



# Taking on Critical Public Health Challenges

September 2019



#### Forward-Looking Statements and Non-GAAP Financial Information

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 or prospects; expectations with respect to the continued growth of the long-acting injectable antipsychotic market and revenue from the company's commercial products, including potential VIVITROL® growth driven by geographic expansion and state policy initiatives, state programs and federal funding and potential ARISTADA® and results from the ALPINE study; opportunities to address the bipolar I market with the potential approval of ALKS 3831; the therapeutic and commercial value of the company's marketed and development products; timelines, plans and expectations for clinical development activities relating to the company's products and product development candidates, including the presentation of efficacy data for ALKS 4230 and ongoing enrollment and other progress across the ARTISTRY clinical development program for ALKS 4230; the company's timelines, plans and expectations for regulatory activities and interactions with, and actions by, the U.S. Food and Drug Administration ("FDA") relating to the company's new drug application ("NDA") submission for diroximel fumarate ("DRF") and the company's planned NDA submission for ALKS 3831, including the expected data to be contained in such NDA for ALKS 3831 and the adequacy of such data to serve as the basis of an NDA for ALKS 3831 for the treatment of schizophrenia and the treatment of bipolar I disorder; the potential financial benefits that may be achieved under the license and collaboration agreement between the company and Biogen for DRF; Biogen's commercialization plans for DRF; the company's growing commercial infrastructure and expectations concerning commercial activities relating to the company's products and product candidates; and the duration of expected patent protection for the company's products and development candidates. The company cautions that forward-looking statements are inherently uncertain. Although the company believes that such 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 may lead to competition from generic drug manufacturers; data from clinical trials may be interpreted by the FDA in different ways than the company interpretes 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, and preliminary or interim results in the company's clinical trials may not be predictive of final results of such clinical trials, results of future clinical trials or real-world results; 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; the potential financial, commercial and therapeutic benefits of collaboration with Biogen under the license and collaboration agreement between Alkermes and Biogen may not be achieved; 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 and on the company's website at 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.

Non-GAAP Financial Measures: This presentation includes information about certain financial measures that are not prepared in accordance with generally accepted accounting principles in the U.S. (GAAP), including non-GAAP net income and non-GAAP earnings per share.

These non-GAAP measures are not based on any standardized methodology prescribed by GAAP and are not necessarily comparable to similar measures presented by other companies. Reconciliations of these non-GAAP financial measures to the most directly comparable GAAP financial measures can be found in the Alkermes plc Current Report on Form 8-K filed with the SEC on Feb. 14, 2019.

Note Regarding Trademarks: The company is the owner of various U.S. federal trademark registrations (\*) and other trademarks (TM), including ARISTADA\*, ARISTADA INITIO\*, VIVITROL\* and VUMERITY\*. 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>



**3M** 

SUFFER FROM BIPOLAR I DISORDER<sup>3</sup>

- 1. Schizophrenia and Related Disorders Alliance of America, <a href="https://sardaa.org/resources/about-schizophrenia/">https://sardaa.org/resources/about-schizophrenia/</a> accessed on Aug. 1, 2019
- 2. Substance Abuse and Mental Health Services Administration (SAMHSA). 2017 National Survey on Drug Use and Health (NSDUH)
- 3. Epidemiology of DSM-5 bipolar I disorder: Results from the national epidemiologic survey on alcohol and related conditions III. Blanco C, Compton WM, Saha TD et al. J Psychiatr Res 84 (2017) 310-317. https://www.ncbi.nlm.nih.gov/pubmed/27814503



#### 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



revenue in 2018
Increased annual proprietary product net sales by 527%<sup>2</sup>

Crossed \$1B in total

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

~1,000 employees in operations and quality

Dedicated culture



~2,400 total employees in Ireland, MA, OH, and U.S.-based field sales force<sup>3</sup>

- 1. Includes years 2014 through 2018
- 2. FY2018 compared to FY2013
- 3. As of Q2 2019





### **Establishing a Leadership Position in Serious Mental Illnesses**



### Developing Important New Medicines for the Treatment of Serious Mental Illnesses



Long-acting injectable prodrug new molecular entity (NME) for the treatment of schizophrenia



#### **ALKS 3831**

Investigational, oral bilayer tablet, olanzapine plus novel NME for the treatment of schizophrenia and for the treatment of bipolar I disorder



#### Integrated Infrastructure Scaled to Address Complex Disease Areas



### 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 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. The first ARISTADA dose may be administered on the same day as ARISTADA INITIO or up to 10 days thereafter.



### Key Differentiating Feature: Treatment Initiation With ARISTADA INITIO®

- ARISTADA® is the first and only long-acting injectable (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>









<sup>\*</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. The first ARISTADA dose may be administered on the same day as ARISTADA INITIO or up to 10 days thereafter. ARISTADA INITIO was approved by FDA on June 29, 2018.

<sup>1.</sup> Truven Health Analytics Marketscan claims database, 2015.

