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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM 8-K**

**CURRENT REPORT  
PURSUANT TO SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934**

Date of Report (Date of earliest event reported): January 7, 2019

**ALKERMES PUBLIC LIMITED COMPANY**

(Exact name of registrant as specified in its charter)

**Ireland**  
(State or other jurisdiction  
of incorporation)

**001-35299**  
(Commission  
File Number)

**98-1007018**  
(IRS Employer  
Identification No.)

**Connaught House, 1 Burlington Road  
Dublin 4, Ireland**

(Address of principal executive offices)

(Zip Code)

**(Registrant's telephone number, including area code): + 353-1-772-8000**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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**Item 2.02. Results of Operations and Financial Condition.**

On January 7, 2019, Alkermes plc (the “Company”) will participate in investor meetings at the J.P. Morgan Healthcare Conference, utilizing a corporate presentation which includes the Company’s current expectations with respect to certain financial results for the year ended December 31, 2018. A copy of the corporate presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K (this “Form 8-K”) and is incorporated in this Item 2.02 by reference.

**Item 7.01 Regulation FD Disclosure.**

The information in Item 2.02 above and in Exhibit 99.1 to this Form 8-K are incorporated in this Item 7.01 by reference.

The information contained in this Form 8-K, including in Items 2.02 and 7.01 above, and in Exhibit 99.1 furnished herewith, shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

<b>Exhibit No.</b>	<b>Description</b>
99.1	<a href="#">Presentation to be used by the Company on January 7, 2019.</a>

**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**ALKERMES PLC**

Date: January 7, 2019

By: /s/ David J. Gaffin  
David J. Gaffin  
Senior Vice President, Chief Legal Officer, Chief Compliance  
Officer and Secretary



# Taking on Critical Public Health Challenges

Richard Pops  
Chief Executive Officer

37<sup>th</sup> Annual J.P. Morgan Healthcare Conference

JANUARY 8, 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<sup>®</sup>, ARISTADA<sup>®</sup> and ARISTADA INITIOF; 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 diroxime fumarate ("DRF"), the timing of topline data from the phase 3b study evaluating ARISTADA<sup>®</sup> and INVEGA SUSTENNA<sup>®</sup>, 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 ALKS 5461 and 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 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.

**Note Regarding Trademarks:** The company is the owner of various U.S. federal trademark registrations (™) and other trademarks (®), including ARISTADA<sup>®</sup>, VIVITROL<sup>®</sup> and ARISTADA INITIOF. Any other trademarks referred to in this presentation are the property of their respective owners. Appearances of such other trademarks herein should not be construed as any indicator that their respective owners will not assert their rights thereto.



# 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



~365K patients<sup>1</sup> treated with VIVITROL® or ARISTADA®

### Enhanced scale of the business



Crossing \$1B in expected total revenue in 2018<sup>2</sup>  
Increased annual proprietary product net sales by 528%<sup>3</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. Reflects Alkermes plc's financial expectations as of Jan. 8, 2019

3. TTM Q3 2018 compared to TTM Q3 2013





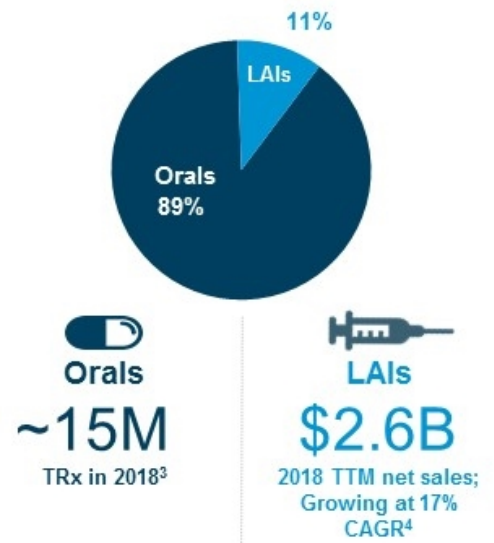


## Establishing a Leadership Position in Schizophrenia

## 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>



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.





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

Long-acting injectable prodrug  
new molecular entity (NME)



**ALKS 3831**

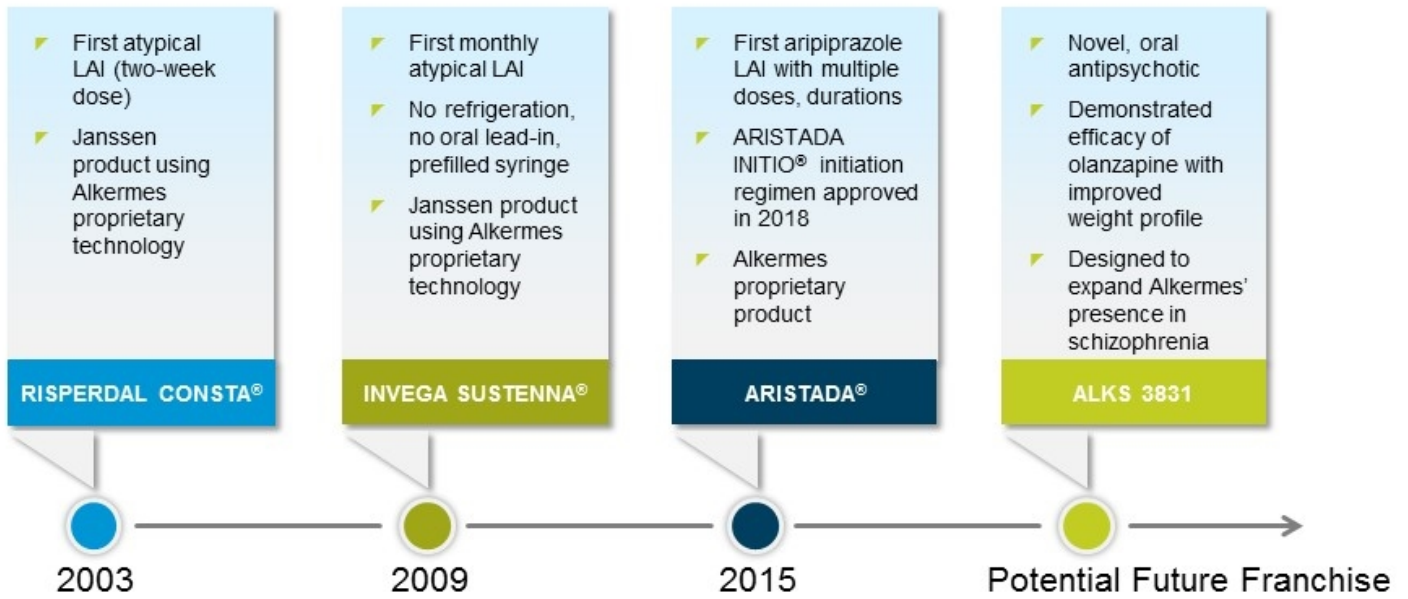
Investigational, oral bilayer tablet,  
olanzapine plus novel NME



# Integrated Infrastructure Scaled to Address Complex Disease Areas



# Evolution of Alkermes' Schizophrenia Franchise



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



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# 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  
 441mg · 662mg · 882mg · 1064mg

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



\*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.

