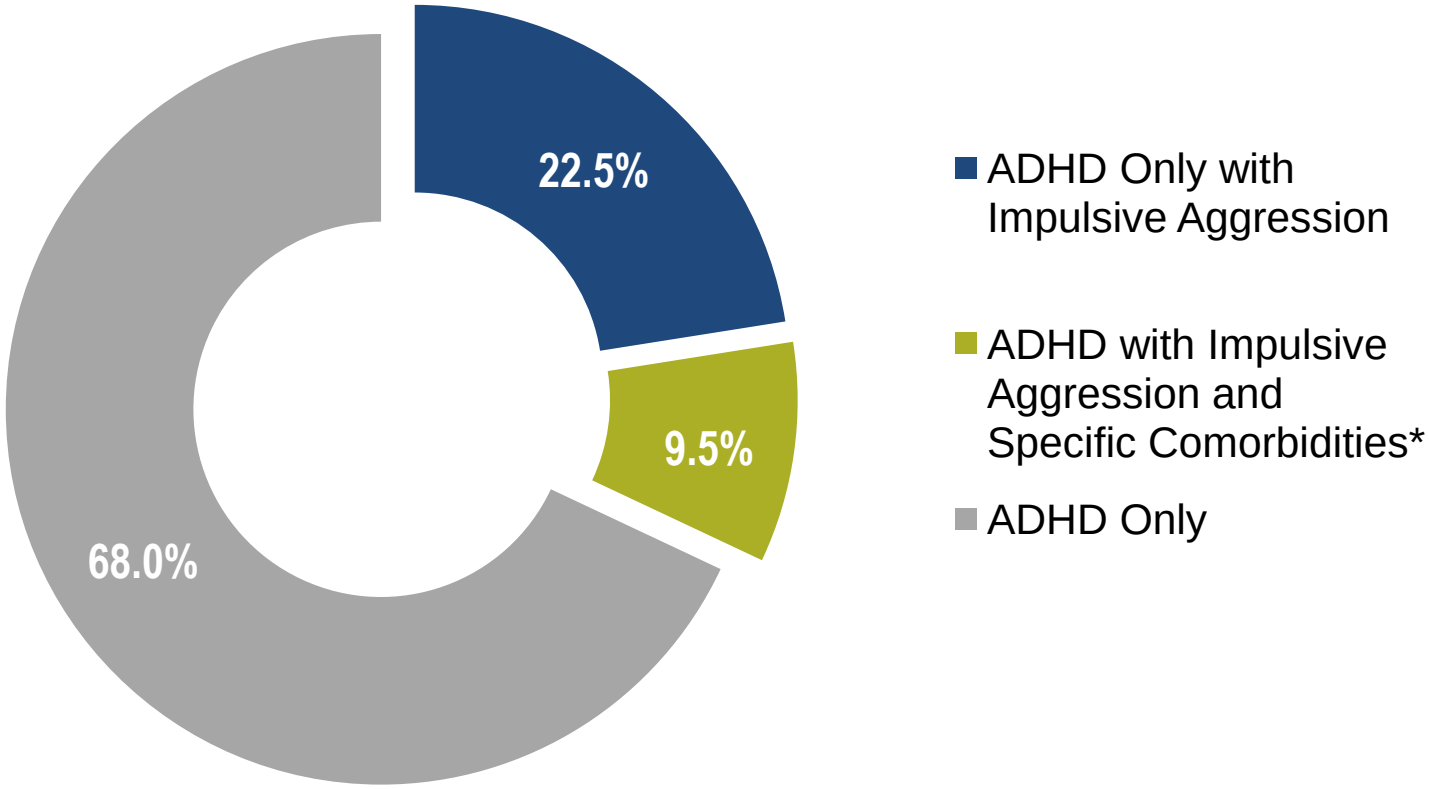
51% of TRxs are adult; 49% are pediatric/adolescent