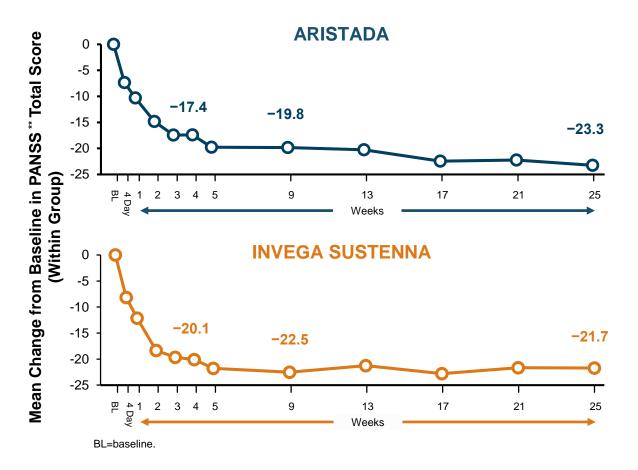
## ALPINE: <u>Aripiprazole Lauroxil and Paliperidone Palmitate:</u> <u>In</u>itiation <u>Effectiveness\* Topline Results</u>

#### Primary Endpoint:

 Statistically significant improvement from baseline to Week 4 for each treatment group

#### **Secondary Endpoints:**

- Within-group reductions in change from baseline in PANSS total scores observed during the 6-month study for each treatment group
- Similar results for PANSS total scores between groups were observed



- Most common adverse events:
  - ARISTADA: injection site pain (17.2%), increase in weight (9.1%) and akathisia (9.1%)
  - INVEGA SUSTENNA: injection site pain (24.8%), increase in weight (16.8%) and akathisia (10.9%)
- Additional weight, akathisia and prolactin data from ALPINE were presented at ASCP<sup>†</sup> 2019
- Study retention by treatment group (completed six-month study)
  - ARISTADA: 56.6%
  - INVEGA SUSTENNA: 42.6%

<sup>&</sup>lt;sup>†</sup>American Society of Clinical Psychopharmacology



<sup>\*</sup>This was not a head-to-head study. This study was not powered to provide comparative efficacy or safety results and should not be interpreted as suggesting ARISTADA as superior or noninferior to INVEGA SUSTENNA

<sup>\*\*</sup> Positive and Negative Syndrome Scale

### ARISTADA®: Differentiated in the Atypical LAI Market

	Treatment Initiation	Dosing Intervals	Dosing Strengths
ARISTADA	Day 1: ARISTADA INITIO® regimen* & ARISTADA dose	One-month, six-week and two-month	5 doses**
INVEGA SUSTENNA®	Day 1: 234 mg injection Day 8: 156 mg injection	One-month	5 doses
INVEGA TRINZA <sup>®</sup>	Initial injection follows ≥ four months of INVEGA SUSTENNA treatment	Three-month	4 doses
RISPERDAL CONSTA®	Initial injection and three weeks of daily oral risperidone or another antipsychotic medication	Two-week	3 doses
ABILIFY MAINTENA®	Initial injection and two weeks of daily oral aripiprazole or current oral antipsychotic	One-month	2 doses†

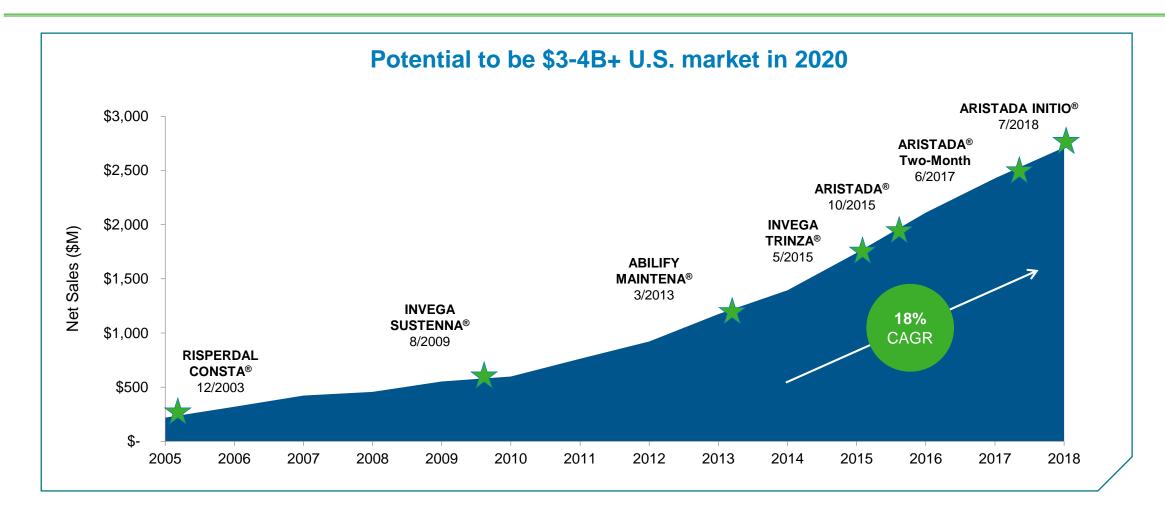
<sup>\*</sup>ARISTADA INITIO + single 30 mg oral dose of aripiprazole provides an alternative for concomitant three weeks of oral aripiprazole for initiation of ARISTADA, with relevant levels of aripiprazole concentration reached within four days. The first ARISTADA dose may be administered on the same day as ARISTADA INITIO or up to 10 days thereafter. ARISTADA INITIO was approved by FDA on June 29, 2018.

\*\* Includes ARISTADA INITIO

<sup>&</sup>lt;sup>†</sup> Includes 300mg dose for patients experiencing adverse events with 400mg



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

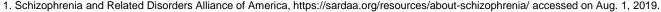


Sources: Johnson & Johnson, Otsuka, Lundbeck and Alkermes quarterly reports.