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- ▶ 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.

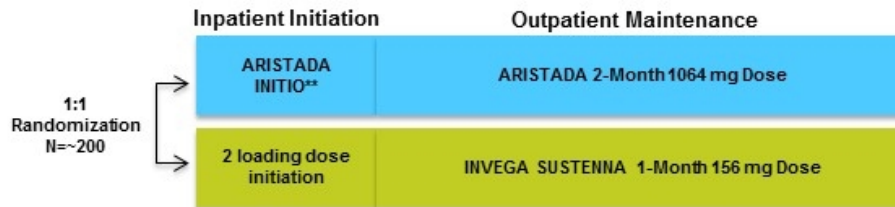
1. Truven Marketscan 2015.





# 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 †

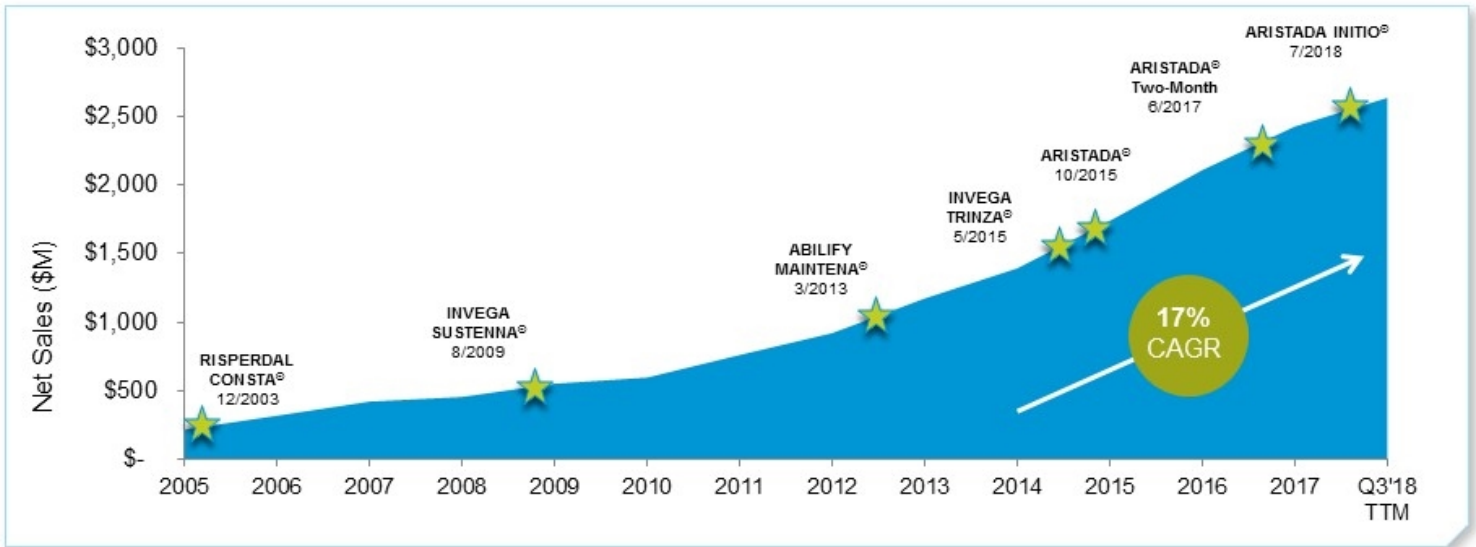
\*ARISTADA INITIO + single 30 mg oral dose of aripiprazole provides an alternative for concomitant three weeks of oral aripiprazole for initiation of ARISTADA, with relevant levels of aripiprazole concentration reached within four days. ARISTADA INITIO was approved by FDA on June 29, 2018.

\*\* Including ARISTADA INITIO

† Excluding low doses for poor metabolizers.



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



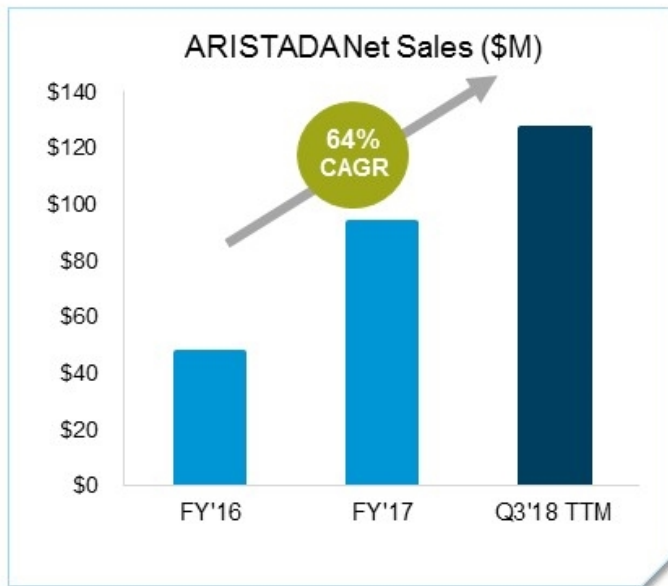
Potential to be \$3-4B+ U.S. market in 2020

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



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# 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

\*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.



## 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>



1. Gilles et al. *Clinical Neuropharmacology*. 33(5):248-249, Sept. 2010.
2. Richie et al. *Nutr Metab Cardiovasc Dis*. 2007 May;17(4):319-26. Epub Nov. 15, 2006.