IQVIA

Supernus® Pharmaceuticals

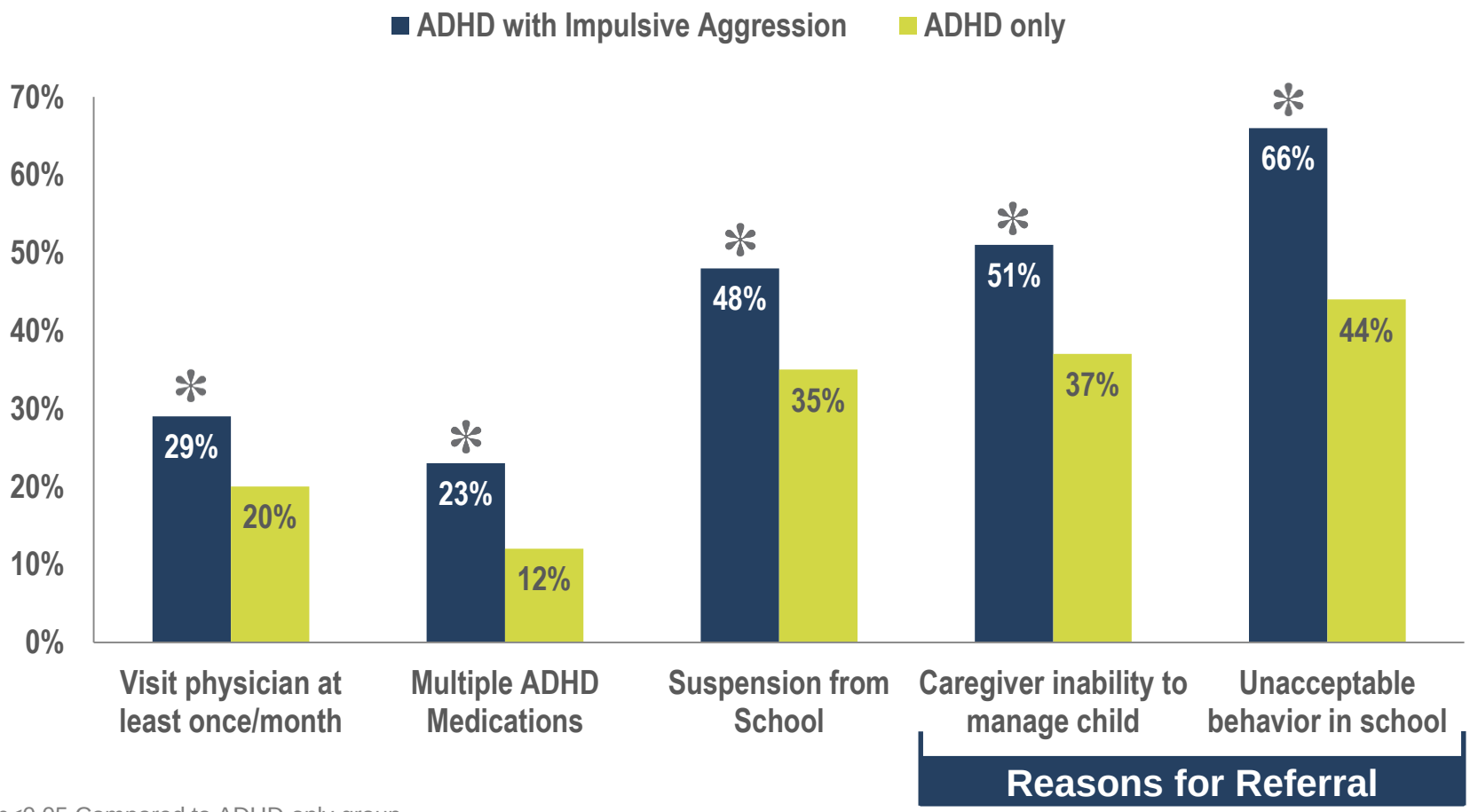
Prevalence of IA in Addressable ADHD Market is 32%

Prevalence of Impulsive Aggression in Children



SPN-810 Market Sizing and Demand Study; April 2015;
*Specific co-morbidities: autism, epilepsy, IQ<70, neurological disorders, bipolar disorder, schizophrenia

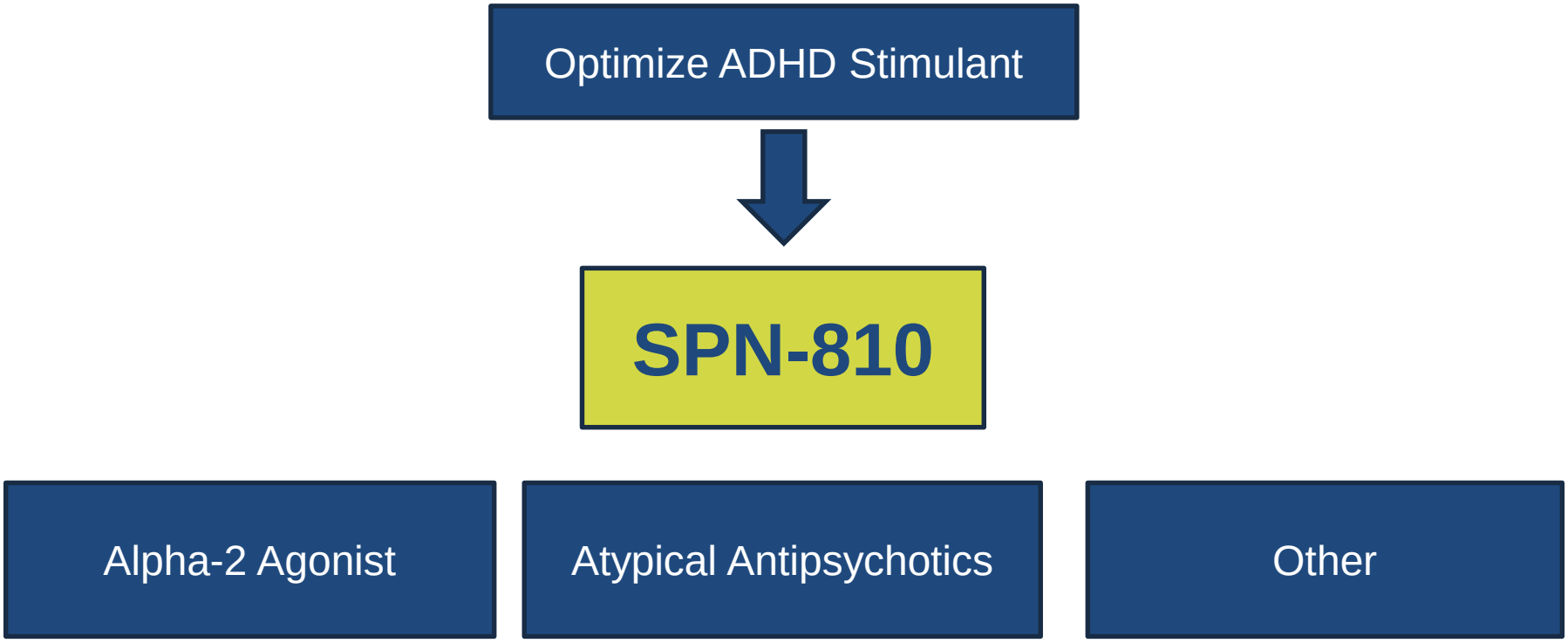
IA in ADHD is a Significant Concern for Physicians, Parents and Caregivers



