



# Taking on Critical Public Health Challenges

February 2019

# Forward-Looking Statements

Certain statements set forth in this presentation constitute “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the company’s expectations with respect to its current and future financial and operating performance, business plans and prospects; the continued growth of the long-acting injectable antipsychotic market and revenue from the company’s commercial products, including VIVITROL®, ARISTADA® and ARISTADA INITIO®; potential expansion and growth of the company’s schizophrenia franchise; improvements to and modernization of the treatment ecosystem for opioid dependence, including related policy initiatives and state and federal funding; the timing, funding, results and feasibility of clinical development activities relating to the company’s products and development candidates, including expansion of the ongoing phase 1 study for ALKS 4230 and initiation of a phase 1 subcutaneous dosing study for ALKS 4230, the timing of topline data from the phase 3 elective study for dioximel fumarate (“DRF”), the timing of topline data from the phase 3b study evaluating ARISTADA® and INVEGA SUSTENNA®, the timing of the availability and presentation of data relating to ALKS 3831 and submission of a new drug application (“NDA”) for ALKS 3831; the company’s expectations and timelines for regulatory interactions with the U.S. Food and Drug Administration (“FDA”), and actions by the FDA, relating to the company’s NDA submissions for DRF and future NDA submission for ALKS 3831; the company’s commercial infrastructure and expectations concerning the timing, results and nature of commercial activities relating to the company’s products, including growth of the company’s hospital sales force for ARISTADA, and preliminary lifecycle management activities, launch planning and payer discussions for ALKS 3831; the potential financial benefits that may be achieved under the license and collaboration agreement between the company and Biogen for DRF; the therapeutic value and commercial potential of the company’s commercial products and development candidates, and funding for, payer coverage of, and patient access to and awareness of, the company’s commercial products and development candidates. Although the company believes that such forward-looking statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to various risks, assumptions and uncertainties. These risks, assumptions and uncertainties include, among others: the unfavorable outcome of litigation, including so-called “Paragraph IV” litigation and other patent litigation, related to any of the company’s products or partnered products, which may lead to competition from generic drug manufacturers; data from clinical trials may be interpreted by the FDA in different ways than the company interprets it; the FDA may not agree with the company’s regulatory approval strategies or components of the company’s filings for its products, including its clinical trial designs, conduct and methodologies or the sufficiency of the results thereof to support approval; clinical development activities may not be completed on time or at all; the results of the company’s clinical development activities may not be positive, or predictive of real-world results or of results in subsequent clinical trials; regulatory submissions may not occur or be submitted in a timely manner; the company and its licensees may not be able to continue to successfully commercialize their products; there may be a reduction in payment rate or reimbursement for the company’s products or an increase in the company’s financial obligations to governmental payers; the FDA or regulatory authorities outside the U.S. may make adverse decisions regarding the company’s products; the company’s products may prove difficult to manufacture, be precluded from commercialization by the proprietary rights of third parties, or have unintended side effects, adverse reactions or incidents of misuse; and those risks, assumptions and uncertainties described under the heading “Risk Factors” in the company’s most recent Annual Report on Form 10-K and in subsequent filings made by the company with the U.S. Securities and Exchange Commission (“SEC”), which are available on the SEC’s website at [www.sec.gov](http://www.sec.gov) and on the company’s website at [www.alkermes.com](http://www.alkermes.com) in the “Investors—SEC filings” section. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation.

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# Patient-Inspired Medicines: Making a Real Impact



## Drug development driven by real-world needs of patients

- Using deep scientific expertise and clinical insights to develop medicines designed to positively impact the lives of patients, families and communities



## Distinctive focus in mental health and addiction

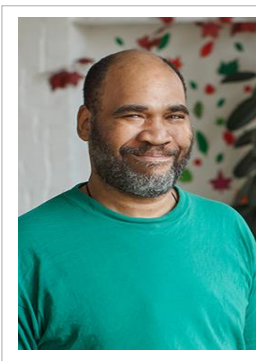
- Targeting chronic, debilitating psychiatric disorders where therapeutic options are available but significant patient needs remain



## Specialized commercial capabilities

- Navigating challenging treatment systems, administered by large commercial and government payers

# Focus on Diseases With Major Public Health Implications



**3.5M**

**SUFFER FROM  
SCHIZOPHRENIA<sup>1</sup>**



**2.4M**

**ARE TREATED FOR  
ALCOHOL USE  
DISORDER<sup>2</sup>**



**2.1M**

**HAVE OPIOID USE  
DISORDER<sup>2</sup>**



**16.2M**

**SUFFER FROM MAJOR  
DEPRESSIVE DISORDER<sup>3</sup>**

1. Schizophrenia and Related Disorders Alliance of America, <https://sardaa.org/resources/about-schizophrenia/> accessed on Jan. 2, 2019

2. Substance Abuse and Mental Health Services Administration (SAMHSA). 2017 National Survey on Drug Use and Health (NSDUH)

3. Rush AJ, et al. *Am J. Psychiatry*. 2006, 163(11): 1905-1917 (STAR\*D Study). Decision Resources 2016

# Transformational Progress Over the Past 5 Years

## Delivering Growth Across Multiple Dimensions

### Meaningful impact on patients



~380K patients<sup>1</sup>  
treated with  
VIVITROL® or  
ARISTADA®

### Enhanced scale of the business



Crossed \$1B in  
total revenue in  
2018  
Increased annual  
proprietary  
product net sales  
by 527%<sup>2</sup>

### Sophisticated commercial infrastructure



Community and  
hospital sales  
organizations  
supported by  
extensive team,  
including: policy,  
patient access  
services,  
managed markets  
and marketing

### World-class science and late-stage pipeline



Expanded  
discovery and  
clinical  
development  
capabilities  
4 NDA  
submissions

### Specialized manufacturing capabilities



950M oral  
solid doses<sup>1</sup>  
30M sterile  
injectable doses<sup>1</sup>  
~1,000 employees  
in operations and  
quality

### Dedicated culture



~2,300 total  
employees in  
Ireland, MA, OH,  
and U.S.-based  
field sales force

1. Includes years 2014 through 2018

2. FY2018 compared to FY2013



## **Establishing a Leadership Position in Schizophrenia**

# Significant Opportunity to Help Address Needs in Schizophrenia

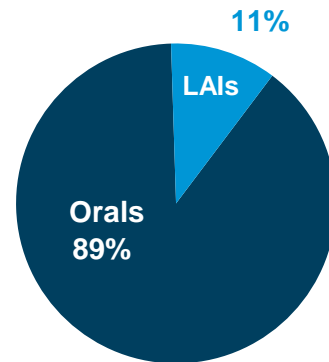
■ Schizophrenia is a serious mental illness that affects ~3.5M patients in the U.S.<sup>1</sup>

- Treatment and other economic costs due to schizophrenia are estimated to be between \$32B - \$65B annually<sup>1</sup>

■ Available antipsychotic treatments present trade-off between efficacy and tolerability

- Oral therapies dominate the treatment paradigm
- Long-acting injectables (LAIs) demonstrate improved outcomes but are currently underutilized<sup>2</sup>

**Atypical Antipsychotics  
TRx for Schizophrenia<sup>3</sup>**



  
**Orals**  
**~15M**  
TRx in 2018<sup>3</sup>

  
**LAIs**  
**\$2.6B**  
2018 TTM net sales;  
Growing at 17%  
CAGR<sup>4</sup>

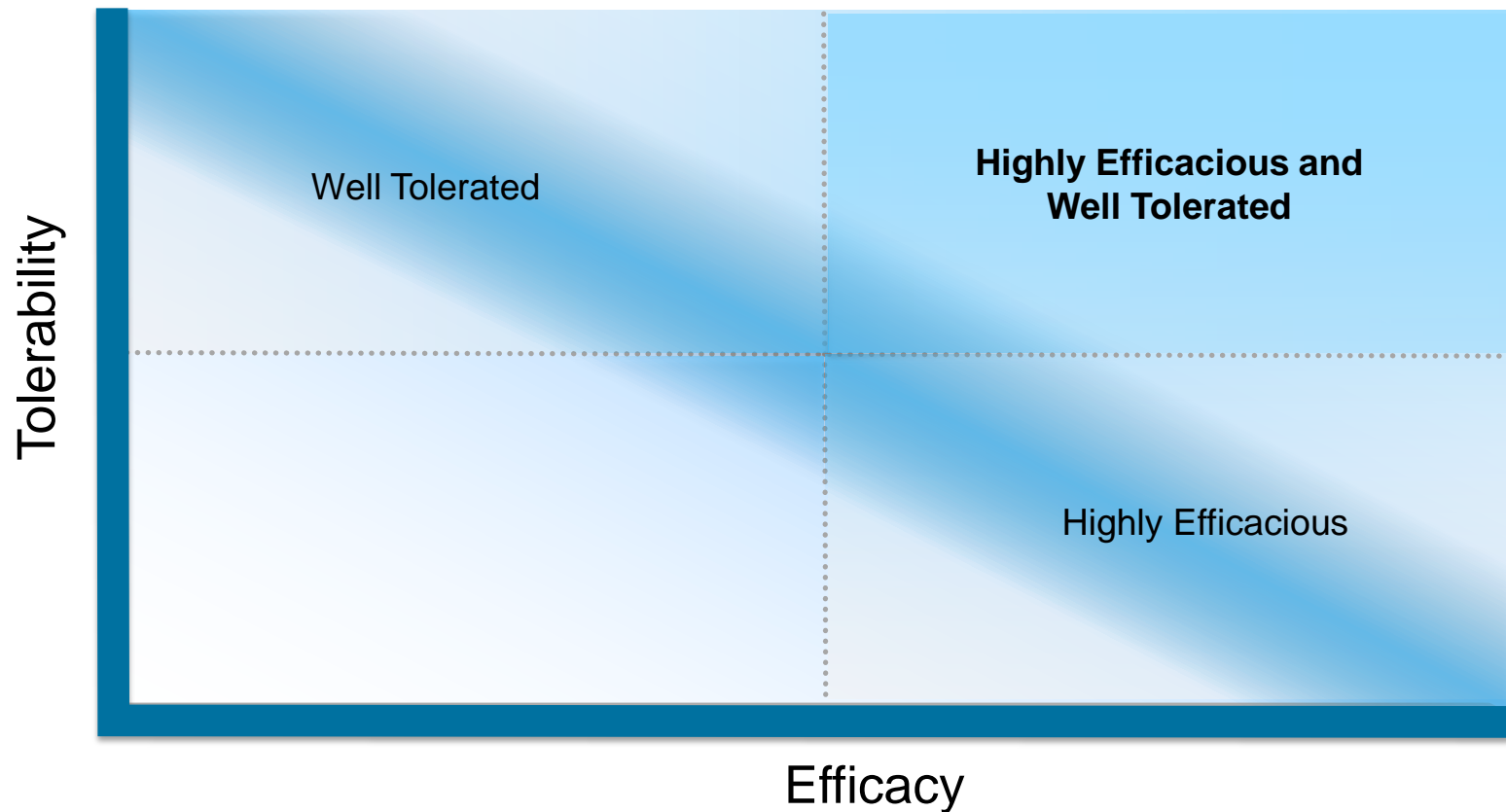
1. Schizophrenia and Related Disorders Alliance of America, <https://sardaa.org/resources/about-schizophrenia/> accessed on Jan. 2, 2019.