## 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 ( $p = 0.004$ )

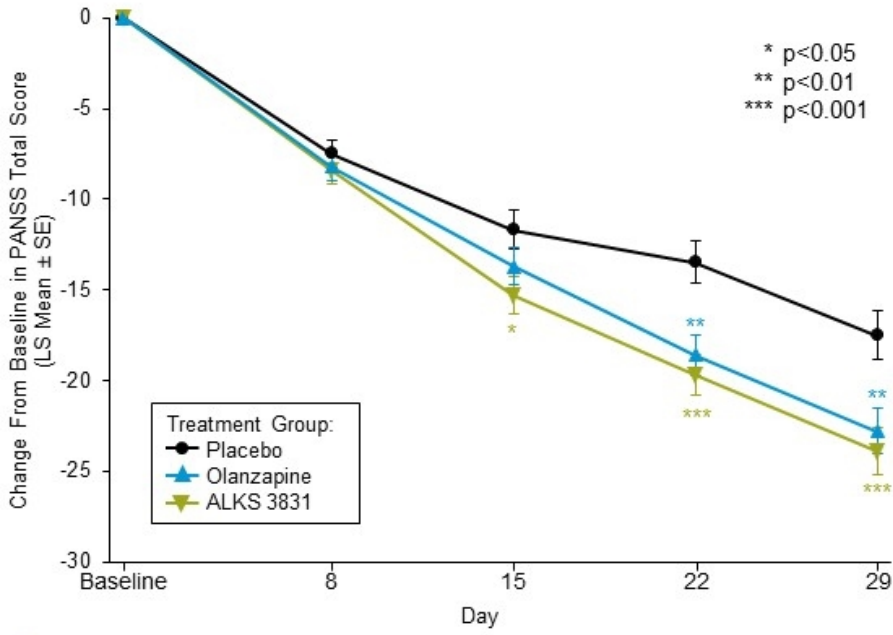


## ENLIGHTEN-2 Weight Study

- 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

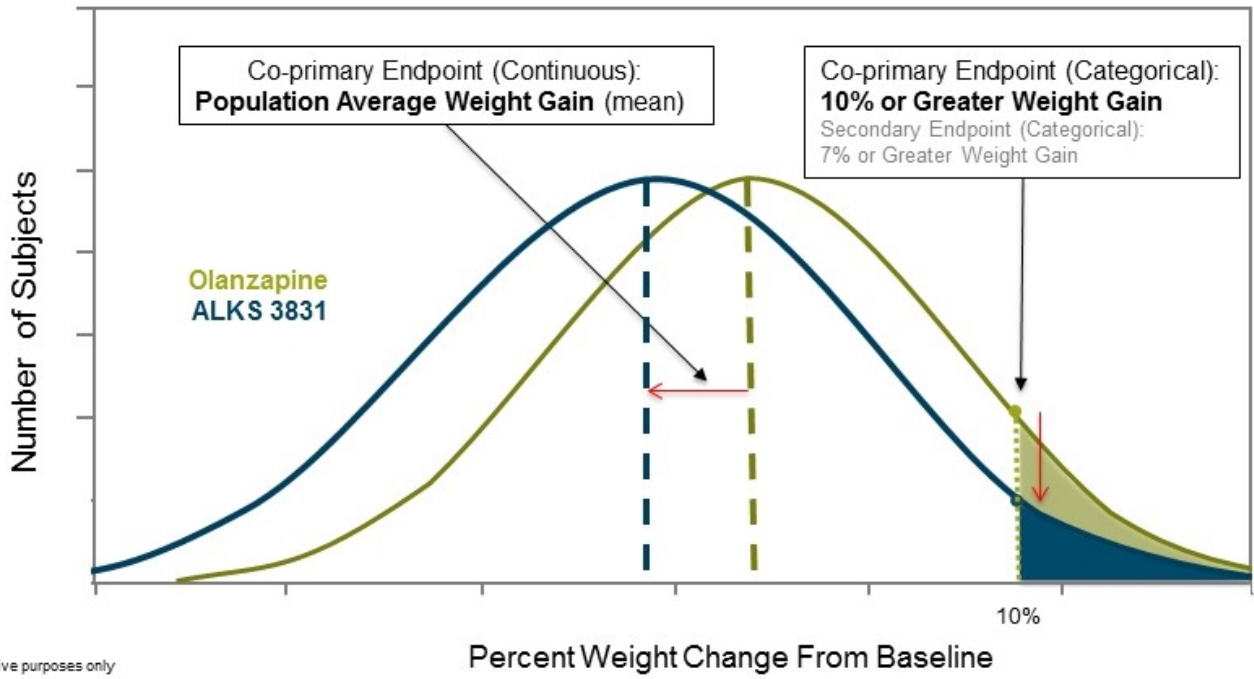


Change from Baseline at Week 4	PBO (N=112)	ALKS 3831 (N=124)	OLZ (N=120)
Mean (SD)	-19.4 (14.80)	-23.7 (12.61)	-22.4 (13.63)
LS Mean (SE)	-17.5 (1.32)	-23.9 (1.28)	-22.8 (1.29)
LS Mean Difference (SE) vs. Placebo		-6.4 (1.83)	-5.3 (1.84)
P-Value		<0.001	0.004