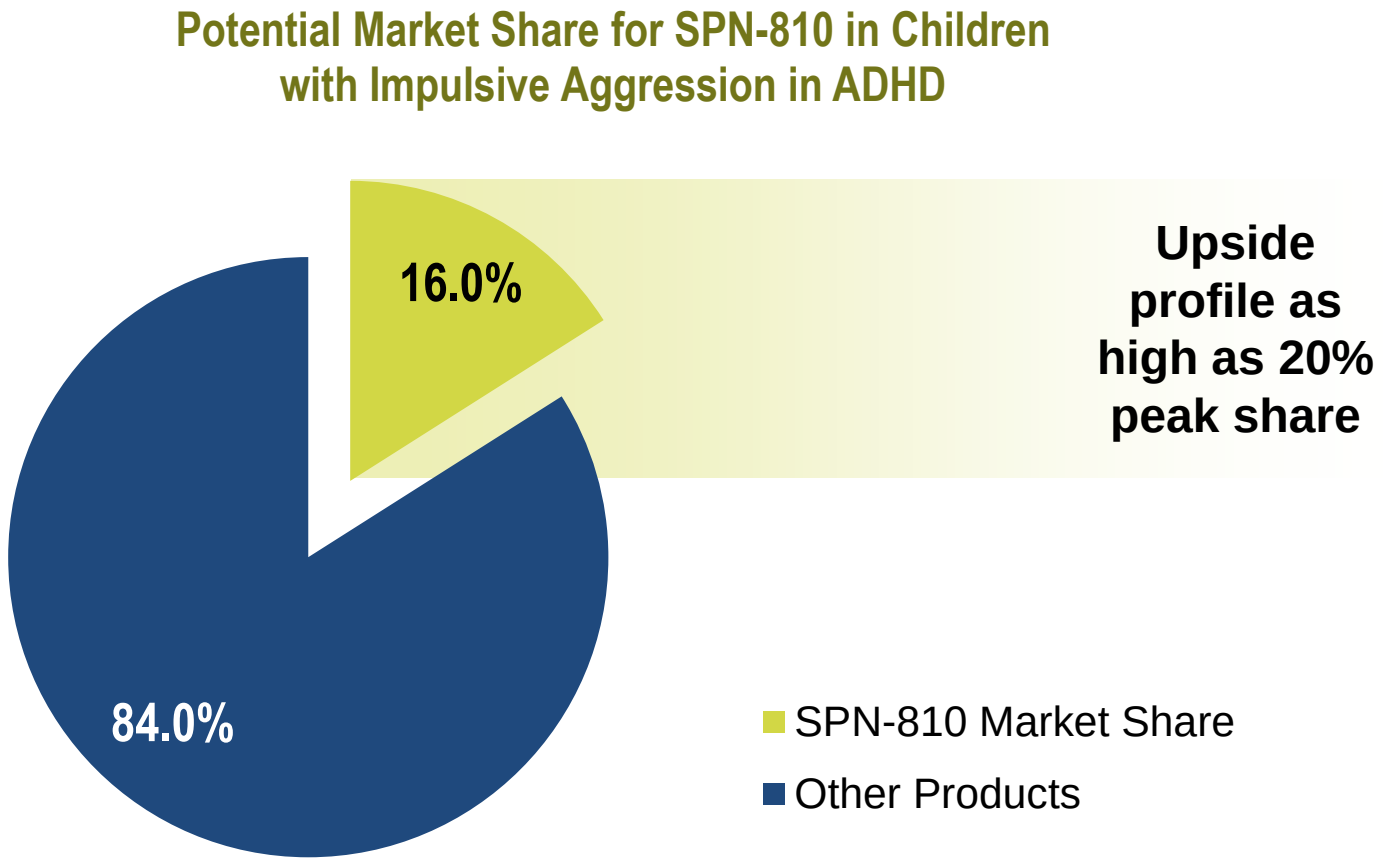
* p<0.05 Compared to ADHD only group

SPN-810 Market Sizing and Demand Study; April 2015

Unmet Needs Exist for Treatments Specific for IA

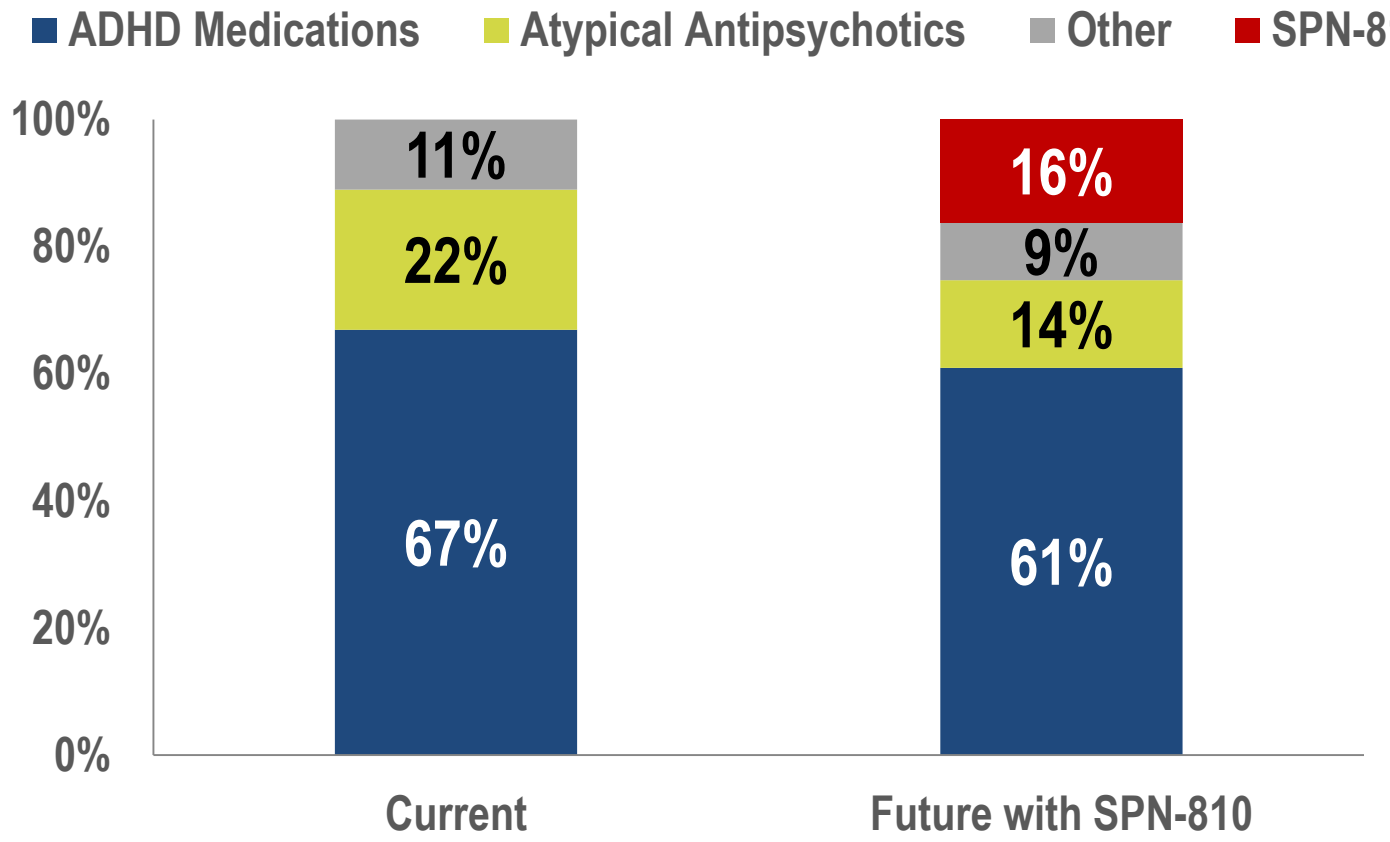


Market Research Suggests 16-20% Market Share for SPN-810 in IA in ADHD



SPN-810 Market Sizing and Demand Study; April 2015

Research Suggests Half of SPN-810 Prescriptions as Replacement for Existing Atypical Antipsychotics



Assumed coverage by Medicaid and by most Insurance plans as a Tier 3 brand

Standard ADHD Medications included stimulants and alpha-2 agonists

SPN-810 Market Sizing and Demand Study; April 2015

Supernus® Pharmaceuticals

SPN-810
Significant Market Opportunity

	Percent	Estimated Prescriptions in Peak Year
ADHD Market Prescriptions		92 - 103 Million
Child and Adolescent ADHD Prescriptions Child Psychiatrists, Child Neurologists, Psychiatrists, and Top Pediatrician Deciles		24 - 28 Million
Prevalence of IA	32%	9.0 Million
	Peak Market Share	**SPN-810 Potential Prescriptions**
SPN-810 Peak Demand	**16 - 20%**	**1.4 - 1.8 Million**

SPN-810 Market Sizing and Demand Study (April 2015); Assumes prevalence and demand from quantitative research are applicable to high ADHD pediatrician prescribers, and peak market share at 5–7 years post launch. Figures in the table above represent management's estimates that are subject to several factors that are beyond our control and actual results may be significantly different from our estimates

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IA Occurs Across Multiple Disorders

- ADHD
- PTSD and Disorders of Traumatic Stress
- Autism Spectrum Disorder
- Bipolar Disorder
- Oppositional Defiant Disorder
- Conduct Disorder
- Intermittent Explosive Disorder
- Disruptive Mood Dysregulation Disorder
- Alzheimer's Disease
- Schizophrenia
- Substance Use Disorder
- Anxiety Disorders
- Psychosis
- Somatic neurological impairments
  - Traumatic Brain Injury
  - Encephalitis
  - Stroke
  - Epilepsy