2. Subotnik KL, et al. JAMA Psychiatry. 2015, 72(8): 822-829.

3. IQVIA NSP & Custom SOB data sets R12M ending September 2018.

4. Johnson & Johnson, Otsuka, Lundbeck and Alkermes quarterly reports.

# Opportunity to Provide New Medicines With Efficacy and Tolerability





# Developing Important New Medicines for the Treatment of Schizophrenia

**ARISTADA<sup>®</sup>**  
aripiprazole lauroxil  
extended-release injectable suspension  
441mg · 662mg · 882mg · 1064mg

Long-acting injectable prodrug  
new molecular entity (NME)



**ALKS 3831**

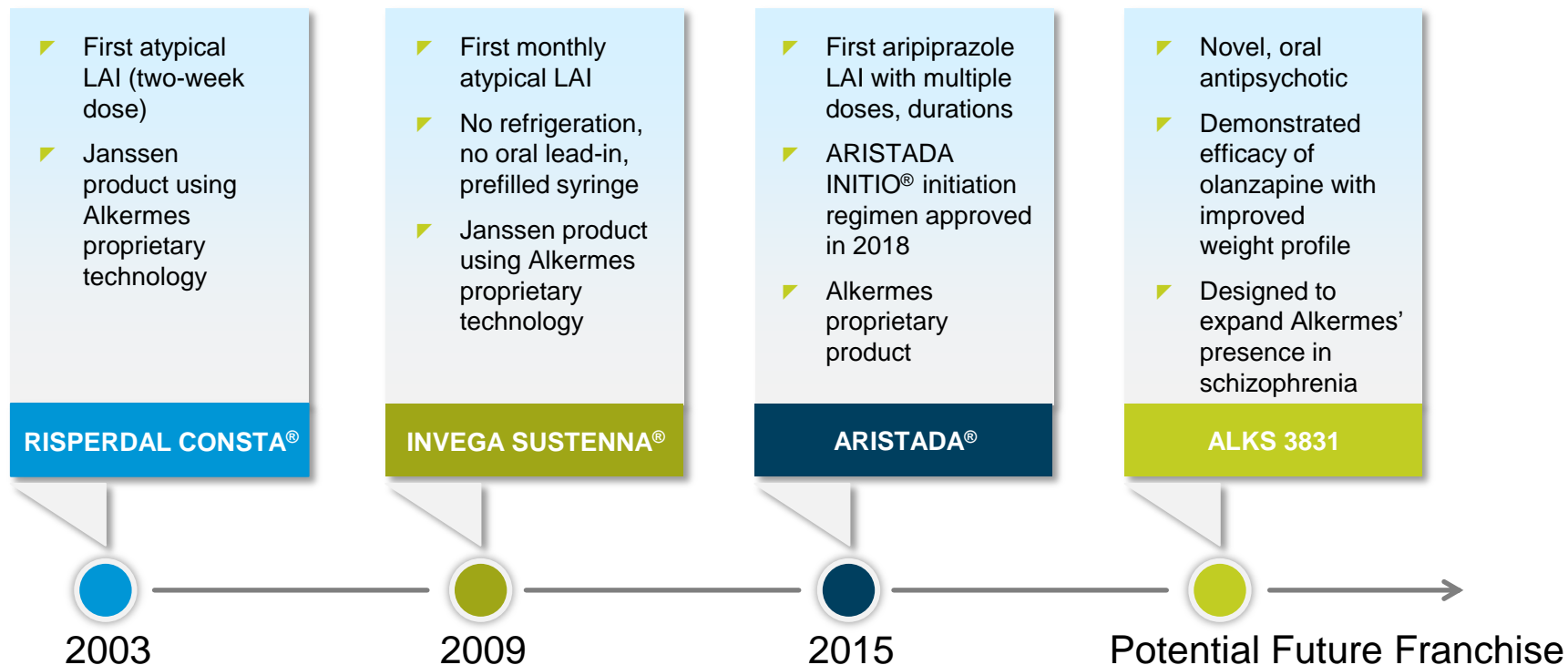
Investigational, oral bilayer tablet,  
olanzapine plus novel NME



# Integrated Infrastructure Scaled to Address Complex Disease Areas



# Evolution of Alkermes' Schizophrenia Franchise



RISPERDAL CONSTA® and INVEGA SUSTENNA® are trademarks of Johnson & Johnson.

# ARISTADA®: Long-Acting Injectable for Treatment of Schizophrenia

- Differentiated medicine provides proven efficacy and safety
  - Four approved doses
  - Three dosing intervals: Monthly, six-week, two-month
  - 1-day initiation with ARISTADA INITIO® regimen\*



**ARISTADA®**  
aripiprazole lauroxil  
extended-release injectable suspension  
441 mg • 662 mg • 882 mg • 1064 mg

**ARISTADA product family is designed to address the  
real-world needs of patients and providers in the community**

# Key Differentiating Feature: Treatment Initiation With ARISTADA INITIO®

- ARISTADA® is the first and only LAI with the ability to fully dose on day one\* for up to two months
- Initiation regimen\* designed with needs of patients, healthcare providers and treatment settings in mind
  - Supports continuity of care from inpatient to outpatient settings
  - One-third of LAI initiations occur in inpatient treatment settings including hospitals and crisis stabilization units<sup>1</sup>

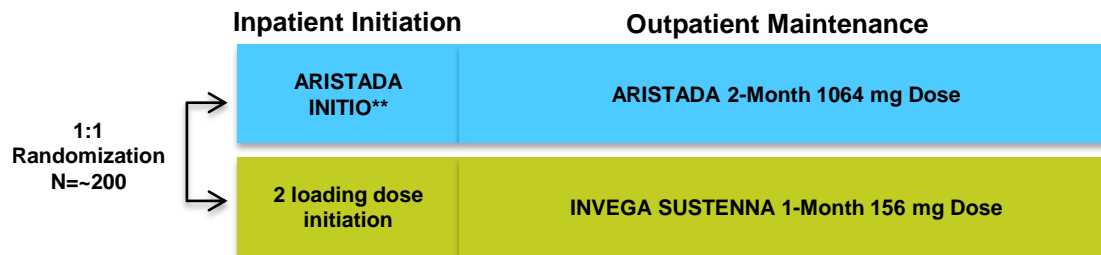


\*ARISTADA INITIO + single 30 mg oral dose of aripiprazole replaces need for concomitant three weeks of oral aripiprazole for initiation of ARISTADA, with relevant levels of aripiprazole concentration reached within four days. ARISTADA INITIO was approved by FDA on June 29, 2018.

1. Truven Marketscan 2015.

# ARISTADA INITIO® Plus Two-Month: Building the Evidence Base

- Phase 3b study designed to provide clinical evidence of efficacy and safety of ARISTADA INITIO plus ARISTADA® two-month dose alongside market leader, INVEGA SUSTENNA®
  - Follows positive data from INVEGA SUSTENNA/ARISTADA switch study presented at U.S. Psych Congress in 2017\*
- Data expected H1 2019



- Primary efficacy endpoint: Change from baseline in PANSS total score at Week 4 within each treatment group
- Secondary endpoints include change in PANSS total score between treatment groups at Week 4 and change from baseline in PANSS total score at six months

\*Claxton, A. et al. Switching Patients with Schizophrenia from Paliperidone Palmitate to Aripiprazole Lauroxil: A 6-month, Prospective, Open-label Study. Presented at U.S. Psych Congress 2017.

\*\*ARISTADA INITIO + single 30 mg oral dose of aripiprazole replaces need for concomitant three weeks of oral aripiprazole for initiation of ARISTADA, with relevant levels of aripiprazole concentration reached within four days.

# ARISTADA®: Differentiated in the LAI Market

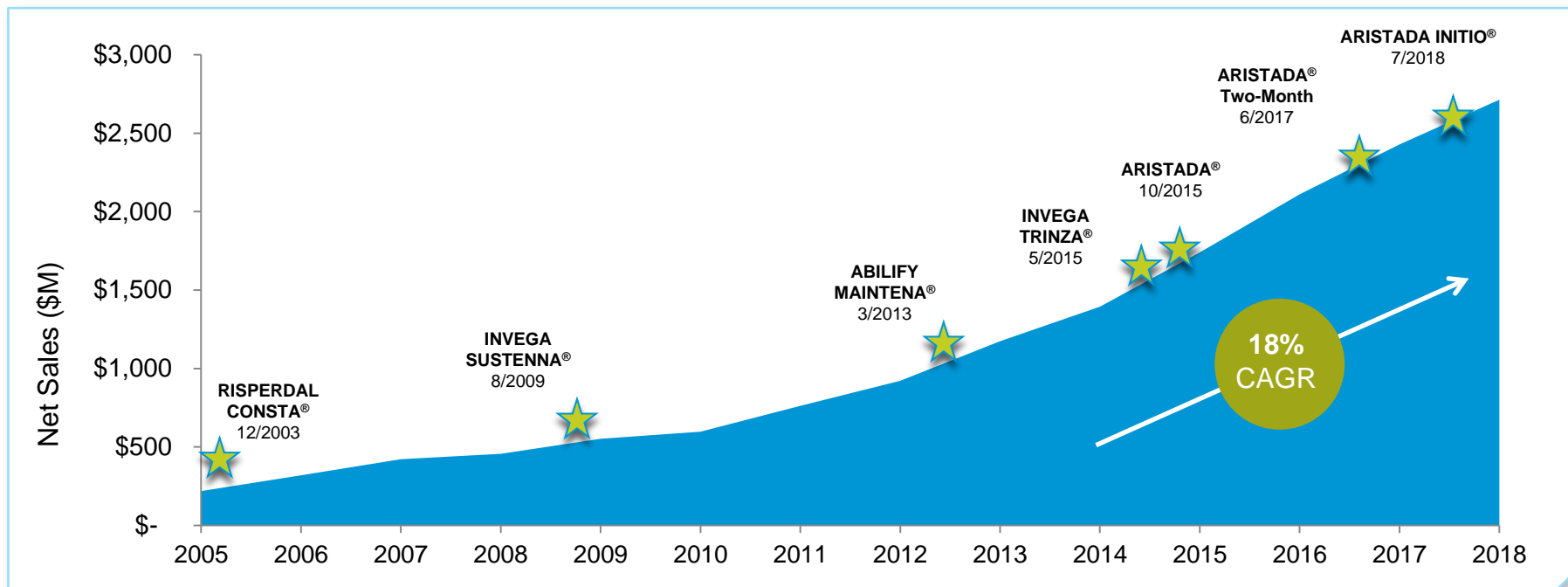
	Treatment Initiation	Dosing Intervals	Dosing Strengths
<b>ARISTADA</b>	ARISTADA INITIO® regimen*	One-month, six-week and two-month	5 doses**
<b>INVEGA SUSTENNA®</b>	2 loading-dose injections	One-month and three-month	5 doses
<b>RISPERDAL CONSTA®</b>	2 weeks daily oral	Two-week	3 main doses†
<b>ABILIFY MAINTENA®</b>	2 weeks daily oral	One-month	1 main dose †

\*ARISTADA INITIO + single 30 mg oral dose of aripiprazole provides an alternative for concomitant three weeks of oral aripiprazole for initiation of ARISTADA, with relevant levels of aripiprazole concentration reached within four days. ARISTADA INITIO was approved by FDA on June 29, 2018.

\*\* Including ARISTADA INITIO

† Excluding low doses for poor metabolizers.