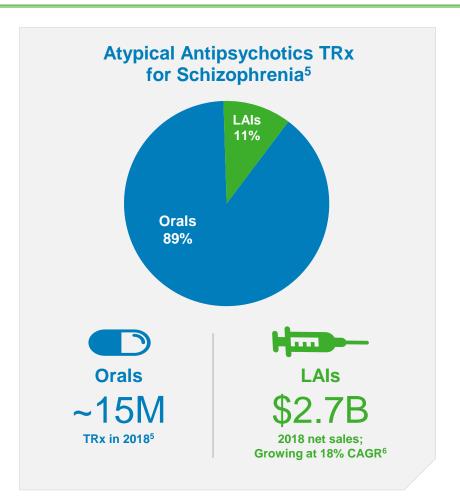


## Significant Opportunity to Help Address Needs in Schizophrenia With Long-Acting Injectables

- Schizophrenia is a serious mental illness that affects
   ~3.5M patients in the U.S.¹
  - Treatment and other economic costs due to schizophrenia are estimated to be between \$32B - \$65B annually<sup>1</sup>
- LAIs demonstrate improved outcomes<sup>2</sup>, reduced relapse<sup>3</sup> and lower mortality<sup>4</sup>, but are currently underutilized in the U.S.<sup>2</sup>
  - Oral therapies dominate the treatment paradigm



<sup>2.</sup> Subotnik KL, et al. JAMA Psychiatry. 2015, 72(8): 822-829; Stahl, Stephen, CNS Spectrums (2014), 19, 3–5; Carpenter, William et al., JAMA Psychiatry. 2015;72(8):745-746.



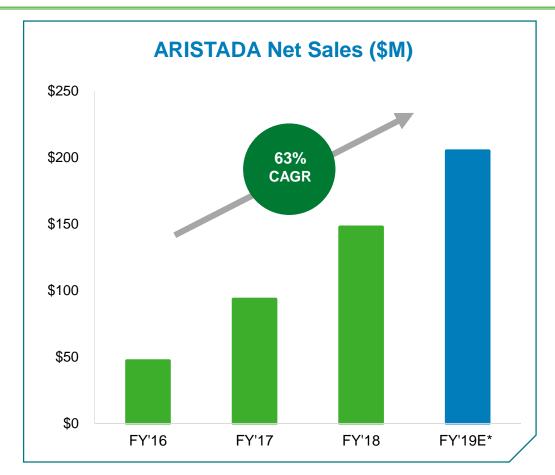
<sup>3.</sup> Tiihonen, Mittendorfer-Rutz et al., 2017.

<sup>4.</sup> Taipale, Mittendorfer-Rutz et al., 2018.

<sup>5.</sup> IQVIA NSP & Custom SOB data sets R12M ending December 2018.

<sup>6.</sup> Johnson & Johnson, Otsuka, Lundbeck and Alkermes quarterly reports.

### ARISTADA®: Growing Into its Potential



#### **Anticipated Growth Drivers**

- ARISTADA INITIO® regimen\*\* plus ARISTADA two-month dose
- Expanded commercial team increasing provider awareness;
   Hospital commercial organization targeting new starts
- Positive results from ALPINE study that evaluated the efficacy, safety and tolerability of ARISTADA and the current market-leader INVEGA SUSTENNA
- ARISTADA underlying prescription trends have continued to demonstrate solid growth
  - On a TRx MOT basis, Q2 sequential growth was 13%, compared to the broader atypical long-acting injectable (aLAI) market growth of 6% sequentially<sup>1</sup>
  - Year-over-year, Q2 ARISTADA TRx MOT grew 43%<sup>1</sup>

<sup>\*\*</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. The first ARISTADA dose may be administered on the same day as ARISTADA INITIO or up to 10 days thereafter. ARISTADA INITIO was approved by FDA on June 29, 2018.

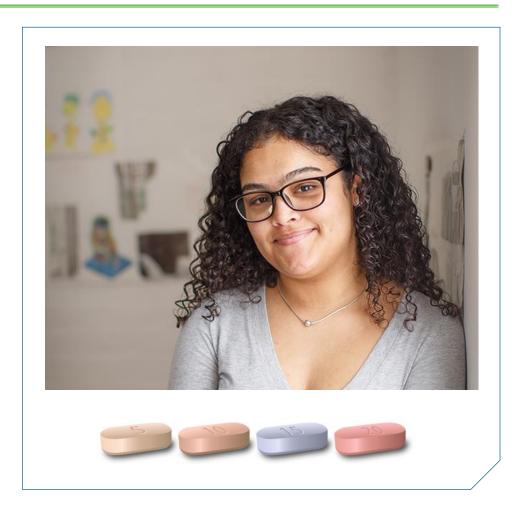
1. IMS NPA



<sup>\*</sup> FY'19E reflects the midpoint of guidance. This financial guidance was initially provided by Alkermes plc (the "Company") in its Current Report on Form 8-K filed with the SEC on July 25, 2019, and is effective only as of such date. The Company expressly disclaims any obligation to update or reaffirm this guidance. The Company only provides guidance in a Regulation FD compliant manner.

## ALKS 3831: A Potential New Oral Treatment for Adults With Schizophrenia and Adults With Bipolar I Disorder

- Designed to offer robust efficacy of olanzapine; addition of Samidorphan intended to mitigate weight gain liability
- Single NDA submission for treatment of adults with schizophrenia and bipolar I disorder planned for Q4 2019
  - Conducted pre-NDA meeting to discuss contents of planned NDA submission including FDA requirements related to efficacy, safety, weight and metabolic profile and expansion to include the treatment of bipolar I disorder
  - NDA will include data from the completed ENLIGHTEN clinical development program in patients with schizophrenia and pharmacokinetic bridging data comparing ALKS 3831 and olanzapine
- Fixed-dose combination
  - Bilayer tablet of olanzapine (5 mg, 10 mg, 15 mg, or 20 mg) with samidorphan (10 mg)