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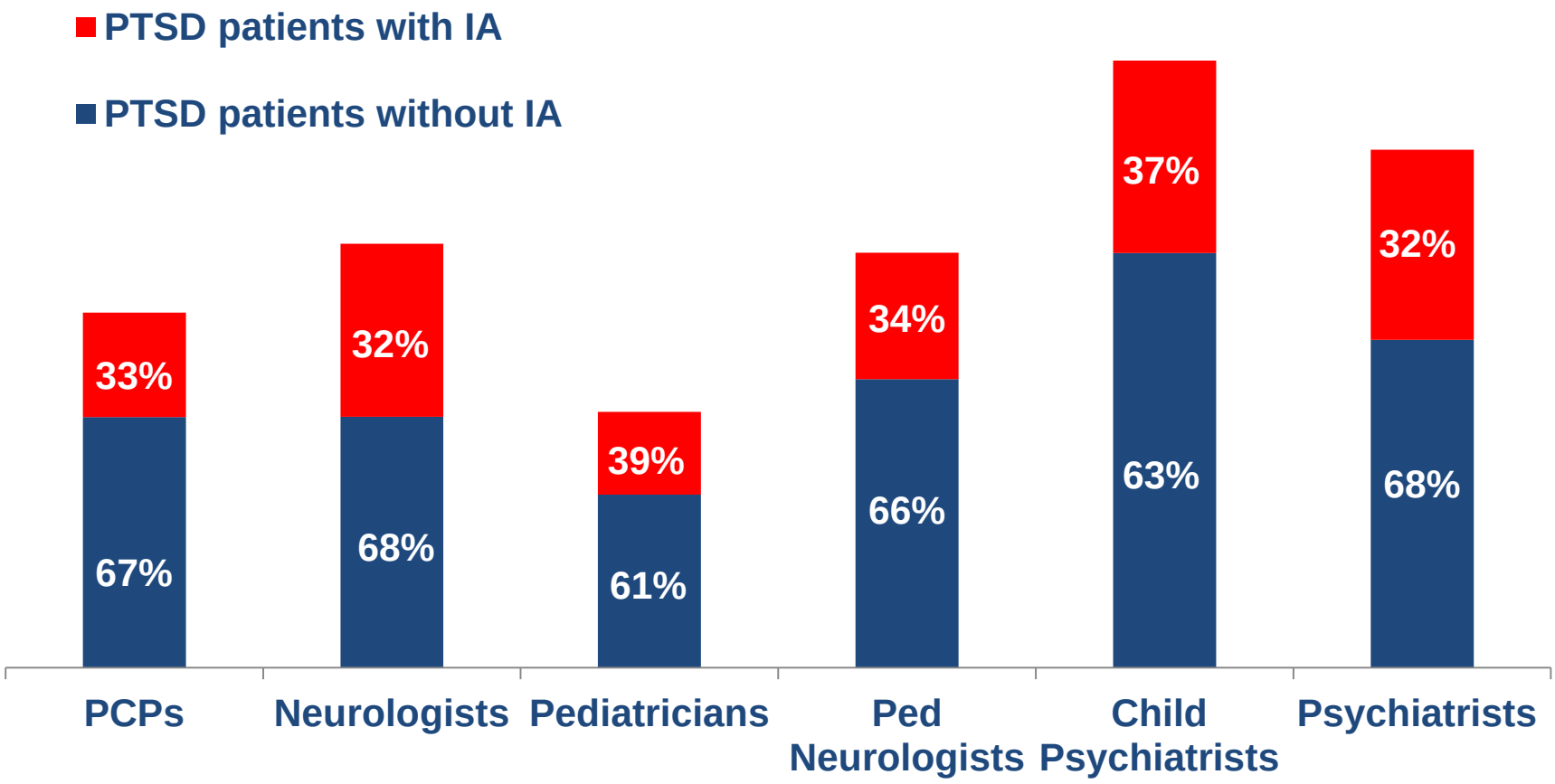
Prevalence of IA in PTSD Consistent Across Specialties in a Large Quantitative Survey



N = 201: PCPs (n=34), Neurologists (n=47), Pediatricians (n=29), PED Neurologists (n=22), Child Psychiatrists (n=20), Psychiatrists (n=49).

IA/PTSD Stems From Various Traumas, Often Associated With Comorbid Psychiatric Conditions

Causes of PTSD

- Abuse (physical, emotional, sexual, verbal)
- Childhood abandonment / neglect
- Sexual assault
- Witness to trauma (domestic violence, murder)
- Combat / war-related
- Bullying
- Natural disasters
- Acts of terrorism
- Other life-threatening traumas (car accident)

Common Comorbidities

- Depression
- Anxiety
- ADHD
- Substance abuse
- Conduct disorder
- Oppositional defiant disorder (ODD)

Supernus market research 8/16
N = 35; child and adult psychiatrists

Supernus® Pharmaceuticals

Satisfaction With Current Products for IA/PTSD is Low

Need for Fewer Side Effects, Better Efficacy, and Approved Indication

#1: Side Effects

- Sedation, weight gain and metabolic effects are particular concerns
- EPS and tardive dyskinesia also worrisome, especially in children

#2: Efficacy

- Difficult to find the right combination of medications / seems ‘hit or miss’
- Products sedate, and do not directly address IA

#3: No FDA Approved Options

- Makes it harder to convince patients to take medication
- Hinders medication approval process / requires prior authorization

Supernus market research 8/16 , N = 35; child and adult psychiatrists

Supernus® Pharmaceuticals

IA Occurs Across Multiple Disorders

- ADHD
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- Schizophrenia
- Substance Use Disorder
- Anxiety Disorders
- Psychosis
- Somatic neurological impairments
  - Traumatic Brain Injury
  - Encephalitis
  - Stroke
  - Epilepsy

Supernus® Pharmaceuticals

FDA-Approved Product for IA in Autism Would Have a Large Impact On Use

% of Autism Patients Age 6-17 with IMPULSIVE AGGRESSION:

38%

(PSYCH avg. 45%, NEURO avg. 31%, PED avg. 30%).