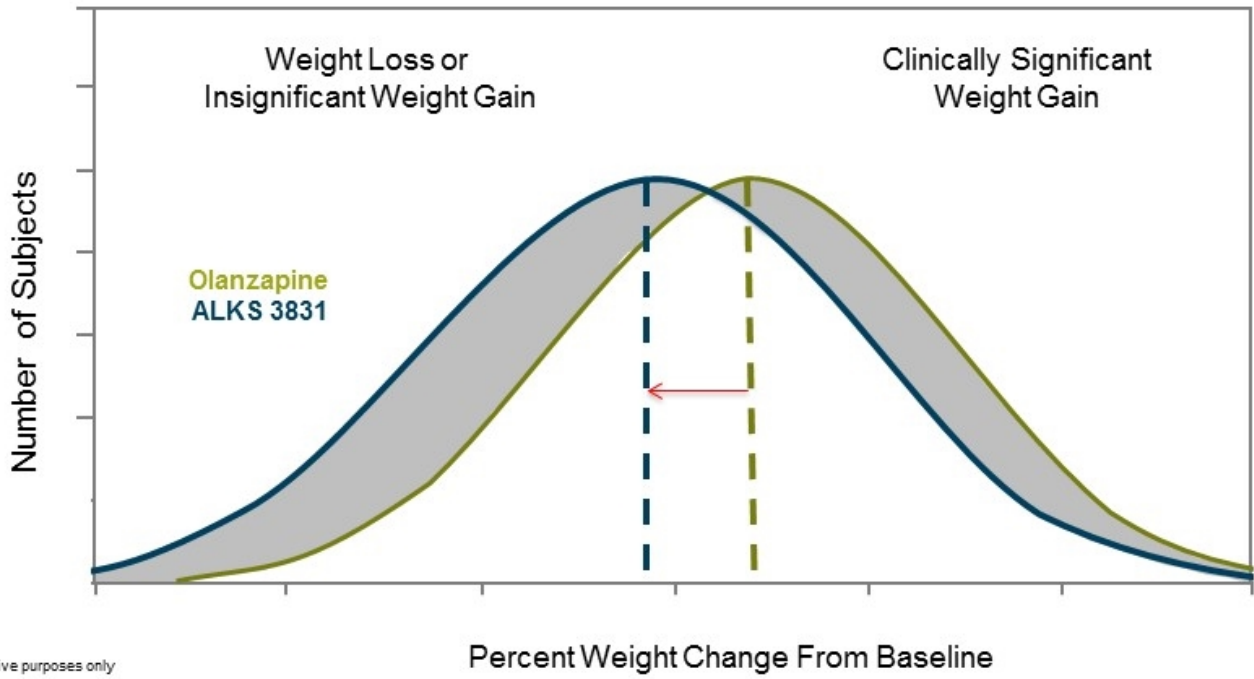
# ENLIGHTEN-2: Primary Analysis Captures Shift in Two Dimensions



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 $\geq 10\%$ From Baseline	29.8%	17.8%
p-value		<b>p=0.003*</b>
<b>Secondary Endpoint:</b>		
Proportion of Subjects with Weight Gain of $\geq 7\%$ 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

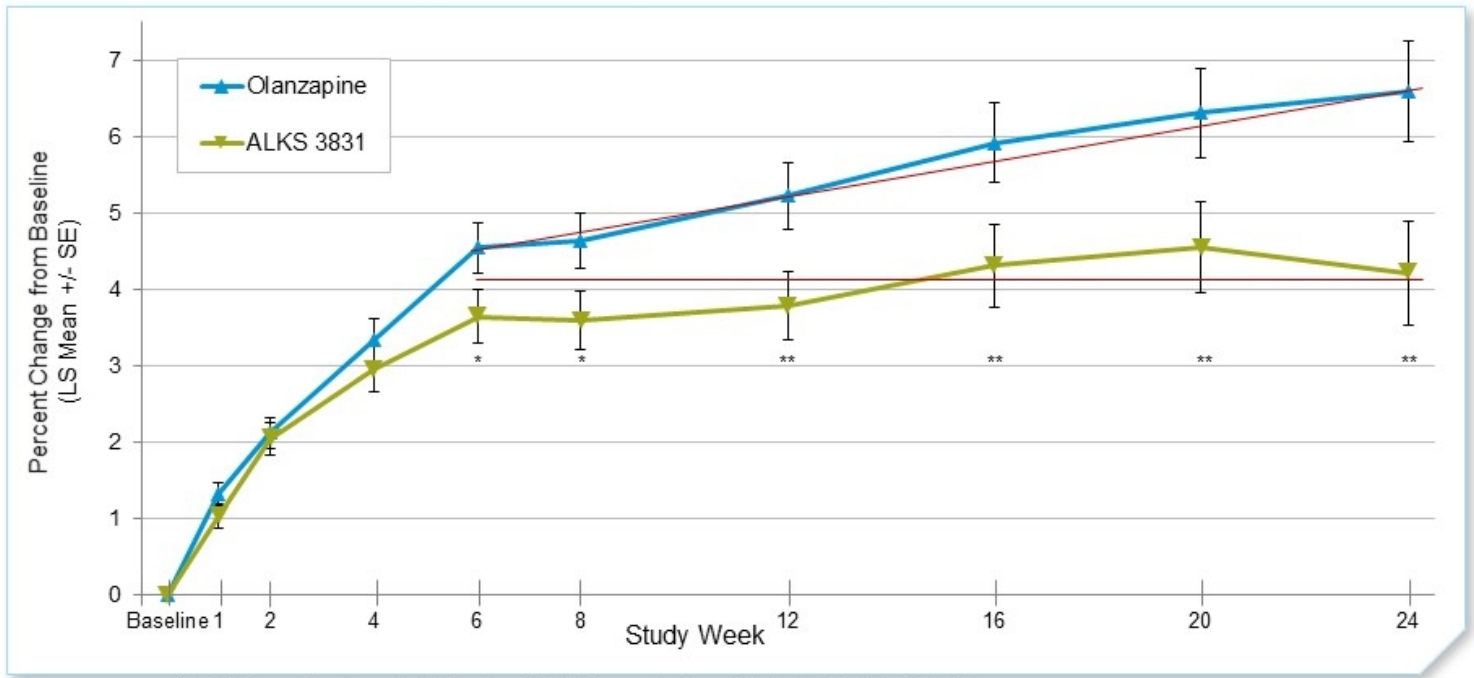
**2.0x** the risk of **clinically meaningful\*** weight gain from baseline with olanzapine vs. ALKS 3831

**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

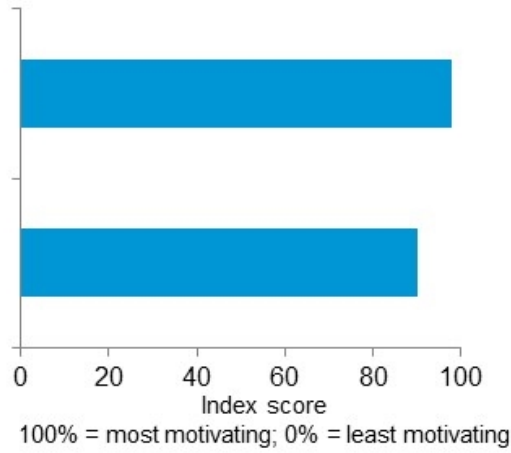
Healthcare Provider Market Research

### Efficacy:

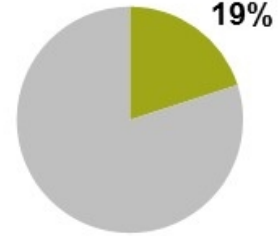
Schizophrenia improvement in PANSS similar to olanzapine