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

#### V

#### **ENLIGHTEN-1 Efficacy Study**

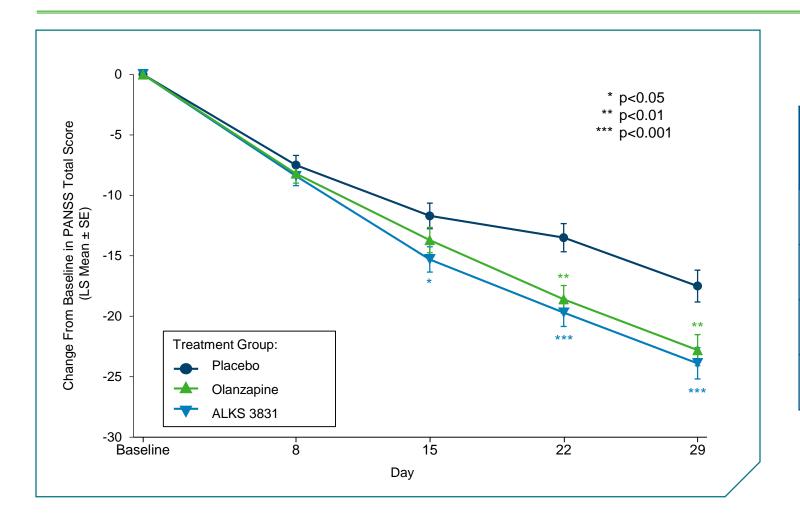
- Antipsychotic efficacy vs. placebo
- 403 patients with acute schizophrenia
- ALKS 3831 demonstrated statistically significant reductions from baseline in PANSS scores at 4 weeks, compared to placebo (p<0.001)</li>
- Olanzapine achieved similar improvements from baseline PANSS scores, compared to placebo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

### V

#### **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 ≥10% weight gain (p=0.003)

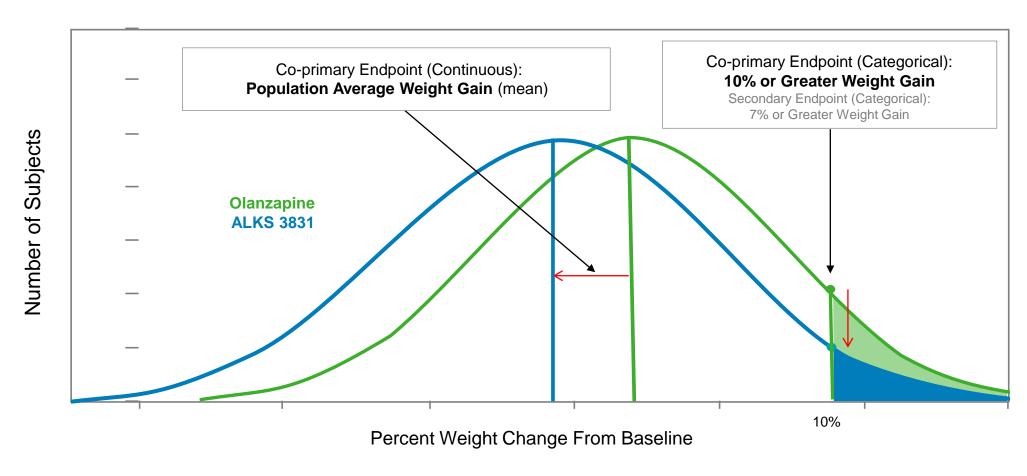
#### **ENLIGHTEN-1: Demonstrated Robust Antipsychotic Efficacy**



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



## ENLIGHTEN-2: Primary Analysis Designed to Capture Shift in Two Dimensions



Graph is for illustrative purposes only and does not reflect actual results of the ENLIGHTEN-2 study.



#### **ENLIGHTEN-2** Results

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

#### **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

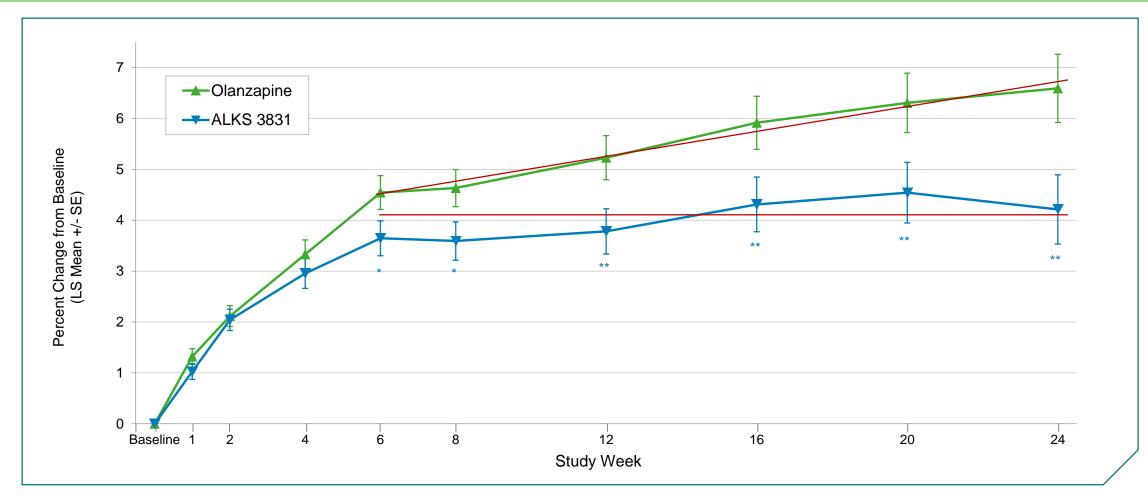
The most common adverse events for ALKS 3831 were weight gain, somnolence and dry mouth.

The most common adverse events for olanzapine were weight gain, somnolence and increased appetite.