# High-Growth U.S. LAI Atypical Antipsychotic Market

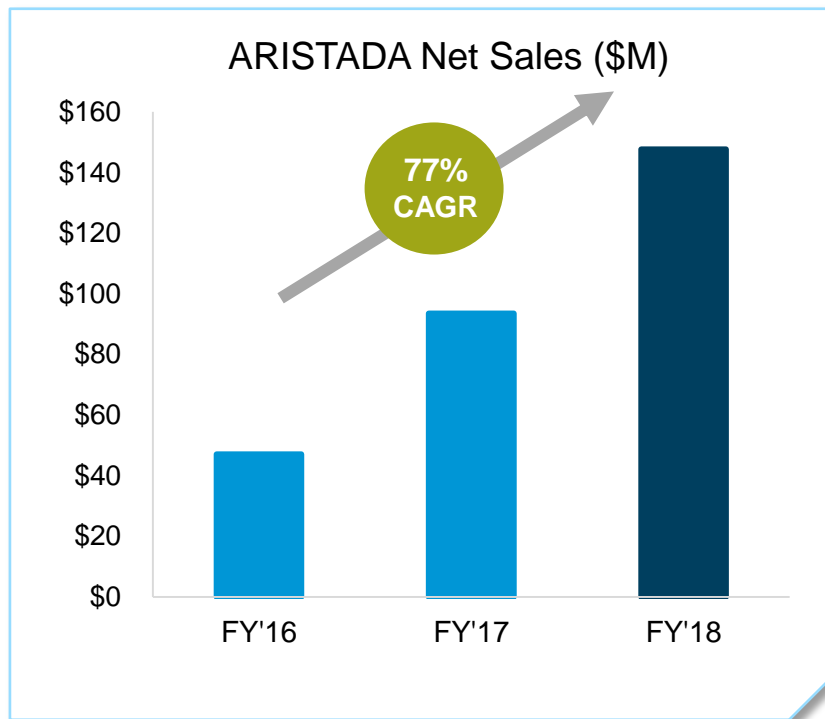


**Potential to be \$3-4B+ U.S. market in 2020**

Sources: Johnson & Johnson, Otsuka, Lundbeck and Alkermes quarterly reports.



# ARISTADA®: Growing Into its Potential



## Anticipated Growth Drivers

- ARISTADA INITIO® regimen\* plus ARISTADA two-month dose
- New clinical data expected in 2019
- Expanded commercial team increasing provider awareness; Hospital commercial organization targeting new starts
- Collaborating with policymakers and industry peers to improve treatment system for serious mental illness

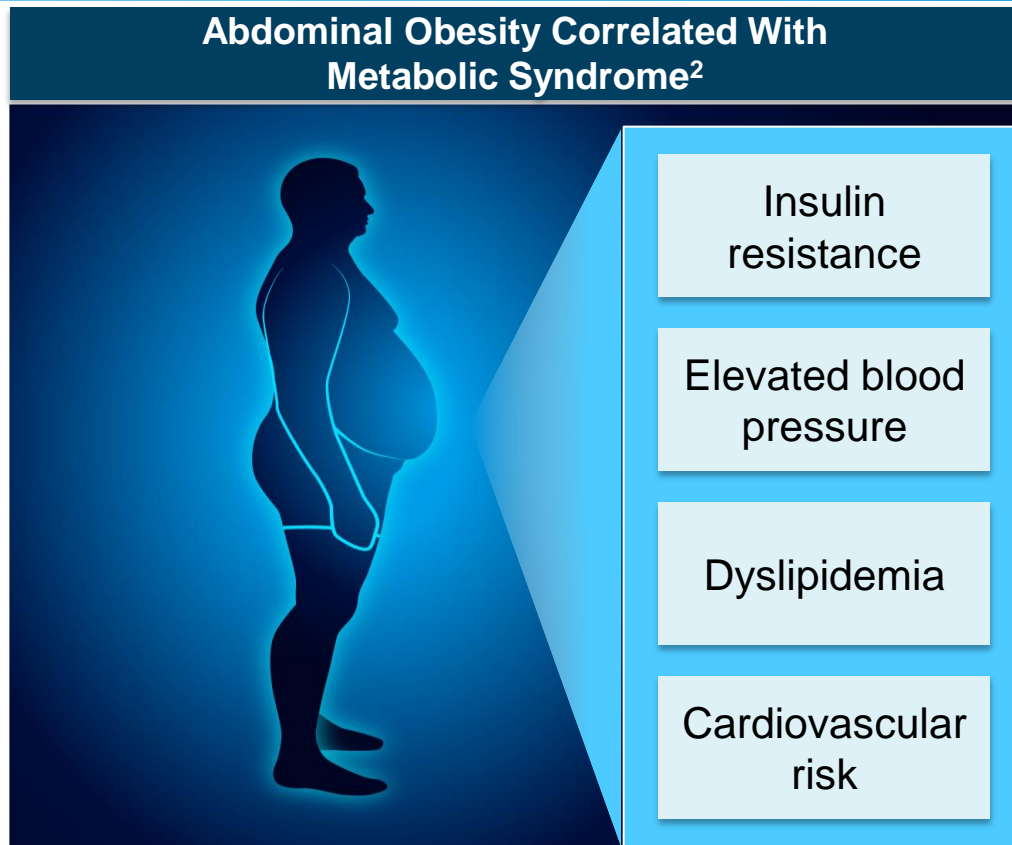
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# ALKS 3831: A New Potential Oral Treatment for Schizophrenia

- Designed to offer robust efficacy of olanzapine with favorable weight and metabolic properties
  - Samidorphan expands olanzapine's spectrum of activity to help mitigate weight gain liability
- Registration studies now complete
  - Efficacy, safety and weight gain profile confirmed in two large, phase 3 studies
  - NDA submission planned for mid-2019
- Fixed-dose combination
  - Bilayer tablet of olanzapine (5 mg, 10 mg, 15 mg, or 20 mg) with samidorphan (10 mg)



# Olanzapine Associated With Abdominal Weight Gain<sup>1</sup>



# ALKS 3831: Efficacy, Safety and Weight Gain Profile Confirmed in Two Large, Phase 3 Studies



## ENLIGHTEN-1 Efficacy Study

- Antipsychotic efficacy vs. placebo
- 403 patients with acute schizophrenia
- ALKS 3831 demonstrated statistically significant reductions from baseline in PANSS scores at 4 weeks, compared to placebo ( $p < 0.001$ )
- Olanzapine achieved similar improvements from baseline PANSS scores, compared to placebo ( $p = 0.004$ )

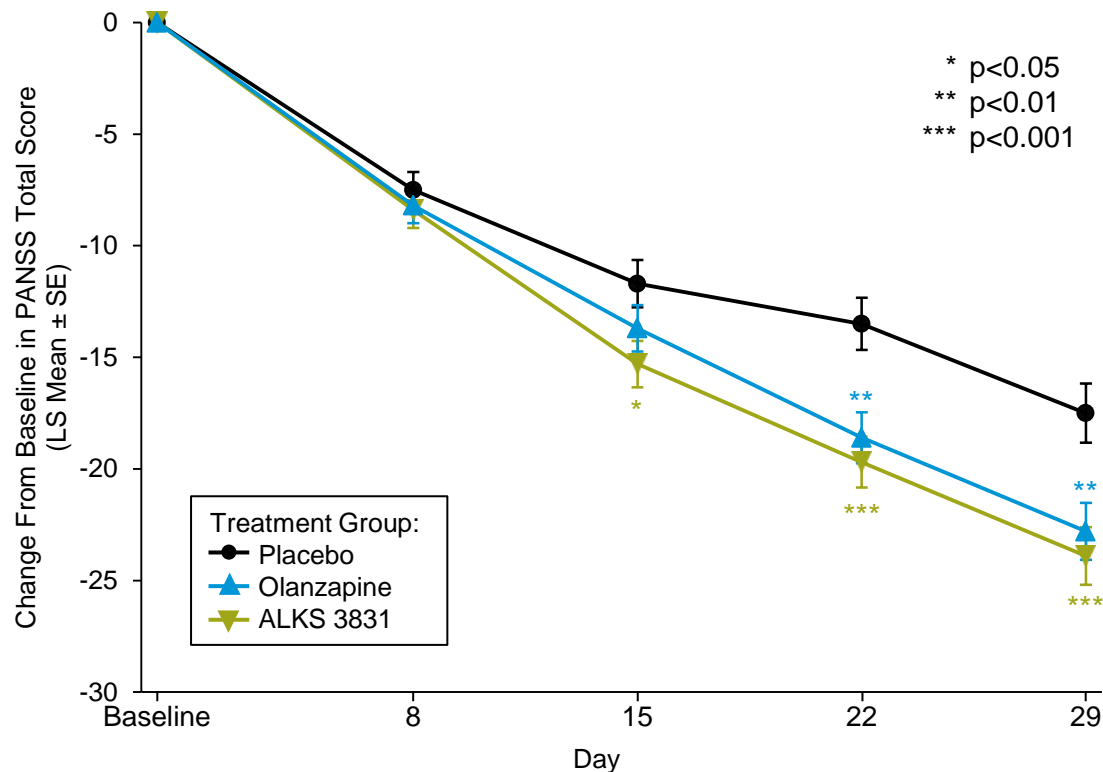


## ENLIGHTEN-2 Weight Study

- Weight change vs. olanzapine
- 561 patients with stable schizophrenia
- Demonstrated statistically significant improvement compared to olanzapine at 6 months for both co-primary endpoints:
  - Percent change from baseline in body weight ( $p = 0.003$ )
  - Proportion of subjects with  $\geq 10\%$  weight gain ( $p = 0.003$ )