### 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

Alkermes research; n=66 Psychs, NPs, PAs



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## Next Steps for ALKS 3831 Program

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- ✔ 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



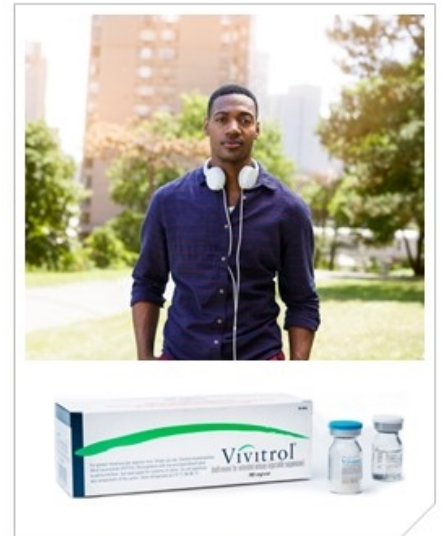


# VIVITROL<sup>®</sup> for Opioid and Alcohol Dependence



# 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\***

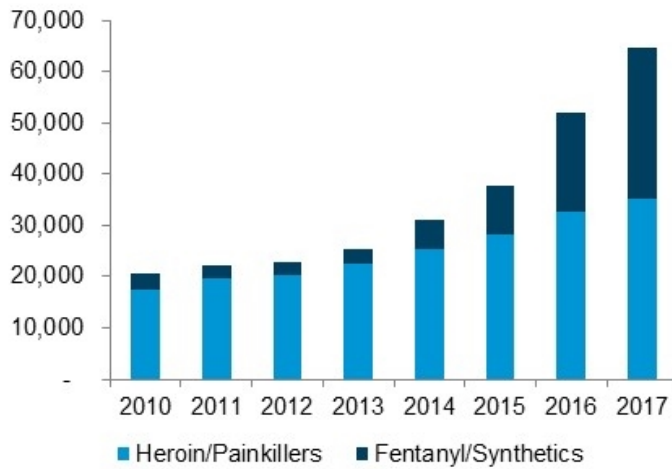
\*To be used in conjunction with psychosocial support

**Alkermes**

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# Opioid Epidemic Continues to Rage Nationwide

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



## In 2017

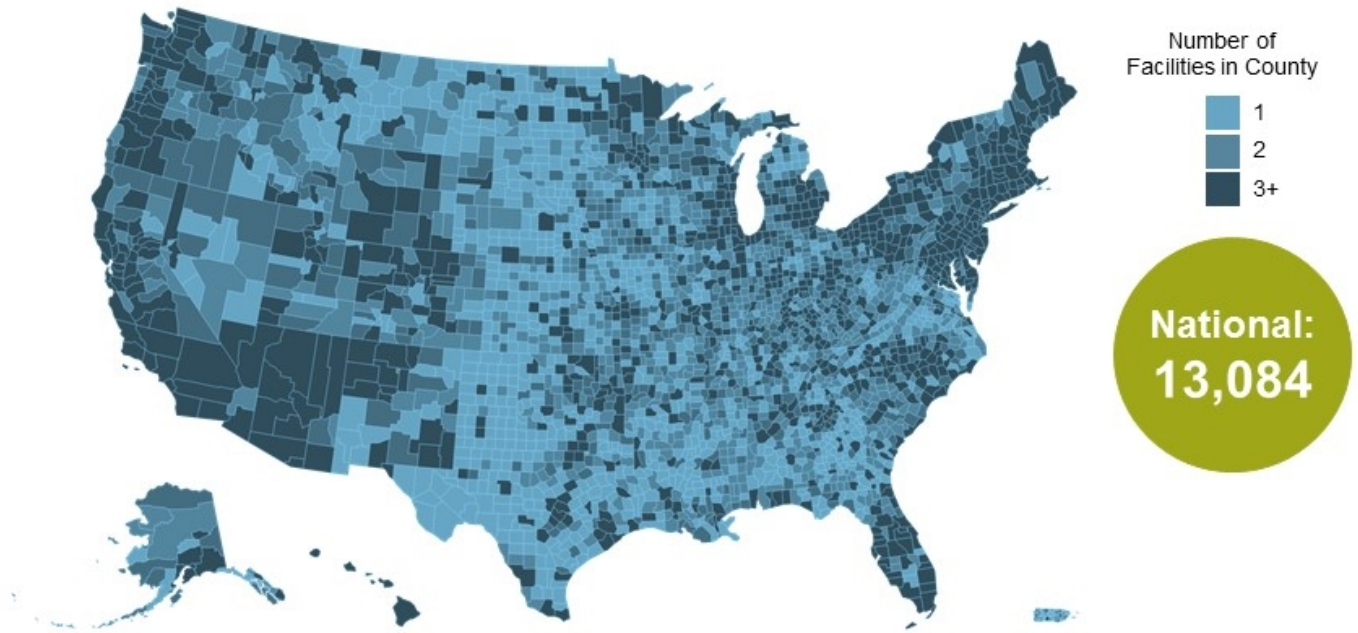
- **11.1M** people misused prescription opioids<sup>1</sup>
- **2.1M** people reported having Opioid Use Disorder<sup>1</sup>
- Fentanyl-related overdose deaths increased **~45%**<sup>2</sup>
- Opioid overdose deaths drove down U.S. life expectancy over the last three years<sup>3</sup>