- Important/useful for patient treatment and caregiver decision making
- More comfort for parents
- FDA approval means important clinical data in younger patients available

Potential Significant use of SPN-810 for IA in autism due to FDA approval and potentially favorable SE/safety profile

SUPN IA/Autism Market Research Study 5/15
18 Qualitative individual depth interviews; 5 Autism KOLs, 7 Child Psychs, 3 Devel Peds, 3 Ped Neuros

Supernus® Pharmaceuticals

SPN-810
Novel Product Candidate for IA

IA occurs across multiple disorders including ADHD, autism, bipolar disorder, PTSD

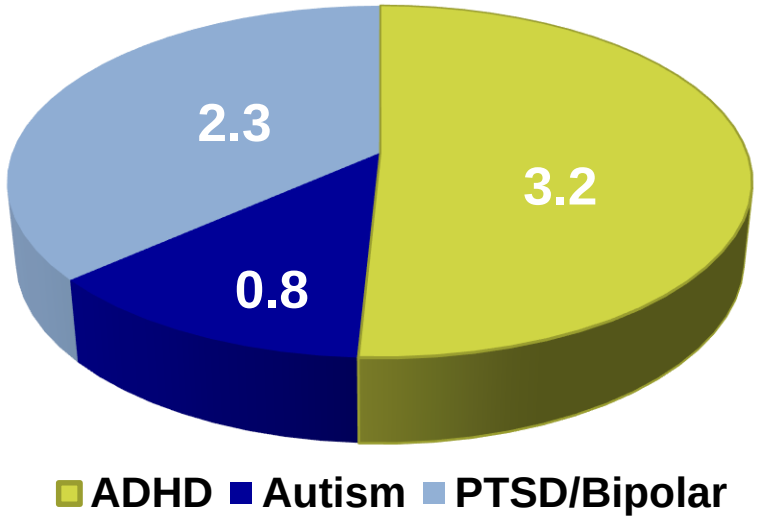
Granted Fast Track Designation

1st **Expected to be First Product Approved to Treat IA**

Building Strong IP with Expirations 2029-2033

2019 **Three Ongoing Phase III Trials**

Market Opportunity[1]
+$6.3B



[1] Initial indication in ADHD population with potential to expand into areas such as Autism and PTSD.
CDC/US Census; IMS; Qualitative Opportunity Assessment Research 2014; * Assumes quantitative research in ADHD is applicable to Autism, PTSD and Bipolar Disorder. Does not account for IA in other CNS areas. Company Research and Estimates
Above figures represent management's estimates that are subject to several factors that are beyond our control and actual results may be significantly different from our estimates

Supernus® Pharmaceuticals

SPN 604:
Bipolar Disorder

Todd Horich Ph.D., MBA
Vice President, Marketing

Supernus® Pharmaceuticals

SPN-604

Novel Product Candidate for Bipolar

50% Use of Oxcarbazepine in Psychiatry

1st Expected to be Only Oxcarbazepine Product Approved to Treat Bipolar

2019 Phase 3 Trials Planned 2H 2019

Market Opportunity
+53 Million Prescriptions

Class of Drugs	% of Prescriptions
Antiepileptics	34
Antipsychotics	29
SSRI's	15
SNRI's	6
Antimania	6
Other Antidepressants	6
Benzodiazepines	4
Total	100

Source: IQVIA 2016

SSRI = Selective serotonin reuptake inhibitor
SNRI = Serotonin & norepinephrine reuptake inhibitor

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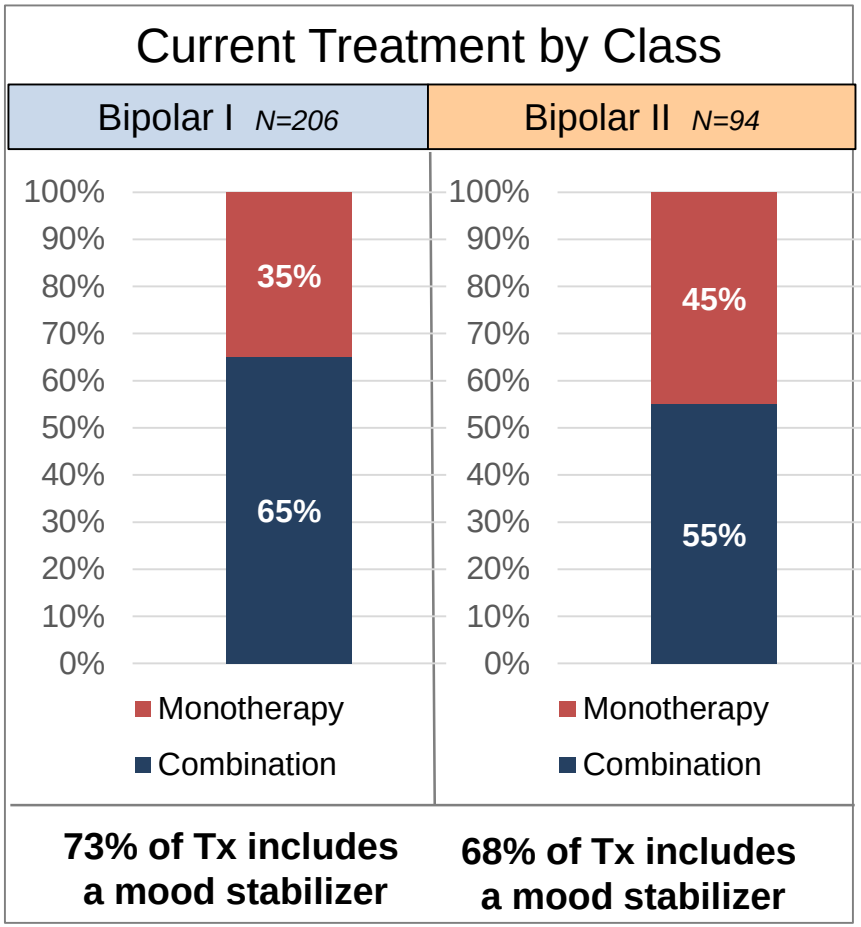
Majority of Treatment For Bipolar I and II Includes Use of Mood Stabilizers