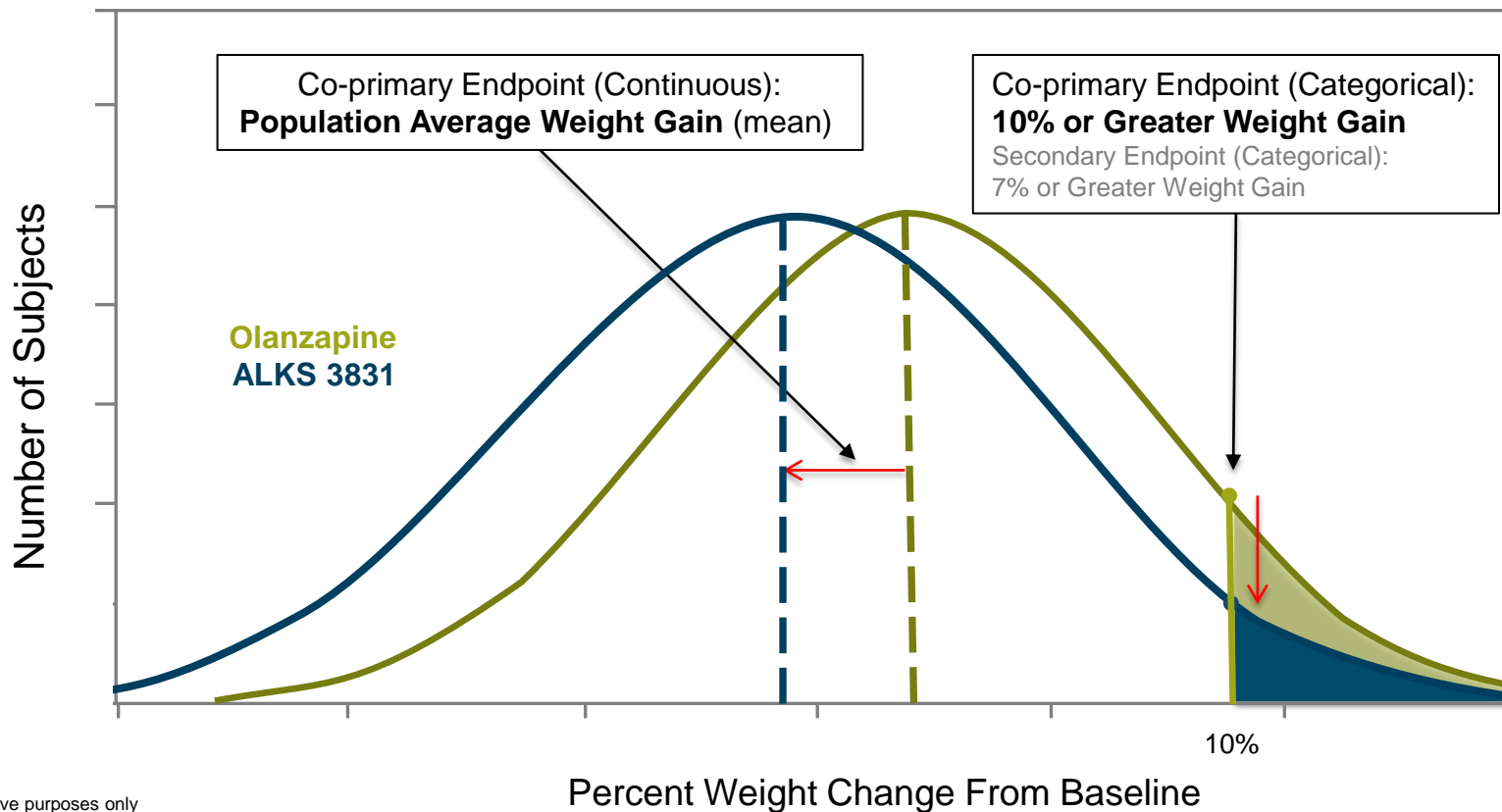
**NDA submission planned mid-2019**

# ENLIGHTEN-1: Demonstrated Robust Antipsychotic Efficacy



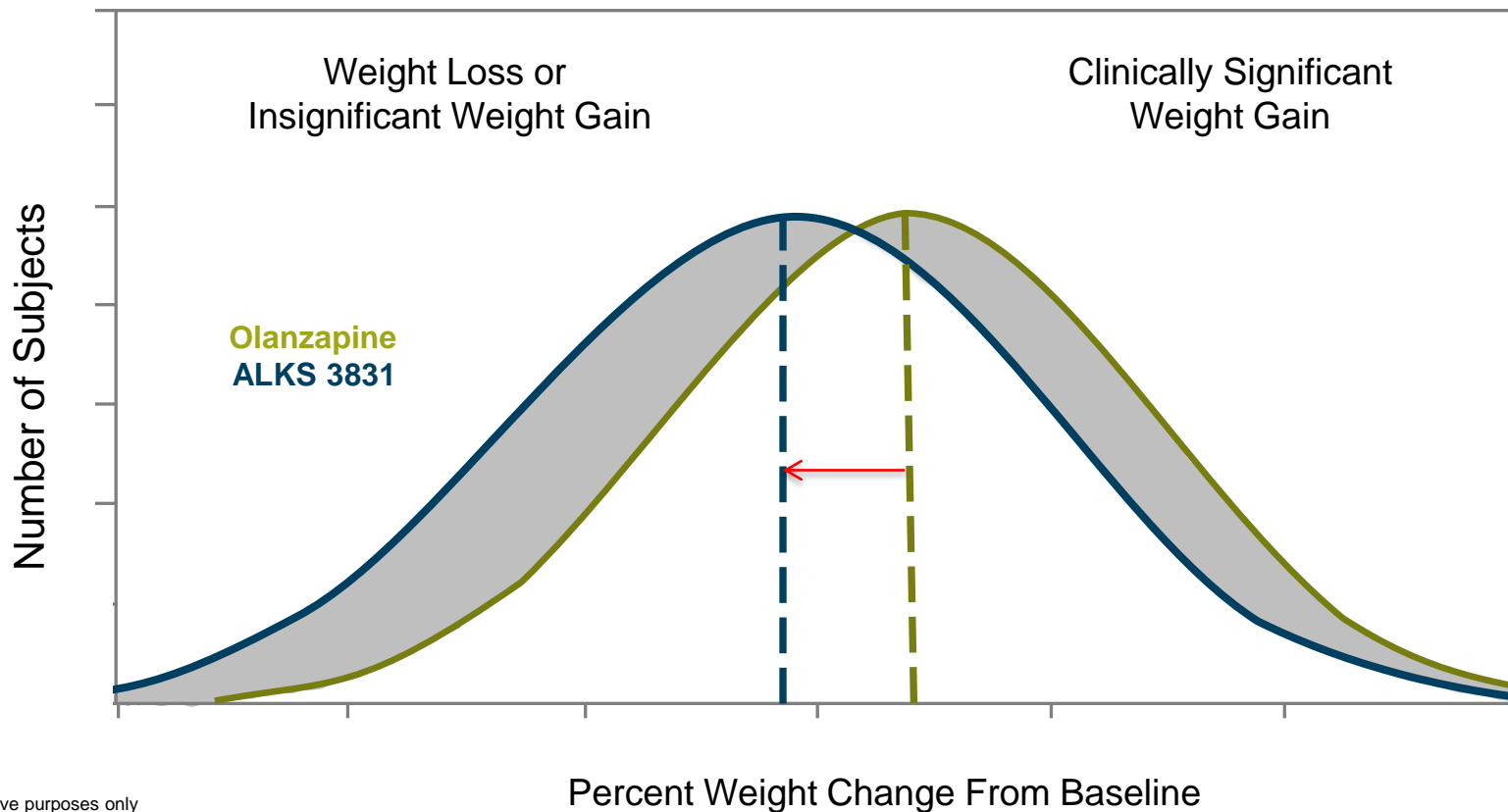
Change from Baseline at Week 4	PBO (N=112)	ALKS 3831 (N=124)	OLZ (N=120)
Mean (SD)	-19.4 (14.80)	-23.7 (12.61)	-22.4 (13.63)
LS Mean (SE)	-17.5 (1.32)	-23.9 (1.28)	-22.8 (1.29)
LS Mean Difference (SE) vs. Placebo		-6.4 (1.83)	-5.3 (1.84)
P-Value		<0.001	0.004

# ENLIGHTEN-2: Primary Analysis Captures Shift in Two Dimensions



For illustrative purposes only


# ENLIGHTEN-2: Shift in Mean has Beneficial Weight Implications for Entire Study Population



For illustrative purposes only

## ENLIGHTEN-2: Pre-Specified Primary and Key Secondary Endpoints

	Olanzapine	ALKS 3831
<b>Co-Primary Endpoints:</b>		
Mean Weight Gain	6.59%	4.21%
p-value		<b>p=0.003*</b>
Proportion of Subjects with Weight Gain of ≥10% From Baseline	29.8%	17.8%
p-value		<b>p=0.003*</b>
<b>Secondary Endpoint:</b>		
Proportion of Subjects with Weight Gain of ≥7% From Baseline	42.7%	27.5%
p-value		<b>p=0.001*</b>

-  The most common adverse events for ALKS 3831 were weight gain, somnolence and dry mouth. The most common adverse events for olanzapine were weight gain, somnolence and increased appetite.



## ENLIGHTEN-2 Results: Clinical Implications for Patients

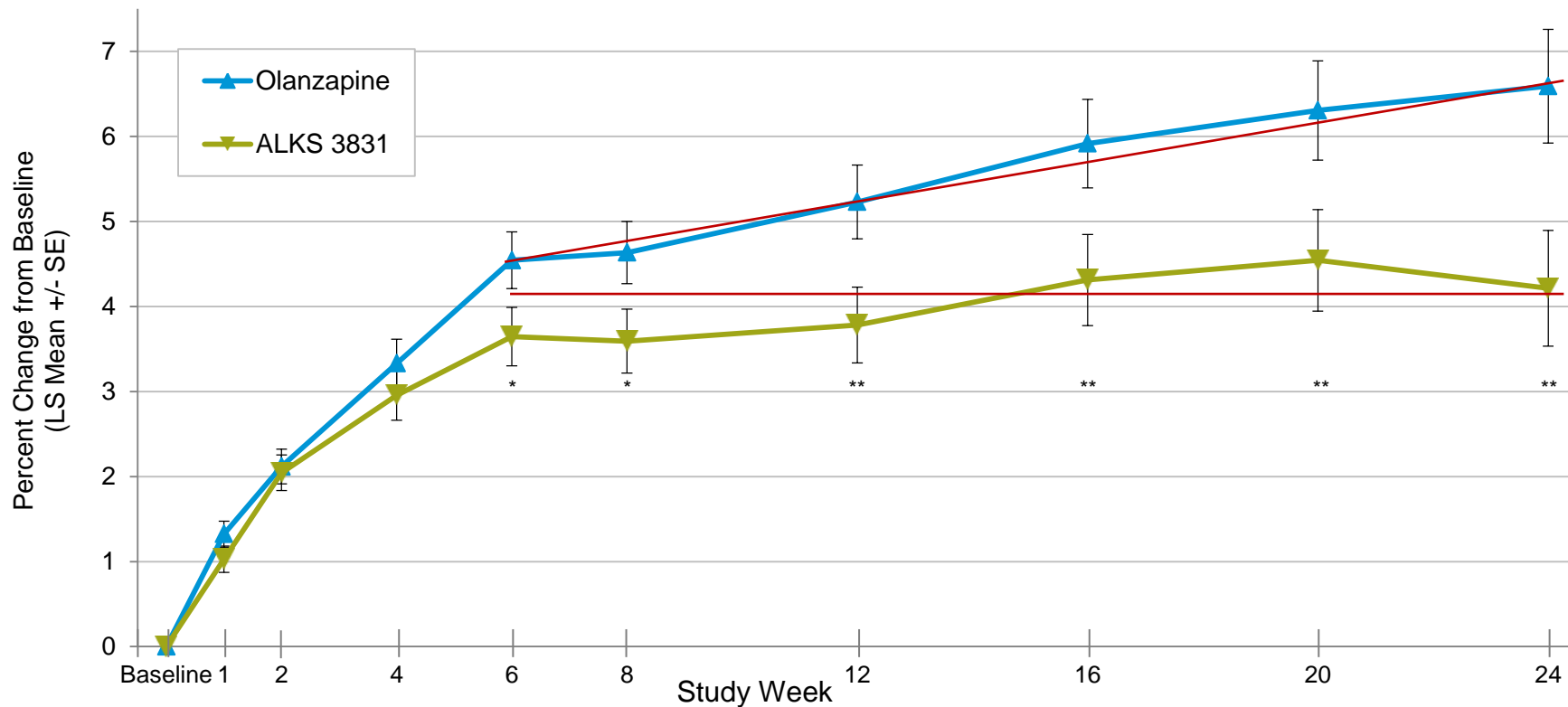
**73%** of ALKS 3831 patients did not gain **clinically meaningful\*** weight from baseline

**2.0x** the risk of **clinically meaningful\*** weight gain from baseline with olanzapine vs. ALKS 3831

**57%** higher mean percent weight change at six months for patients who received olanzapine vs. ALKS 3831

\*Using at least 7% increase from baseline body weight as the benchmark of clinical significance.