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

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

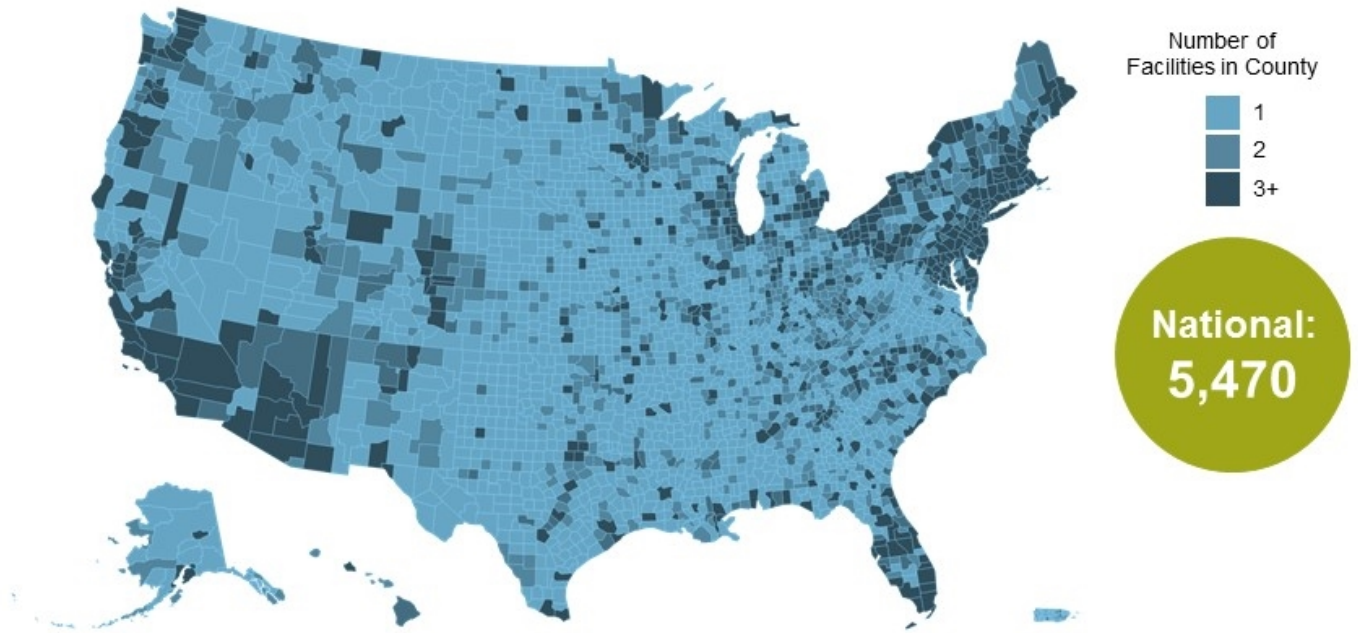
# Facilities Providing Substance Abuse Services



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



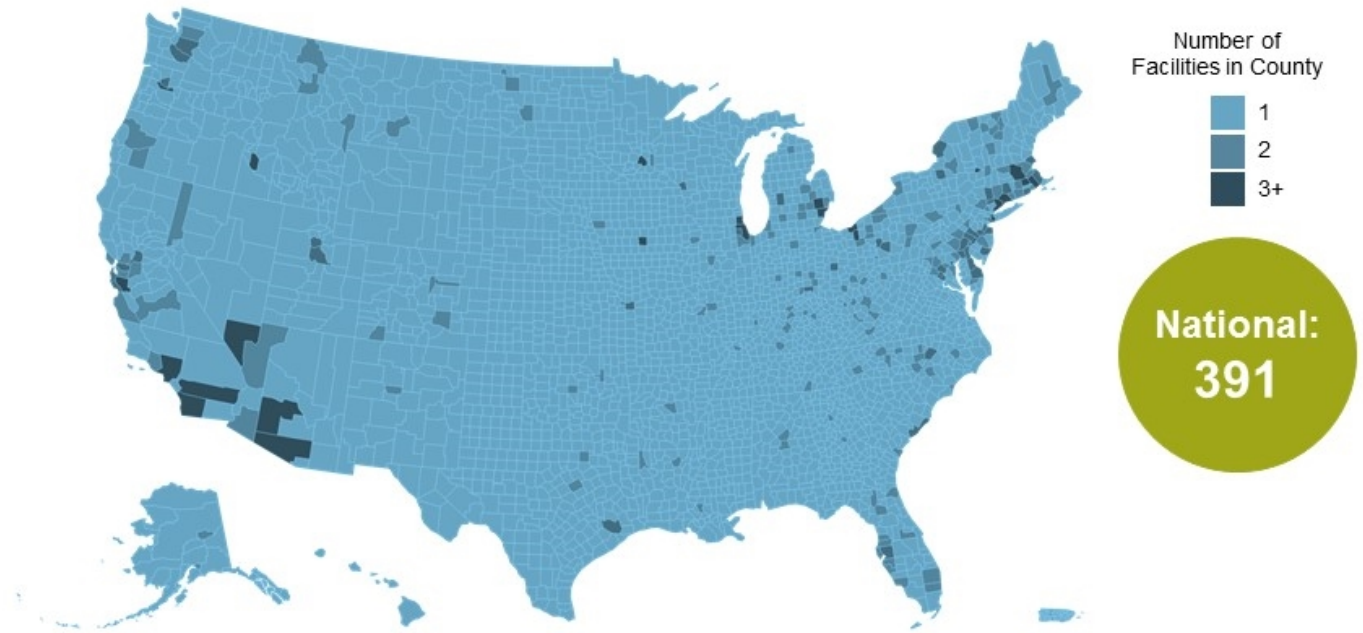
# Fewer Than 50% Offer Any FDA-Approved Opioid Use Disorder Medication



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



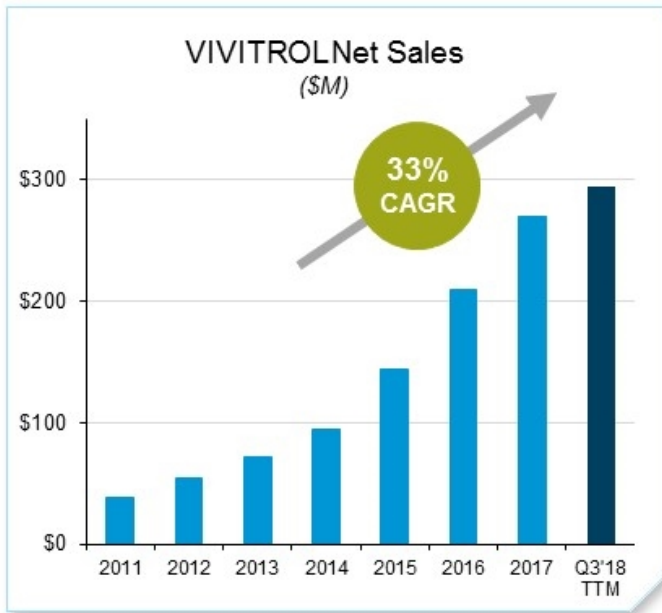
# Fewer Than 5% Offer All Three Types of FDA-Approved Opioid Use Disorder Medications