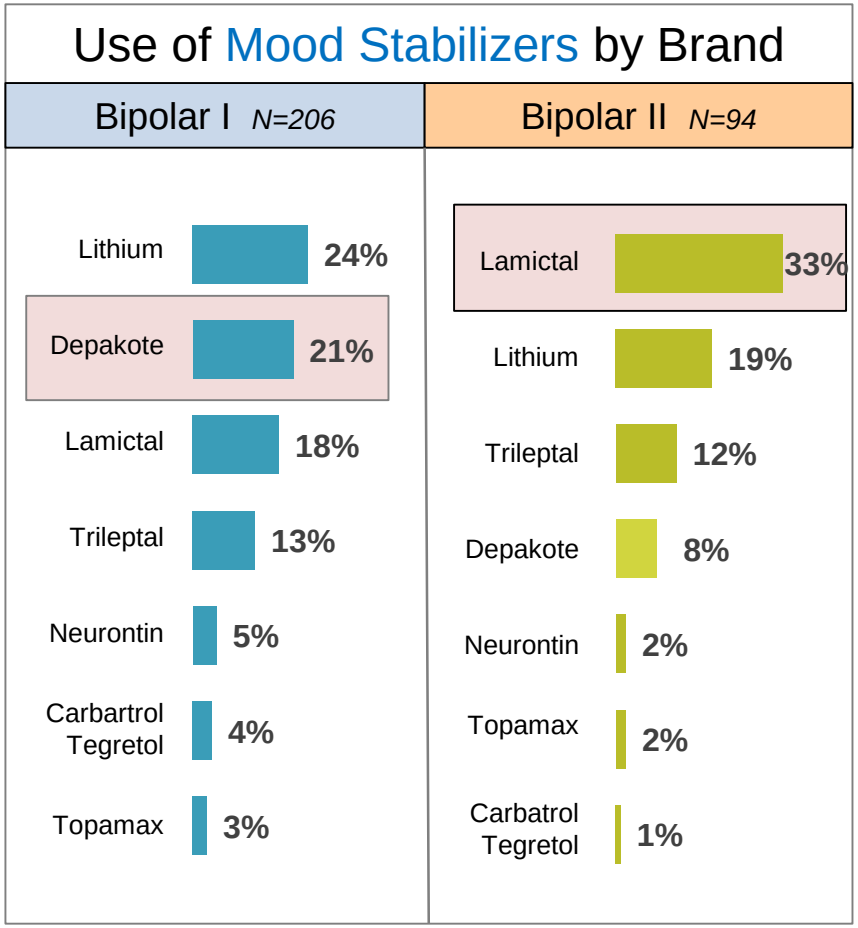


Supernus Bipolar Landscape Study; 2/19. N=150 psychiatrists

Base: Random Patient Charts (n=300)
Trileptal Patient Charts (n=214)

Majority of Treatment For Bipolar I and II Includes Use of Mood Stabilizers

Depakote used most often after Lithium for Bipolar I, Lamictal is preferred in Bipolar II
Off-label Trileptal use is ~12% of patients, or 7% of total bipolar scripts

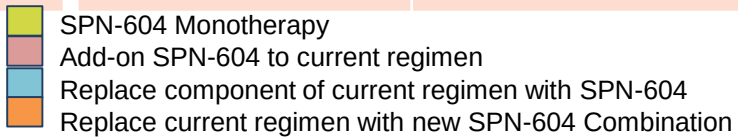


Supernus Bipolar Landscape Study; 2/19. N=150 psychiatrists

Base: Random Patient Charts (n=300)
Trileptal Patient Charts (n=214)

>25% of Bipolar Patients Considered Suitable for SPN-604 at their Last Treatment Change; 50% of Trileptal Patients are Candidates

	All Patients (Random Arm Records)	Bipolar I (Random Arm Records)	Bipolar II (Random Arm Records)	Trileptal Treated (All Trileptal Records)
% Suitable Patients	26%	26%	27%	50%
Type of Anticipated SPN-604 Regimen Adjustment	8% / 48% / 39% / 5%	6% / 53% / 36% / 5%	13% / 37% / 46% / 4%	22% / 22% / 54% / 1%



Supernus Bipolar Landscape Study; 2/19. N=150 psychiatrists

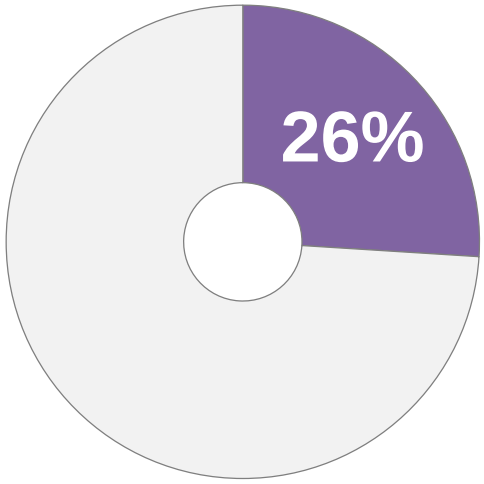
Base: Random Patient Charts (n=300)
Trileptal Patient Charts (n=214)