## ENLIGHTEN-2: ALKS 3831 Weight Profile Stabilized



Note: Weight curve based on analysis of covariance (ANCOVA) approach using multiple imputation (MI) for missing data.

\*p<0.05 vs. olanzapine; \*\*p<0.01 vs. olanzapine

# Antipsychotic Efficacy Key Attribute for Healthcare Providers

## Motivating Elements of the ALKS 3831 Profile

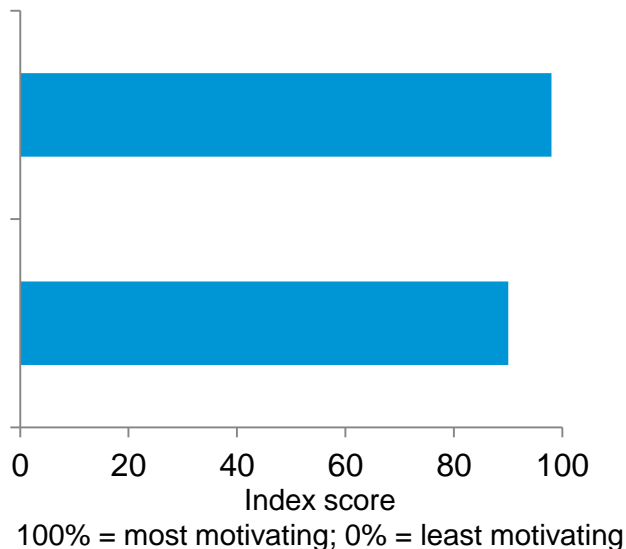
Healthcare Provider Market Research

### Efficacy:

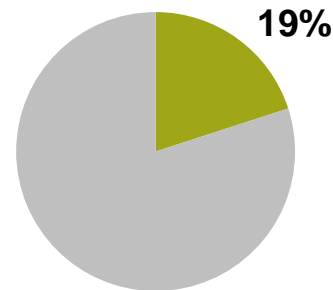
Schizophrenia improvement in PANSS similar to olanzapine

### Weight gain:

Demonstrated a significantly lower weight gain vs. olanzapine



## Olanzapine Market Share 19% Despite Weight Liabilities



U.S Atypical Antipsychotic Market  
TRx for Schizophrenia

Sources: IMS NPA Audit R12M Sep 2018, IMS SOB File

## Next Steps for ALKS 3831 Program

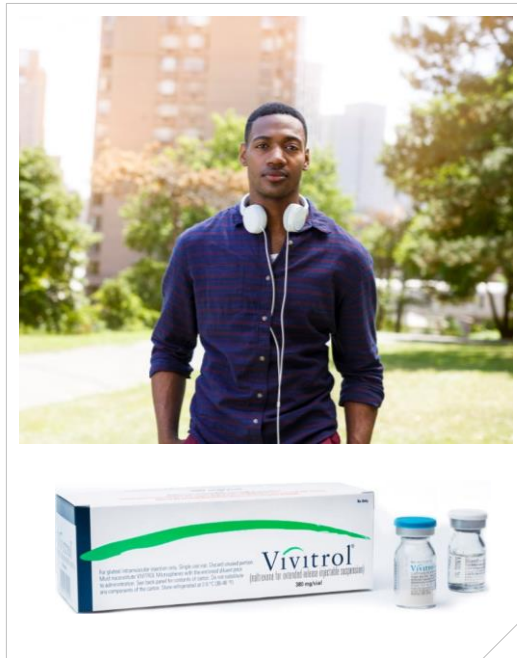
- Advancing toward regulatory submission for schizophrenia
  - Anticipated pre-NDA meeting to discuss key FDA requirements including efficacy, safety, weight and metabolic profile
  - NDA submission planned for mid-2019
- Publication of data and scientific education
  - Plan to present ENLIGHTEN-2 data at spring medical meeting
- Enrollment ongoing for ENLIGHTEN-Early phase 3 study in young adults
  - Early-in-illness study in multiple indications
  - Topline data expected in 2020
- Launching lifecycle management initiatives
  - Evaluating bipolar opportunity
- Commercial launch planning and preliminary payer discussions



## **VIVITROL® for Opioid and Alcohol Dependence**

# VIVITROL® for Opioid and Alcohol Dependence

- Long-acting injectable opioid antagonist provides therapeutic levels of naltrexone for a one-month period
- Only medication approved for prevention of relapse to opioid dependence, following opioid detoxification
- Approved for treatment of alcohol dependence
- Non-narcotic, no abuse potential



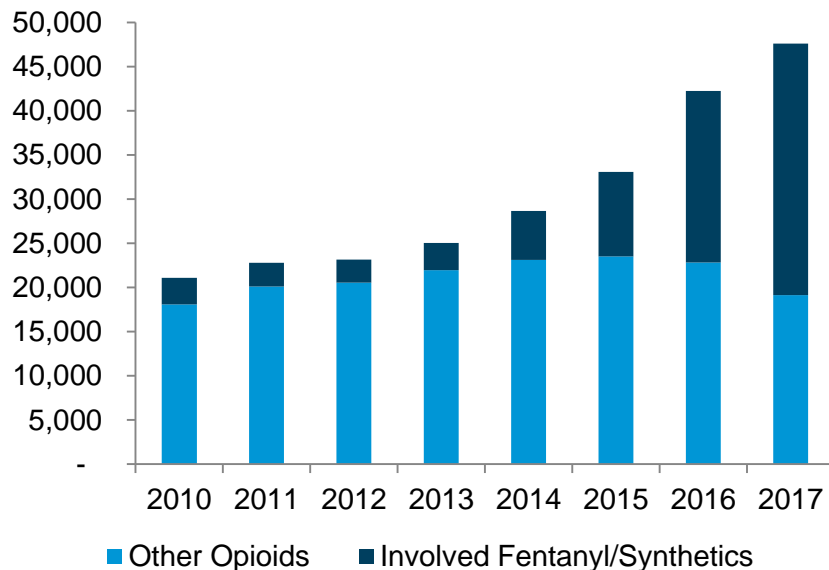
**VIVITROL is 1 of 3 FDA-approved treatment options for opioid dependence\***

\*To be used in conjunction with psychosocial support



# Opioid Epidemic Continues to Rage Nationwide

Opioid Overdose Deaths in the U.S.<sup>1</sup>



## In 2017

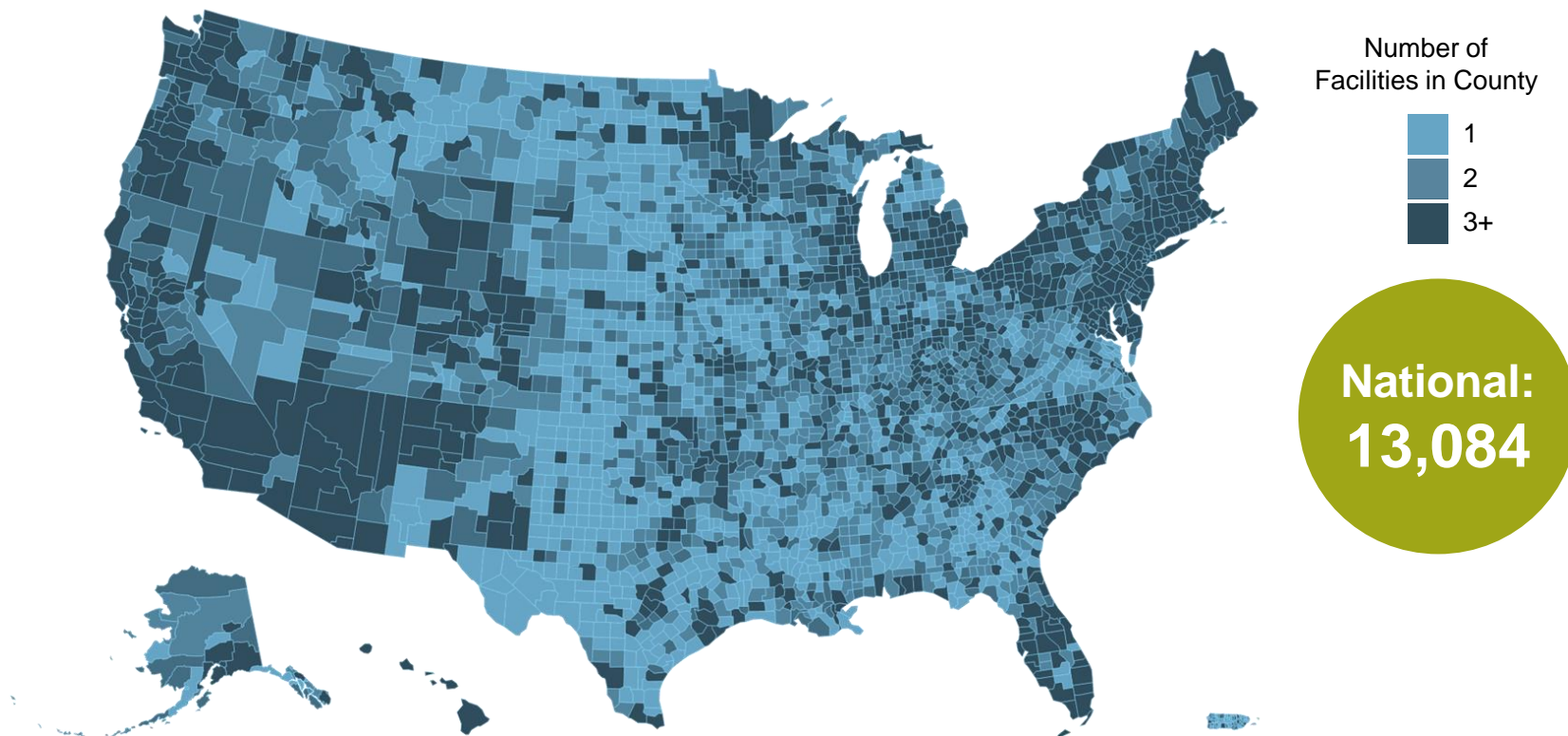
- **11.1M** people misused prescription opioids<sup>1</sup>
- **2.1M** people reported having Opioid Use Disorder<sup>1</sup>
- Fentanyl-related overdose deaths increased **~45%**<sup>2</sup>
- Opioid overdose deaths drove down U.S. life expectancy over the last three years<sup>3</sup>

1. Substance Abuse and Mental Health Services Administration (SAMHSA). 2017 National Survey on Drug Use and Health (NSDUH); Deaths involving more than one opioid category (e.g., a death involving both methadone and a natural and semisynthetic opioid) are counted in both categories

2. National Institute on Drug Abuse provisional 2017 data set

3. Kochanek KD, Murphy SL, Xu JQ, Arias E. Mortality in the United States, 2016. NCHS Data Brief, no 293. Hyattsville, MD: National Center for Health Statistics, 2017