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**
  - 27 states have demonstrated more than 25% growth year-over-year (Q3'18 YTD)
- ▶ **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 ~730 at the end of Q3'18**



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

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

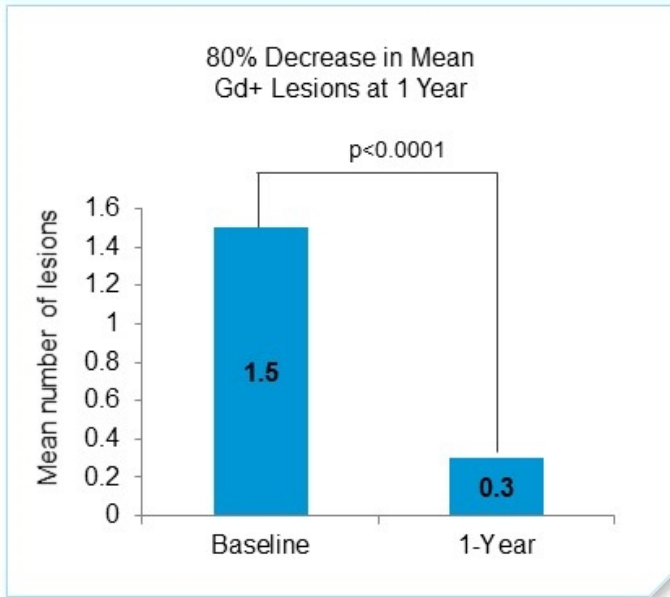
- ▶ Novel, oral investigational fumarate for the treatment of relapsing forms of MS (RRMS), designed to provide differentiated features vs. dimethyl fumarate
  - Administered in oral, micro pellet, controlled-release dosage form
  - Composition of matter patent extends into 2033
- ▶ NDA submitted in 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



 **VUMERITY™**  
(diroximel fumarate)



# 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.

**Alkermes**

**EVOLVE-MS-1: A Phase 3, Open-Label, Long-Term Safety Study of ALKS 8700 in Relapsing-Remitting Multiple Sclerosis**

Robert T. Naismith, MD, Richard A. Leigh-Pemberton, MD, David Raczunas, MD, Hans-Joachim Haas, PhD, Emily Kandel, PhD, Lisa von Mallin, MD, Jerry G. Wolinsky, MD  
Washington University School of Medicine, St. Louis, MO; Alkermes, Inc., Walling, MA; Washington Medical School, UHealth, Houston, TX

	Patients, n (%)
<b>Months 0-1 after treatment initiation (n=580)</b>	
Discontinuations due to GI AEs	3 (0.5)
Serious GI AEs	0
<b>Most common TEAEs (&gt;5% of patients)</b>	
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 adverse event.

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)

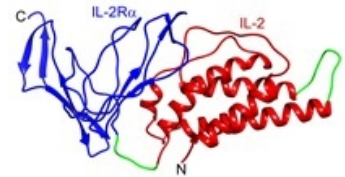




## **ALKS 4230 and Emerging Biologics Capabilities**

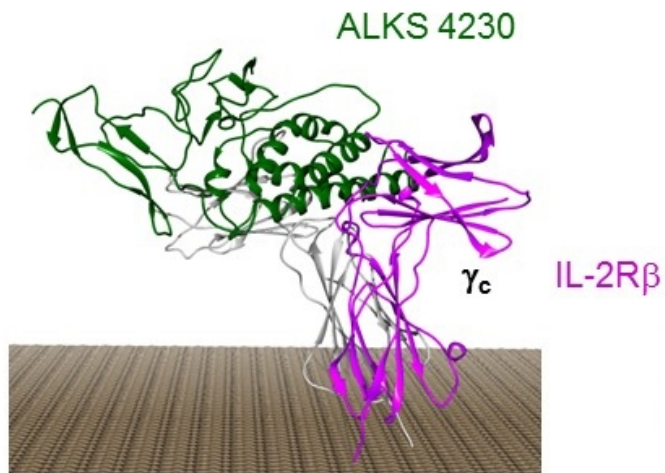
## ALKS 4230: Selective IL-2 Fusion Protein