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



#### ENLIGHTEN-2: ALKS 3831 Weight Profile Stabilized



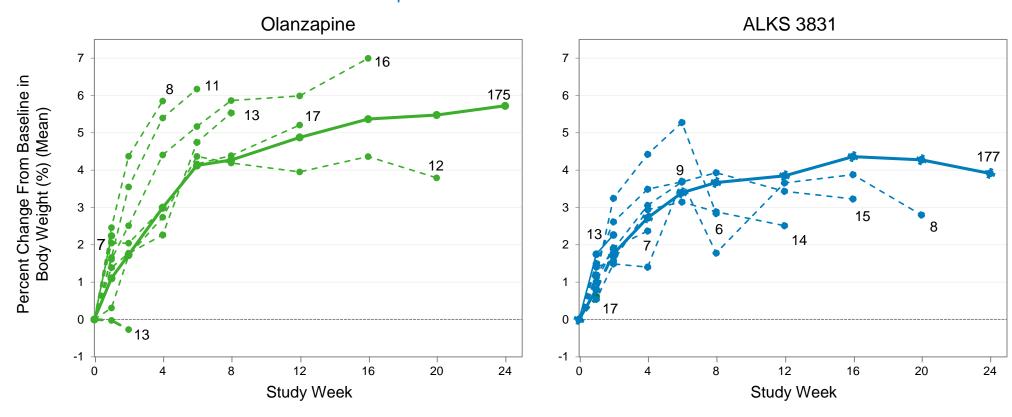
Note: Weight curve based on analysis of covariance (ANCOVA) approach using multiple imputation (MI) for missing data. \*p<0.05 vs. olanzapine; \*\*p<0.01 vs. olanzapine



#### ENLIGHTEN-2: Weight Gain Trajectory of Early Discontinuations

#### **Percent Change From Baseline in Body Weight by Treatment\***

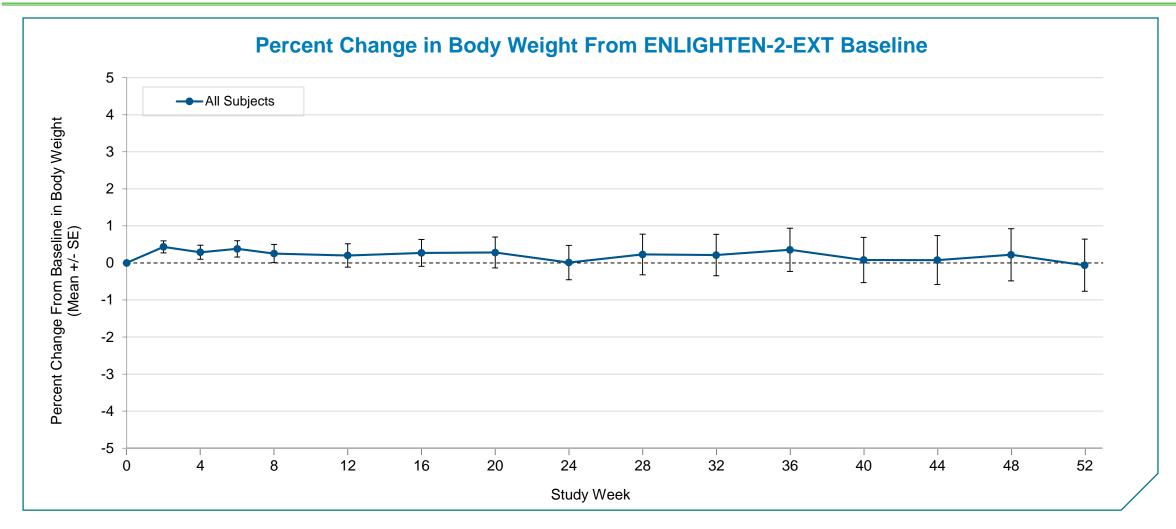
Completers vs. Premature Discontinuations



<sup>\*</sup>Solid lines denote the weight gain curve of patients who completed the study. Dashed lines denote weight gain curves of subjects who prematurely discontinued at given visits. Numbers of patients summarized in each curve are noted.



## ENLIGHTEN-2-EXT Interim Results: Weight Remains Stable Over 52 Weeks

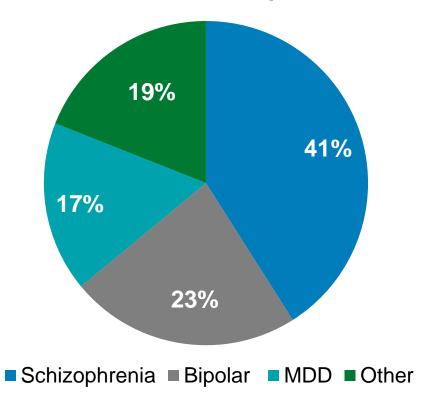




#### Opportunity to Address Unmet Need in the Bipolar Market

	Schizophrenia	Bipolar
Oral atypical antipsychotic market <sup>1</sup>	~15.1M TRx	~17.0M TRx
Olanzapine	~3.0M TRx	~1.9M TRx

U.S. Atypical Antipsychotic Market TRx for Olanzapine<sup>2</sup>



<sup>2.</sup> IMS NPA R12M May 2019



<sup>1.</sup> IQVIA NPA Audit R12M May 2019, IQVIA SOB File





### 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

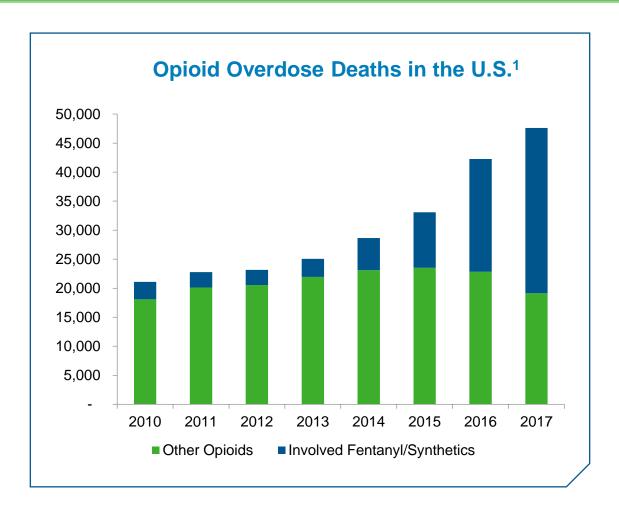


VIVITROL is 1 of 3 FDA-approved treatment options for opioid dependence\*

\*To be used in conjunction with psychosocial support



#### Opioid Epidemic Continues to Rage Nationwide



#### 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%²
- Opioid overdose deaths drove down U.S. life expectancy over the last three years<sup>3</sup>