# Facilities Providing Substance Abuse Services

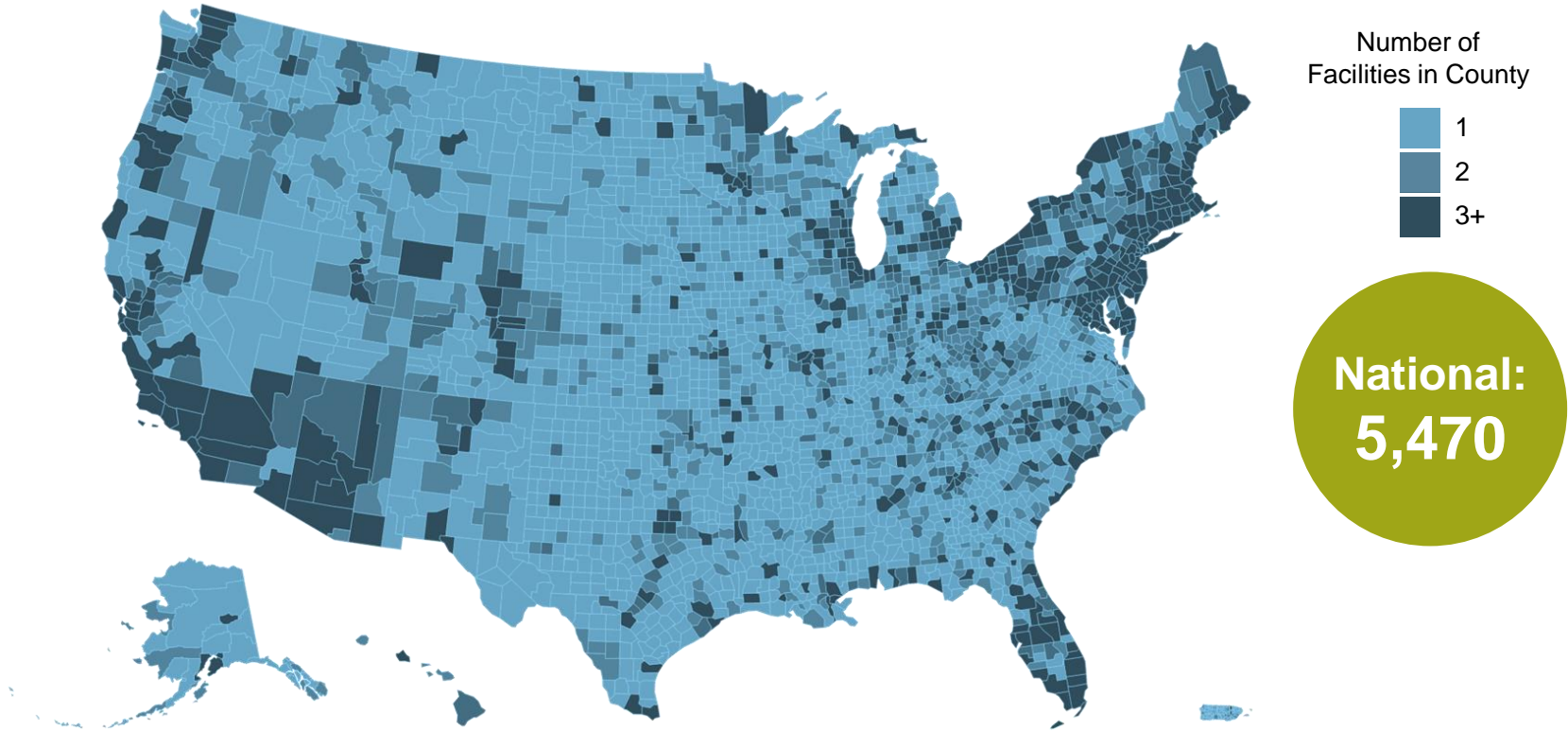


Source: [opioid.amfar.org](http://opioid.amfar.org) accessed on Jan. 2, 2019



# Fewer Than 50% Offer Any FDA-Approved Opioid Use Disorder Medication

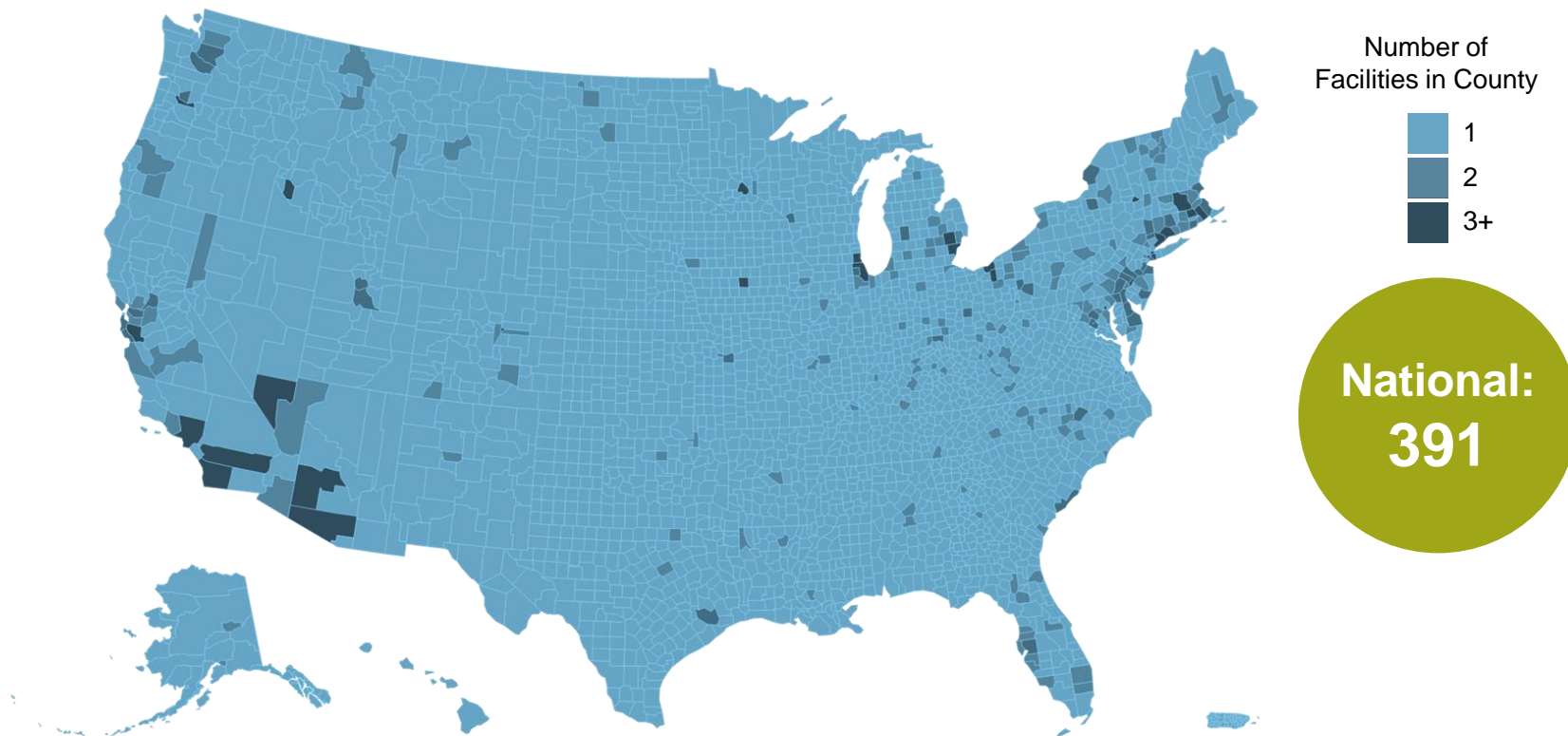
33



Source: [opioid.amfar.org](http://opioid.amfar.org) accessed on Jan. 2, 2019

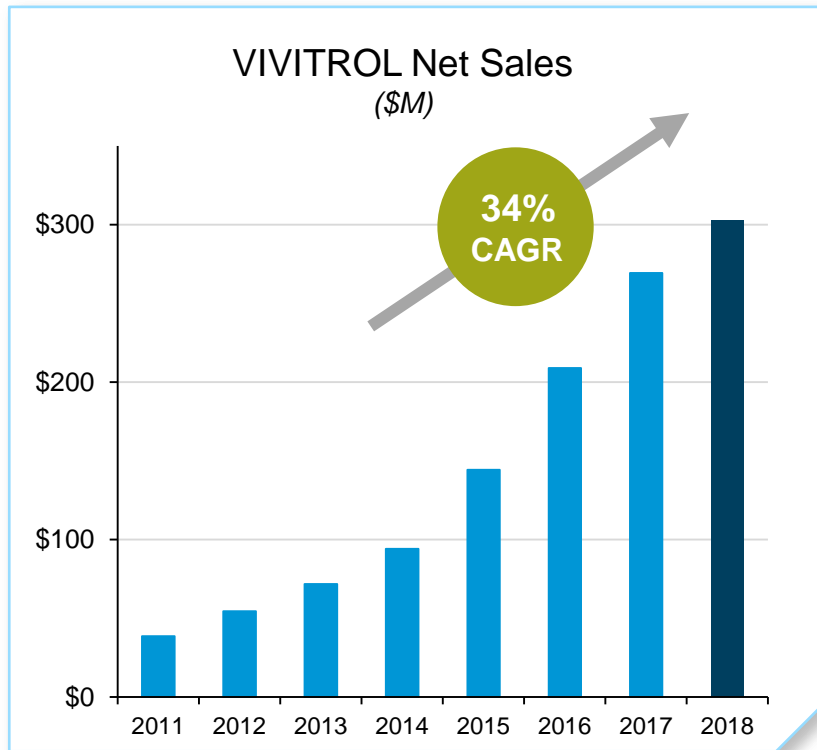
# Fewer Than 5% Offer All Three Types of FDA-Approved Opioid Use Disorder Medications

34



Source: [opioid.amfar.org](http://opioid.amfar.org) accessed on Jan. 2, 2019

# VIVITROL®: Demonstrated Growth With New Opportunities Arising



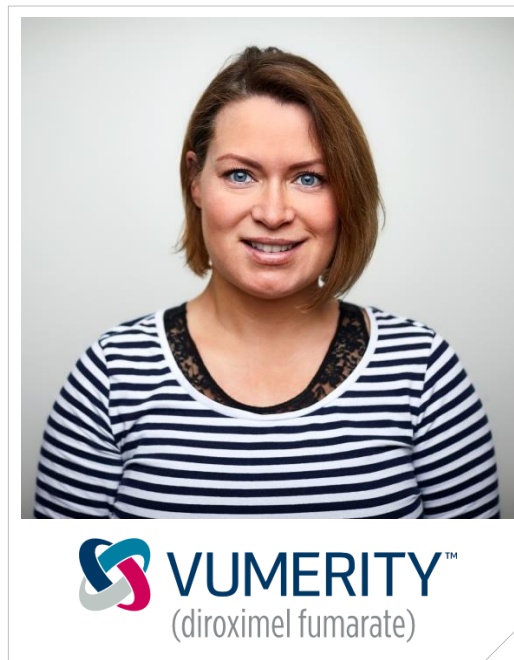
- Public policy initiatives and improved access driving strong growth in new states
  - 28 states have demonstrated more than 25% growth year-over-year (FY'18)
- New state and federal funding slowly catalyzing changes in treatment systems
  - ~\$2B of federal funding distributed to states via block grants
  - SUPPORT for Patients and Communities Act extends State Targeted Response Grant program: Additional \$500M per year 2019-2021
- State programs incorporating VIVITROL expanded to ~750 at year-end '18