- 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

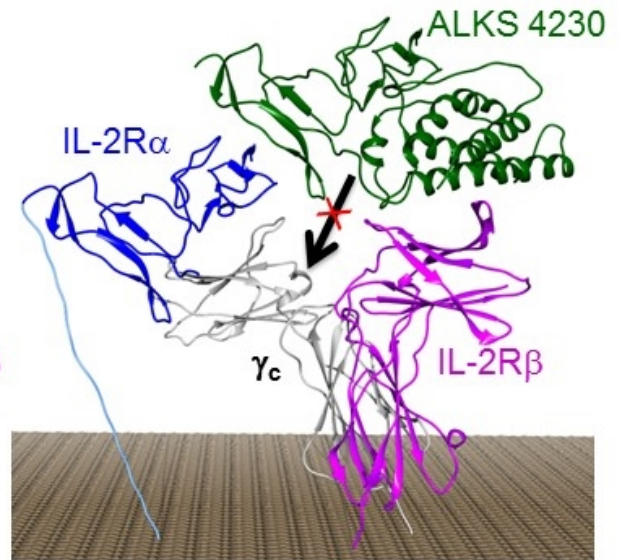


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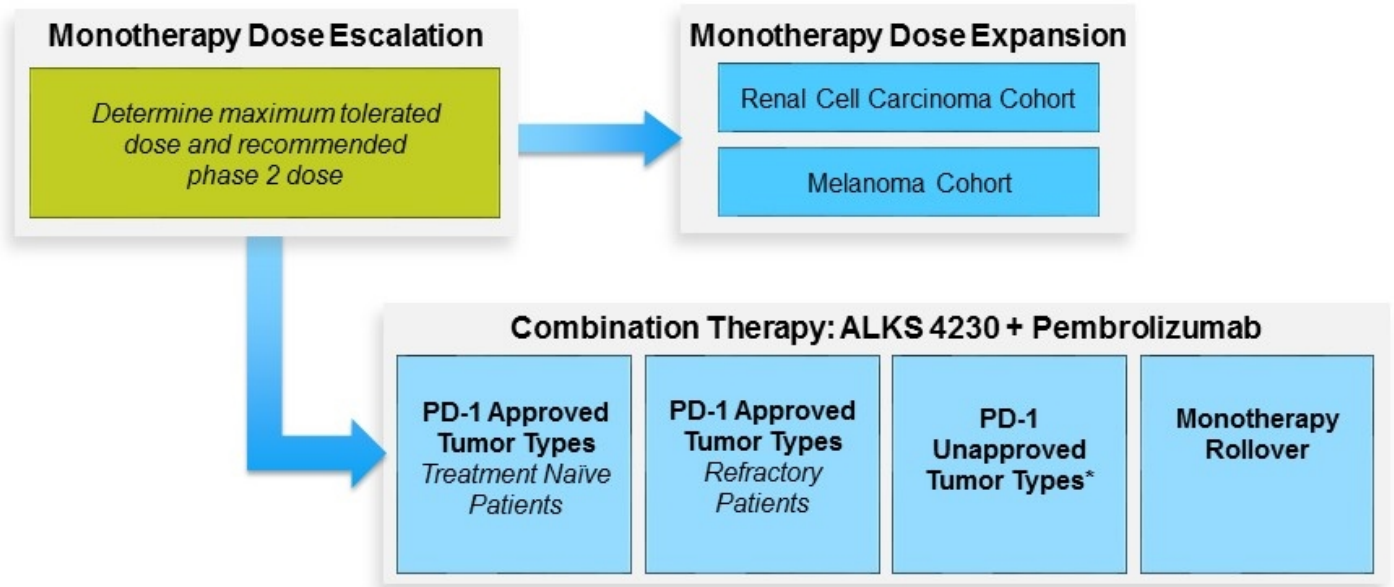
### IL-2 Intermediate-Affinity Receptors



### IL-2 High-Affinity Receptors

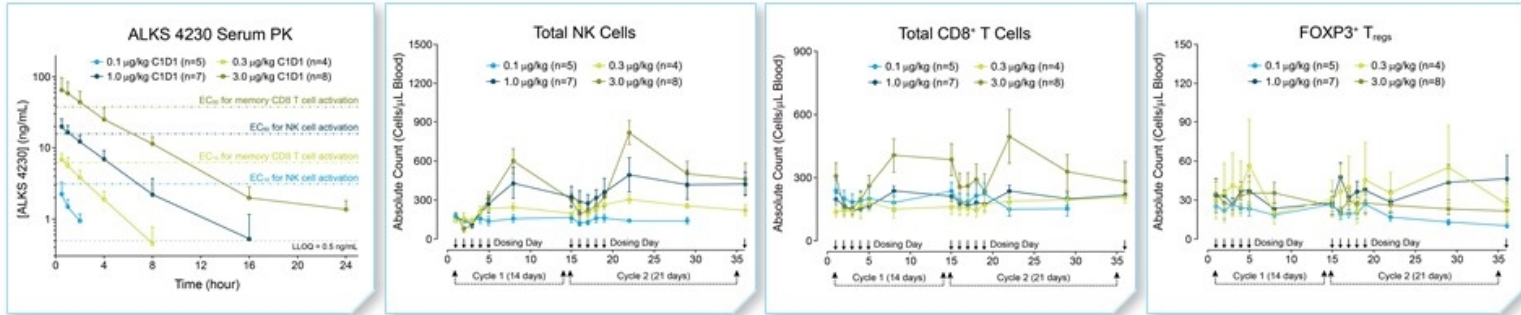


# ALKS 4230 Phase 1 Study Design



\*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 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).





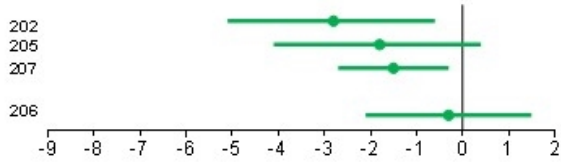
## ALKS 5461 for Adjunctive Treatment of Major Depressive Disorder



- ▶ Investigational opioid system modulator
  - Administered once daily as a single, sublingual tablet
- ▶ Efficacy and safety data from FORWARD-4 and FORWARD-5 published in *Molecular Psychiatry*
- ▶ NDA submitted January 2018; PDUFA target action date Jan. 31, 2019
  - Expecting Complete Response Letter; Determining next steps

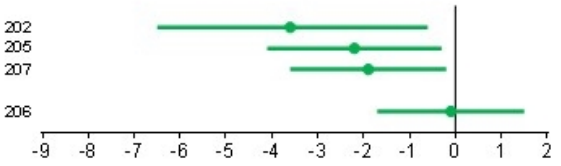


# Consistent Efficacy for ALKS 5461



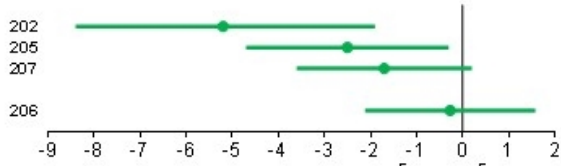
Pre-specified Primary endpoint

2 of the 4 pivotal trials met their primary endpoint



MADRS-10<sub>AVG</sub>

3 of the 4 trials demonstrate evidence of efficacy



MADRS-10<sub>EOT</sub>

2 of the 4 trials demonstrate evidence of efficacy

ALKS 5461 2/2 vs. Placebo  
Least Squares Mean Difference (95% CI)

← Favors ALKS 5461 +ADT      Favors Placebo +ADT →



## Consistent Safety and Tolerability Profile of ALKS 5461

- ▶ Data from FORWARD core efficacy studies demonstrate consistent safety and tolerability profile
  - High completion rate (85%)
  - Most common adverse events included nausea, constipation and dizziness
    - Generally mild, transient and occurring around treatment initiation
- ▶ Extensive dataset
  - >1,500 subjects participated in clinical efficacy program
  - >1,500 patients enrolled in long-term safety study
    - >700 patients have completed 12 months of treatment
- ▶ Consistent evidence of low abuse potential

DEVELOPMENT CANDIDATES	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	FDA REVIEW
<b>ALKS 5461</b> (Major Depressive Disorder)	[REDACTED]				
<b>ALKS 3831</b> (Schizophrenia)	[REDACTED]				
<b>Diroximel Fumarate (BII098)*</b> (Multiple Sclerosis)	[REDACTED]				
<b>ALKS 4230</b> (Immuno-oncology)	[REDACTED]				

\*Diroximel fumarate New Drug Application submitted to FDA December 2018



## 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)
- 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

### Depression

#### ALKS 5461

- PDUFA date Jan. 31, 2019; Determine next steps



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



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