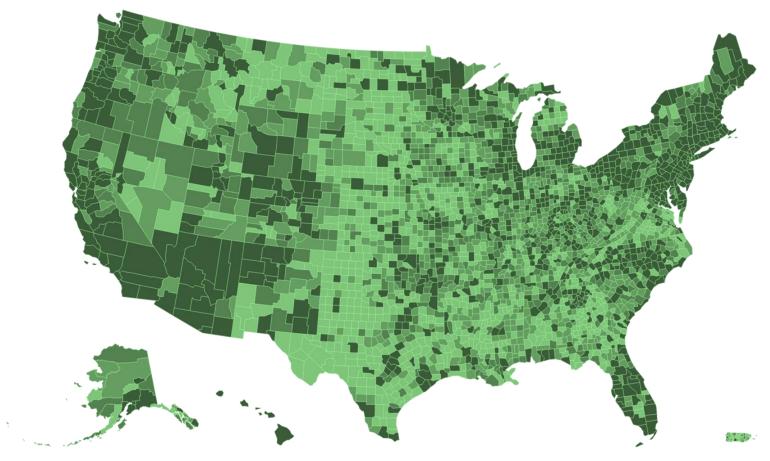


Substance Abuse and Mental Health Services Administration (SAMHSA). 2017 National Survey on Drug Use and Health (NSDUH); Deaths involving more than one opioid category (e.g., a death involving both methadone and a natural and semisynthetic opioid) are counted in both categories.

<sup>2.</sup> National Institute on Drug Abuse provisional 2017 data set.

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



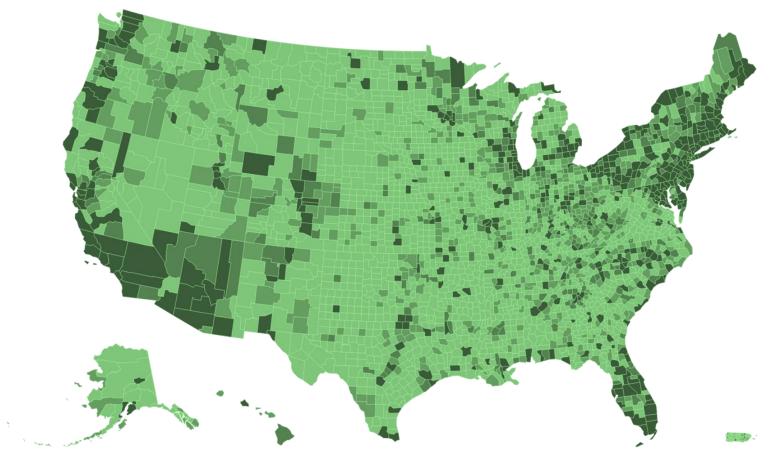




Source: opioid.amfar.org accessed on June 13, 2019



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

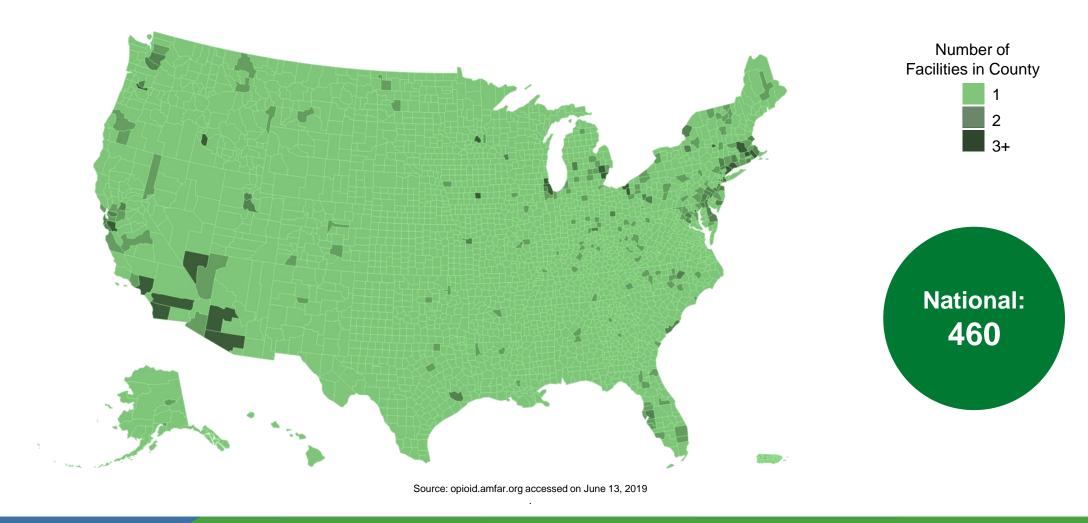






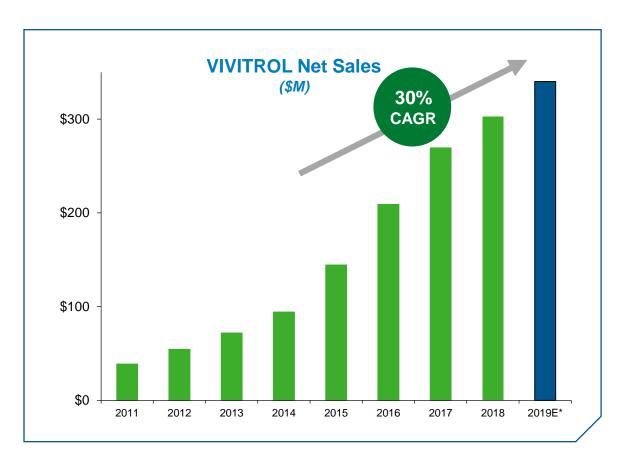
Source: opioid.amfar.org accessed on June 13, 2019