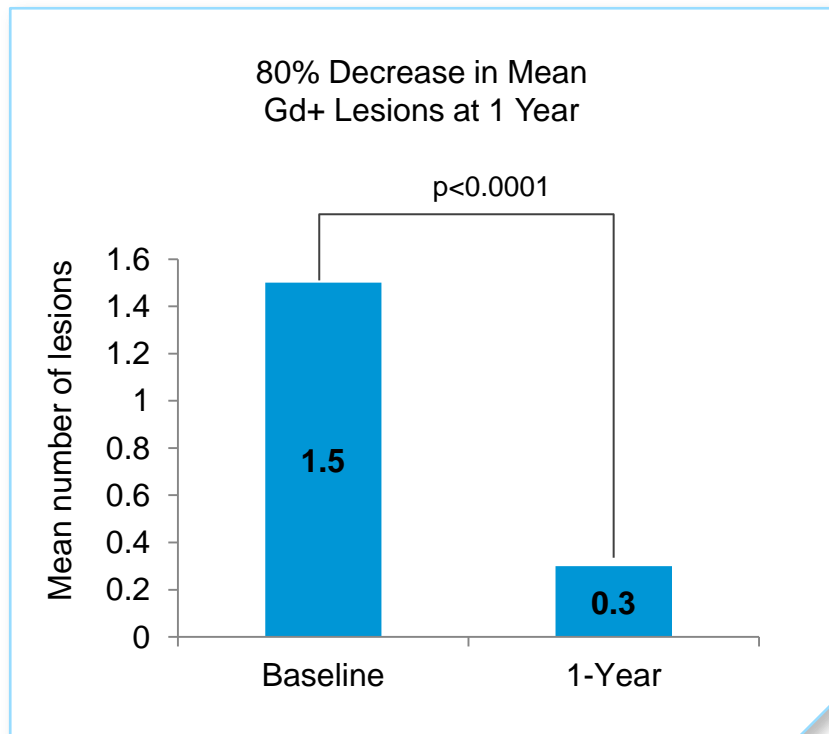
## **Diroxime Fumarate for Multiple Sclerosis (Formerly BIIB098)**

## Diroximel Fumarate (DRF) for Multiple Sclerosis (MS)

- Novel, oral investigational fumarate for the treatment of relapsing forms of MS (RRMS), designed to provide differentiated features vs. dimethyl fumarate
  - Administered in oral, micro pellet, controlled-release dosage form
  - Composition of matter patent extends into 2033
- NDA submitted in December 2018
  - Streamlined regulatory pathway – 505(b)(2)
- Elective head-to-head GI tolerability study underway
  - Designed to assess GI tolerability profile compared to TECFIDERA® (dimethyl fumarate)
  - Data expected mid-2019



# Diroximel Fumarate: EVOLVE-MS-1 Reveals Efficacy and Tolerability



Data from exploratory efficacy analysis: Leigh-Pemberton, R. et al. MRI and Relapse Results for ALKS 8700 (diroximel fumarate) in RRMS: 1-year Interim Results from the Phase 3 EVOLVE-MS-1 Study. Presented at the American Academy of Neurology Annual Meeting 2018. \*N=374 as of January 2018.



Patients, n (%)	
<b>Months 0 - 1 after treatment initiation (n=580)</b>	
Discontinuations due to GI AEs	3 (0.5)
Serious GI AEs	0
Most common TEAEs (>5% of patients)	
Flushing	184 (31.7)
Pruritus	43 (7.4)
Diarrhea	38 (6.6)
<b>Months 0-3 after treatment initiation (n=574)</b>	
Deaths	0
Serious AEs	13 (2.3)
Discontinuations due to AEs	21 (3.7)

Preliminary data from safety population as of July 27, 2017; study recruitment is ongoing.  
AE, adverse event; GI, gastrointestinal; TEAE, treatment-emergent AE.

Naismith, R. et al. Presented at MSParis2017, the 7<sup>th</sup> Joint Meeting of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) and the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS).

# Multiple Sclerosis is a Large and Growing Market

- Approximately 325K patients are treated for multiple sclerosis in the U.S. (~75% RRMS)<sup>1</sup>
  - 15K MS patients new to therapy each year
  - 60K MS patients change therapy each year
- Total market growth of 17% from 2013-2016<sup>2</sup>
  - Orals make up ~45% of this growth
- Additional indications and ex-U.S. opportunities under evaluation

1. Decision Resources MS Disease Landscape (Nov. 2016)

2. IMS SMART Solutions (% of sales in MS factored using InVentiv Health Research & Insights TreatmentAnswers™ Generator).

## Biogen License and Collaboration Agreement

- Granted Biogen an exclusive, worldwide license to commercialize DRF
- Mid-teens percentage royalty to Alkermes on worldwide net sales of DRF
- Received \$50M payment in Q2 2018 following Biogen's preliminary review of GI tolerability data
- \$150M milestone upon FDA approval by 12/31/21
- Biogen responsible for development and commercial expenses (as of 1/1/18)

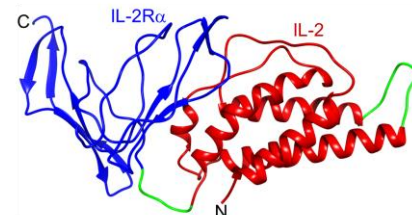


## **ALKS 4230 and Emerging Biologics Capabilities**



# ALKS 4230: Selective IL-2 Fusion Protein

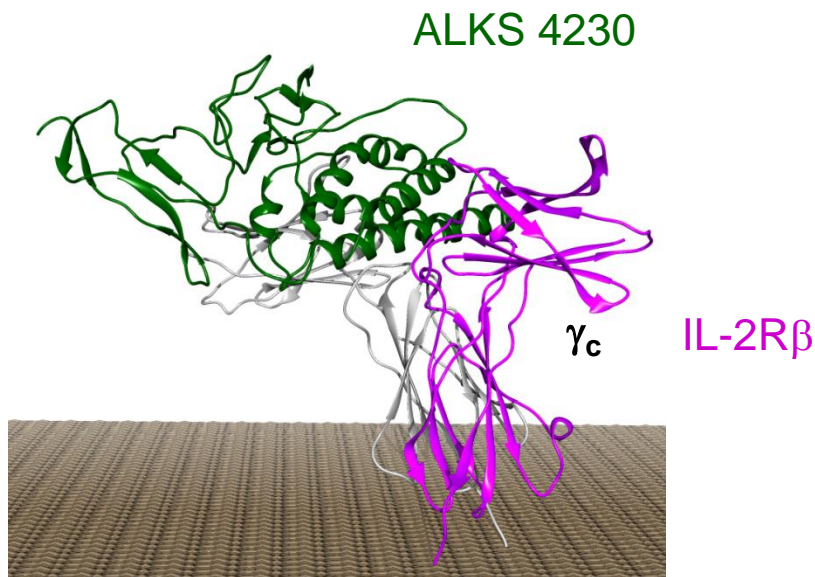
- Novel investigational immunotherapy designed to enhance tumor-killing T cells
- Selective activation of IL-2 intermediate affinity receptors
  - Demonstrated preferential expansion of Natural Killer and CD8+ T cells with minimal expansion of regulatory T cells
  - Potential to be complementary to a range of cancer therapies
- Phase 1 study underway
  - Monotherapy dose escalation ongoing: evaluating safety, tolerability and immunological-pharmacodynamic effects in patients with solid tumors
  - Monotherapy dose expansion planned in renal cell carcinoma and melanoma
  - Evaluation of combination with pembrolizumab ongoing; Initiated September 2018
- Dose optimization
  - Subcutaneous dosing phase 1 study expected to initiate Q1 2019
  - Once-weekly and once-every-three-weeks dosing to be evaluated



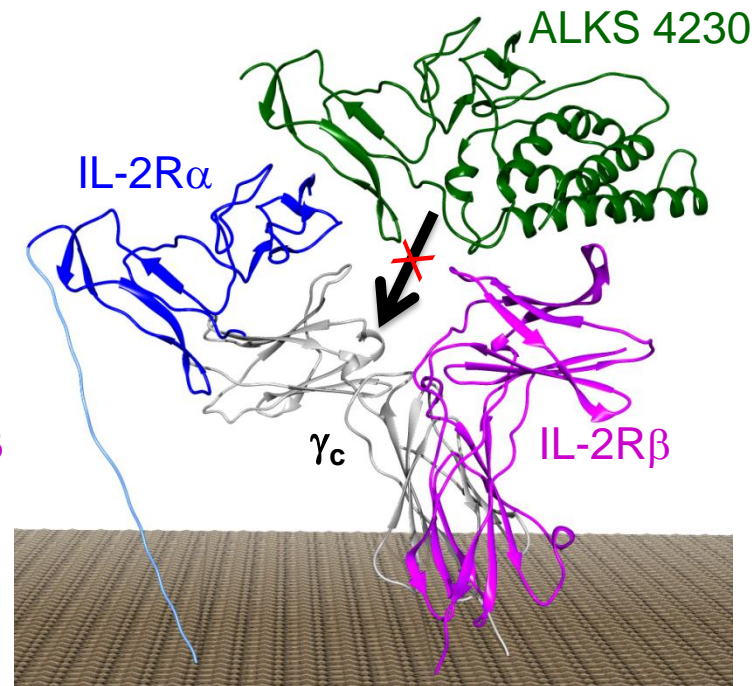
# ALKS 4230 has Increased Preference for Binding to IL-2 Intermediate-Affinity Receptors