Supernus® Pharmaceuticals

SPN-604 Receptivity
Anticipation of Future Use Based on Profile

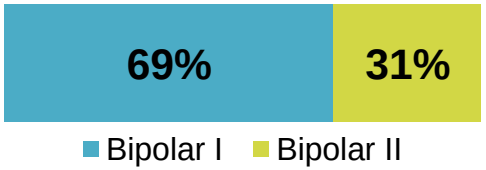
SPN-604 considered suitable for 26% of patients
(which accounts for use of atypical antipsychotics, mood stabilizers and antidepressants)

% of SPN-604 Suitable Patients (at Last Treatment Change)

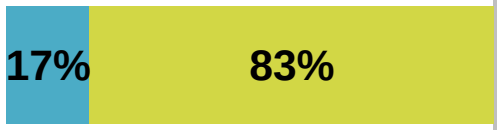


Random arm (N=300)

Bipolar I vs. Bipolar II Use



Monotherapy vs. Combination therapy Use



% Replace Trileptal

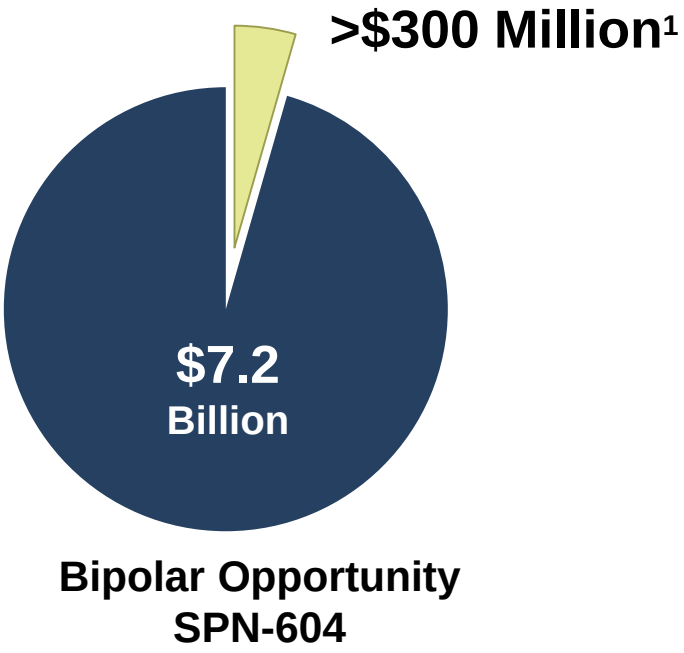
Supernus Bipolar Landscape Study; 2/19. N=150 psychiatrists

Supernus® Pharmaceuticals

SPN-604

Target Market Opportunity in Psychiatry of $7.2 Billion

Potential Peak Sales - SPN-604 >$300 Million



1- Anti-epileptic drugs represent 34% of 53 million prescriptions for bipolar (IQVIA). Average net price per prescription of $400. Peak share of ~5%. Above figures represent management's estimates that are subject to several factors that are beyond our control and actual results may be significantly different from our estimates

Supernus® Pharmaceuticals

SPN-604 Bipolar: Background

- Limited literature on controlled oxcarbazepine studies in bipolar disorder
- Literature review suggests that oxcarbazepine may have more efficacy in Bipolar I disorder in the treatment of mania, hypomania, impulsivity and irritability
- Review of IQVIA prescription data in the National Disease & Therapeutic Index (NDTI)
  - Oxcarbazepine is mostly used adjunctively in bipolar disorder; antipsychotics (55%), antidepressants (26%), lamotrigine (11%), lithium (8%)

Supernus® Pharmaceuticals

SPN-604 Bipolar: Background

- High prescriber interviews sponsored by Supernus:
  - Psychiatrists described oxcarbazepine as an effective treatment for reducing irritability and impulsivity
  - Oxcarbazepine was viewed as an effective treatment for prevention and reduction of hypomanic/ manic symptoms
  - Psychiatrists did not view oxcarbazepine as an effective treatment for depressive symptoms
  - Oxcarbazepine is primarily prescribed adjunctively in Bipolar I disorder

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SPN-604 Bipolar: Background

- Virtually all of psychiatrists interviewed treat bipolar disorder in an outpatient setting
- Patients presenting with manic-related symptoms are being referred to them after experiencing a manic episode (Bipolar I) managed in an in-patient setting

Two most common symptomatologies that would sway psychiatrists to either initiate, switch, or adjust Oxcarbazepine dosing

Presentation of Irritability	Presentation of Impulsivity
• Aggression • Agitation • Anger • Violence	• Euphoria • Hyperactivity • Hyper sexuality • Excessive involvement in pleasurable activities

SPN–604 Bipolar: Clinical Development Plan

- Potential Indication: Acute Treatment of Manic and Mixed Episodes associated with Bipolar I
- Number of clinical studies required: Two positive studies
- Number of subjects: Roughly 360 subjects in Study 1 and 540 subjects in Study 2
- Dosing: TBD (may include one fixed and one flexible dose study)
- Duration of study: Six weeks for an adjunctive outpatient study and three weeks for a monotherapy inpatient study
- Initiation of study: 4Q 2019
- Completion of studies: Approximately 2 years for topline results

General Q&A

Vision

Multi-Billion Dollar Market Value

Neurology Portfolio

>$500 Million in Peak Revenue

Psychiatry Portfolio

Multi-Billion in Peak Revenue

Strong R&D Capability

Corporate Development

Supernus® Pharmaceuticals