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





### VIVITROL®: Demonstrated Growth With New Opportunities Arising



- Public policy initiatives and improved access driving strong growth in new states
  - 25 states had demonstrated more than 25% growth year-over-year (as of May'19)
- 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 ~815 at end of Q2'19

<sup>\*</sup> FY'19E reflects the midpoint of guidance. This financial guidance was initially provided by the Company in its Current Report on Form 8-K filed with the SEC on Feb. 14, 2019. This financial guidance was reiterated by the Company in its Current Report on Form 8-K filed with the SEC on July 25, 2019 and is effective only as of such date. The Company expressly disclaims any obligation to update or reaffirm this guidance. The Company only provides guidance in a Regulation FD compliant manner.



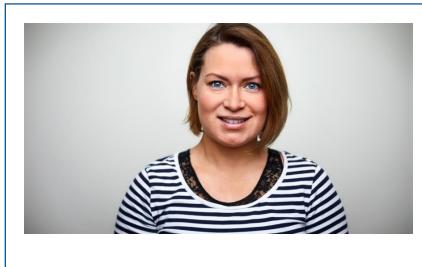


### Diroximel Fumarate for Multiple Sclerosis (Formerly BIIB098)



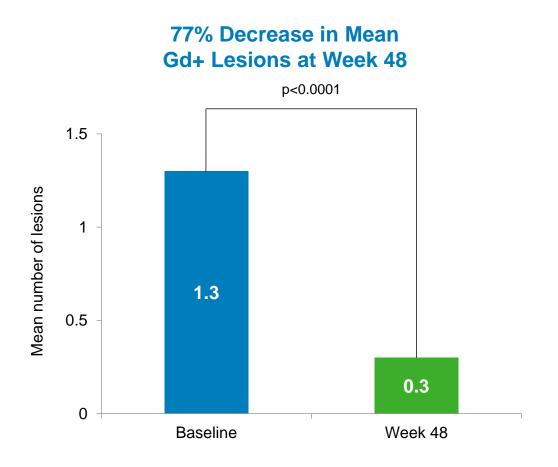
### Diroximel Fumarate (DRF) for Multiple Sclerosis (MS)

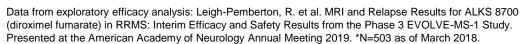
- Diroximel fumarate is an investigational, novel oral fumarate candidate with a distinct chemical structure in development for the treatment of relapsing forms of MS
  - Administered in oral, micro pellet, controlled-release dosage form
  - Composition of matter patent extends into 2033
- NDA accepted for review in February 2019
  - Streamlined regulatory pathway 505(b)(2)
  - PDUFA target action date: Q4 2019
- Announced positive topline results of EVOLVE-MS-2 elective head-to-head gastrointestinal (GI) tolerability study in July 2019
- If approved, Biogen intends to market DRF under the conditionally approved brand name VUMERITY™

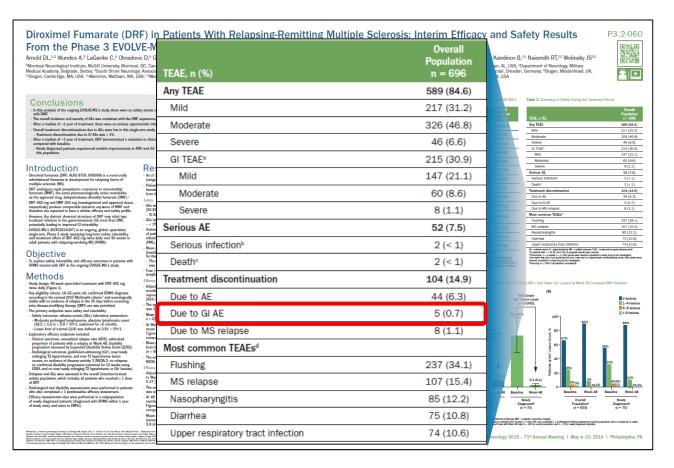




#### Diroximel Fumarate: EVOLVE-MS-1 Reveals Efficacy and Tolerability







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).



#### Diroximel Fumarate (DRF): EVOLVE-MS-2 Positive Topline Results

- Elective, phase 3 study in 506 patients with relapsingremitting multiple sclerosis
- Designed to assess GI tolerability profile of DRF compared to TECFIDERA® (DMF)
- DRF demonstrated statistically superior GI tolerability on primary endpoint assessing self-reported GI events (p = 0.0003)
  - Patients treated with DRF self-reported significantly fewer days of key GI symptoms with intensity scores ≥2 on the Individual Gastrointestinal Symptom and Impact Scale, as compared to DMF
- Results were consistent with the safety and tolerability profile of DRF observed in ongoing EVOLVE-MS-1 study in nearly 700 patients
  - Discontinuation rates due to GI adverse events (AEs) of less than 1%

- Overall proportion of patients with AEs leading to study discontinuation were 1.6% for DRF and 6.0% for DMF
  - Proportion of patients with GI AEs leading to study discontinuation were 0.8% for DRF and 4.8% for DMF

Most Common Adverse Events	DRF	DMF
Flushing	32.8%	40.6%
Diarrhea	15.4%	22.3%
Nausea	14.6%	20.7%

#### 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
- Potential for additional indications and ex-U.S. opportunities<sup>3</sup>

### **Biogen License and Collaboration Agreement**

- Granted Biogen exclusive, worldwide license to commercialize DRF
- Mid-teens percentage royalty to Alkermes on worldwide net sales of DRF
- \$150M milestone upon regulatory approval by FDA by 12/31/21
- Biogen responsible for development and commercial expenses (since 1/1/18)

<sup>3.</sup> Under License and Collaboration Agreement, Biogen controls the pursuit of any additional indications and/or ex-U.S. opportunities.