42

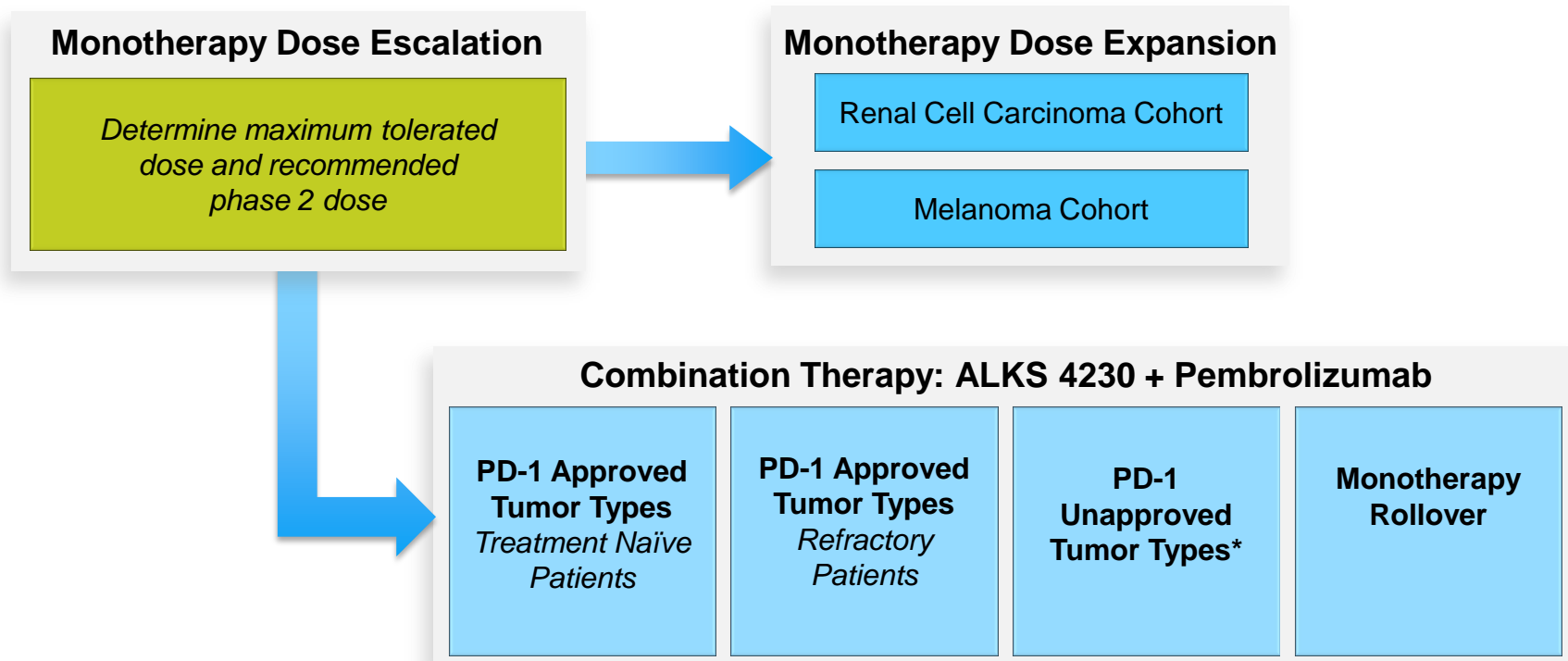
## IL-2 Intermediate-Affinity Receptors



## IL-2 High-Affinity Receptors



# ALKS 4230 Phase 1 Study Design

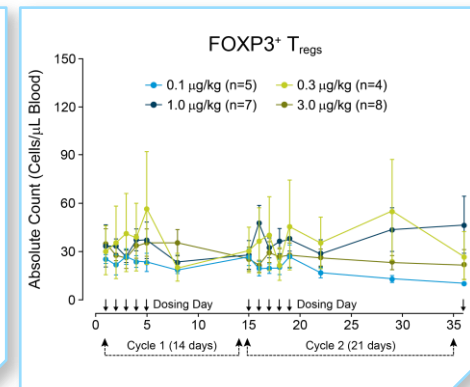
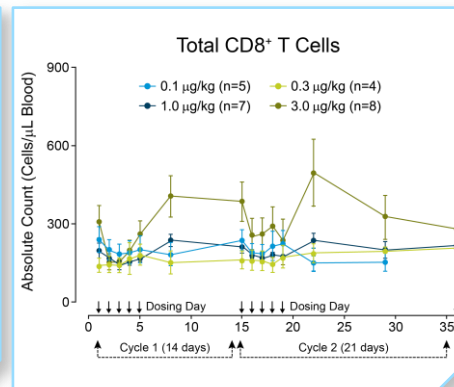
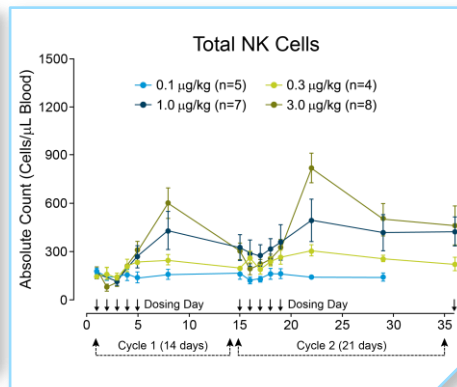
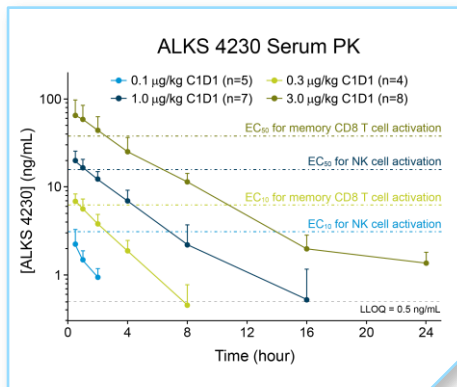


\*Includes colorectal, triple-negative breast, ovarian carcinoma, soft tissue sarcomas, and subjects with metastatic non-small cell lung cancer whose tumors express low or undetectable PD-L1.

# ALKS 4230 Pharmacokinetics and Pharmacodynamic Effects From Phase 1 Ongoing Dose Escalation Study

44

- ALKS 4230 resulted in a dose-dependent increase in circulating NK and CD8<sup>+</sup> T cells with an approximately 4-fold and 2-fold expansion at 3 µg/kg/day, respectively, and minimal, non-dose dependent change in T<sub>regs</sub>



Fever and chills were the most common treatment-related AEs for ALKS 4230 and were generally manageable and transient.

Vaishampayan, U. et al. Safety, Pharmacokinetics, and Pharmacodynamic Effects of ALKS 4230 in Patients With Advanced Solid Tumors From the Ongoing Dose Escalation Portion of a First-In-Human (FIH) Study. Presented at the 2018 Society for Immunotherapy of Cancer (SITC).

# Significant News Flow Expected in 2019

## Schizophrenia

### ARISTADA®

- Report topline results for phase 3b ARISTADA-INVEGA SUSTENNA® study (H1)

### ALKS 3831

- Present ENLIGHTEN-2 data at medical meeting (H1)
- Submit NDA for schizophrenia (mid-year)

## Addiction

### VIVITROL®

- Present and publish data on detox and induction strategies

## Multiple Sclerosis

### Diroximel fumarate

- Report topline data for EVOLVE-MS-2 head-to-head vs. TECFIDERA® (mid-year)
- Expected FDA regulatory action

## Immuno-oncology

### ALKS 4230

- Initiate subcutaneous dosing study (Q1)
- Complete monotherapy dose-escalation stage of phase 1 study
- Initiate monotherapy dose-expansion stage of phase 1 study

# Alkermes: 2019 Financial Expectations†

<i>(in millions, except per share amounts)</i>	Financial Expectations for Year Ending Dec. 31, 2019†
Revenues	\$1,140 – 1,190
COGS	\$180 – 190
R&D Expense	\$450 – 480
SG&A Expense	\$590 – 620
Amortization of Intangible Assets	~\$40
Net Interest Expense	\$5 to \$10
Income Tax Expense	\$10 to \$15
GAAP Net Loss	\$(135) – (165)
GAAP Net Loss Per Share	\$(0.87) – (1.06)
Non-GAAP Net Income‡	\$40 – 70
Non-GAAP Earnings Per Share (Basic)	\$0.26 – 0.45
Non-GAAP Earnings Per Share (Diluted)	\$0.25 – 0.43

## Revenues:

- VIVITROL® net sales of \$330M - \$350M
  - Q1 VIVITROL net sales of ~\$70M
- ARISTADA® net sales of \$210M - \$230M
  - Q1 ARISTADA net sales of ~\$40M
- License revenues: \$150M milestone anticipated upon FDA approval of diroximel fumarate (expected Q4 2019)

† This financial guidance, provided by Alkermes plc (the "Company") in its Current Report on Form 8-K filed with the SEC on Feb. 14, 2019, is effective only as of such date. The Company expressly disclaims any obligation to update or reaffirm this guidance. The Company only provides financial guidance in a Regulation FD compliant manner.



‡ Non-GAAP net income adjusts for one-time and non-cash charges by excluding from GAAP results: share-based compensation expense; amortization; depreciation; non-cash net interest expense; certain other one-time or non-cash items; and the income tax effect of these reconciling items. Reconciliation of this non-GAAP financial measure to the most directly comparable GAAP financial measure can be found in the Alkermes plc Current Report on Form 8-K filed with the SEC on Feb. 14, 2019.

# Alkermes: 2019 Financial Expectations<sup>†</sup> - Operating Expenses

- Investments in R&D to support current development programs and pipeline expansion
  - R&D expected to be in the range of \$450M to \$480M, driven by:
    - Ongoing studies related to ARISTADA®, ALKS 3831 and diroximel fumarate that are carrying over from 2018, as well as life-cycle management initiatives related to ARISTADA and ALKS 3831
    - Intensified activity for the clinical development program for ALKS 4230
    - Investment in internal research and discovery efforts
- Commercial infrastructure provides a platform to capture efficiencies as commercial portfolio expands, particularly as we prepare for the planned launch of ALKS 3831 in schizophrenia
  - SG&A expected to be in the range of \$590M to \$620M, driven by:
    - Full-year impact of the expansion of the ARISTADA commercial team that took place at the end of 2018
    - Infrastructure investments to support long-term growth

<sup>†</sup> This financial guidance, provided by the Company in its Current Report on Form 8-K filed with the SEC on Feb. 14, 2019, is effective only as of such date. The company expressly disclaims any obligation to update or reaffirm this guidance. The company only provides financial guidance in a Regulation FD compliant manner.

# Diverse Commercial Portfolio With Long Patent Lives

	Description	Patent Life
 <small>(naltrexone for extended-release injectable suspension) 300mg/vial</small>	Once-monthly medication for treatment of alcohol and opioid dependence	<b>2029</b> in U.S.
 <small>aripiprazole lauroxil extended-release injectable suspension 441mg • 662mg • 882mg • 1064mg</small>	Long-acting atypical antipsychotic for treatment of schizophrenia with once-monthly, six-week and two-month dosing	<b>2035</b> in U.S.
<b>RISPERDAL CONSTA®</b> <small>(A Janssen product)</small>	Long-acting atypical antipsychotic for treatment of schizophrenia and bipolar 1 disorder	<b>2023</b> in U.S. <b>2021</b> in EU
<b>INVEGA SUSTENNA® / XEPLION®</b> <small>(Janssen products)</small>	Long-acting atypical antipsychotic for treatment of schizophrenia and schizoaffective disorder	<b>2031</b> in U.S. <b>2022</b> in EU
<b>AMPYRA® / FAMPYRA®</b> <small>(An Acorda product)</small>	First and only approved treatment to improve walking in patients with multiple sclerosis	<b>2018</b> in U.S. <b>2025</b> in EU
<b>BYDUREON®</b> <small>(An Astra-Zeneca product)</small>	First once-weekly GLP-1 for treatment of type 2 diabetes	<b>2026</b> in U.S. <b>2024</b> in EU

Please refer to the company's Annual Report on Form 10-K for the fiscal period ended Dec. 31, 2018 for specific royalty agreement rates and terms, which may differ from the Patent Life set forth above.

AMPYRA® (dalfampridine) Extended Release Tablets, 10 mg is being developed and marketed in the U.S. by Acorda Therapeutics, Inc. and outside the U.S. by Biogen, under a licensing agreement with Acorda Therapeutics, as FAMPYRA® (prolonged-release fampridine tablets). RISPERDAL CONSTA® and INVEGA SUSTENNA® are trademarks of Johnson & Johnson, and are products developed and sold by Janssen Pharmaceuticals Inc. using Alkermes technology.



# Patent Protection for Pipeline Candidates Extends Into Next Decade and Beyond

49

	Description	Patent Life (U.S.)
<b>ALKS 3831</b>	Method of Treatment Composition of Matter	<b>2032</b> <b>2031</b>
<b>BIIB098</b> (formerly ALKS 8700)	Composition of Matter Method of Treatment	<b>2033</b> <b>2033</b>
<b>ALKS 4230</b>	Composition of Matter	<b>2033</b>

# Alkermes Values and Mission

Our purpose

**Great Science**  
**Deep Compassion**  
**Real Impact**

**Collaboration  
at our core**

Sharing success  
All is possible

**Respect each voice**

Value every person  
Driven by trust

**Unwavering commitment**

Do the right thing  
Beyond passionate

Our values



[www.alkermes.com](http://www.alkermes.com)