<sup>1.</sup> Decision Resources MS Disease Landscape (Nov. 2016)

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

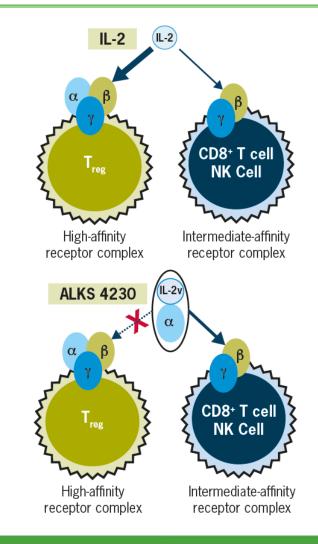


### **ALKS 4230 and Emerging Biologics Capabilities**

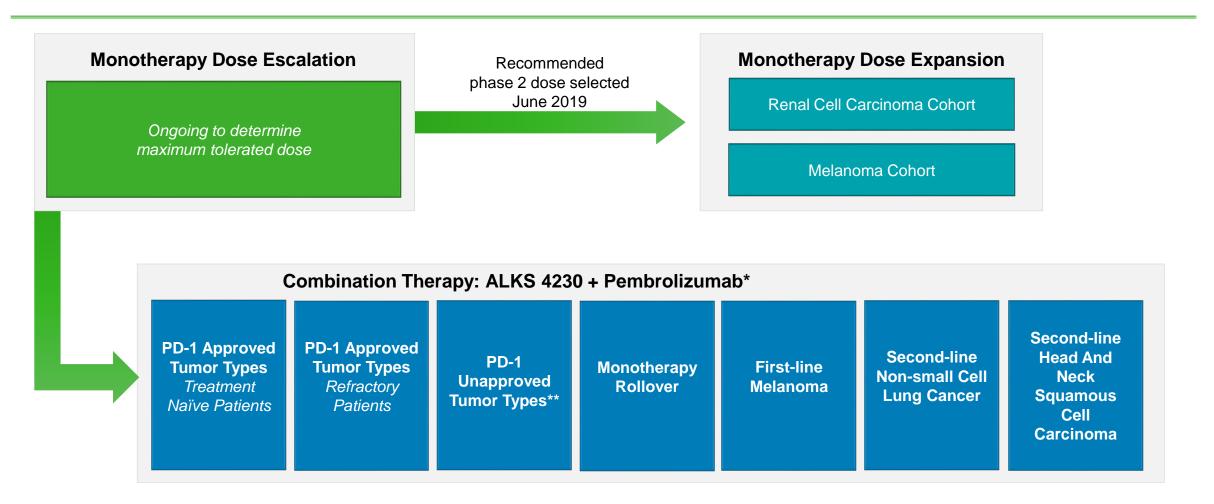


#### ALKS 4230: Selective IL-2 Fusion Protein

- ALKS 4230 is a novel investigational drug designed to leverage the proven anti-tumor effects of existing interleukin-2 (IL-2) therapy while mitigating certain limitations
  - Stable, single polypeptide comprised of modified IL-2 and the high affinity IL-2 alpha receptor chain
- Novel design enables ALKS 4230 to selectively bind to the intermediate-affinity IL-2 receptor, thereby selectively expanding tumor-killing CD8+ and Natural Killer T cells
- Fusion design of ALKS 4230 sterically hinders its ability to bind to high-affinity IL-2 receptors, which minimizes the activation of immunosuppressive regulatory T cells, which are associated with poor tolerability and potential capillary leak syndrome



#### ALKS 4230: ARTISTRY-1 Phase 1/2 Study Design



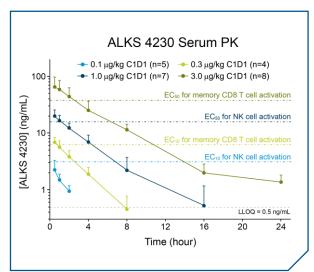
<sup>\*</sup>Expanded the combination-therapy portion of ARTISTRY-1 in Q2'19 to add three additional cohorts evaluating patients with first-line melanoma, second-line non-small cell lung cancer and second-line head and neck squamous cell carcinoma.

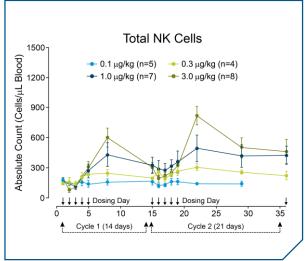
<sup>\*\*</sup>Includes colorectal, triple-negative breast, ovarian carcinoma, soft tissue sarcomas, and subjects with metastatic non-small cell lung cancer whose tumors express low or undetectable PD-L1.

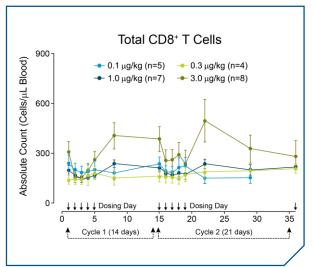


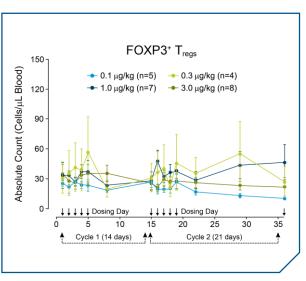
## ALKS 4230: Pharmacokinetics and Pharmacodynamic Effects From ARTISTRY-1 Monotherapy Dose Escalation Stage\*

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









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

<sup>\*</sup>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).



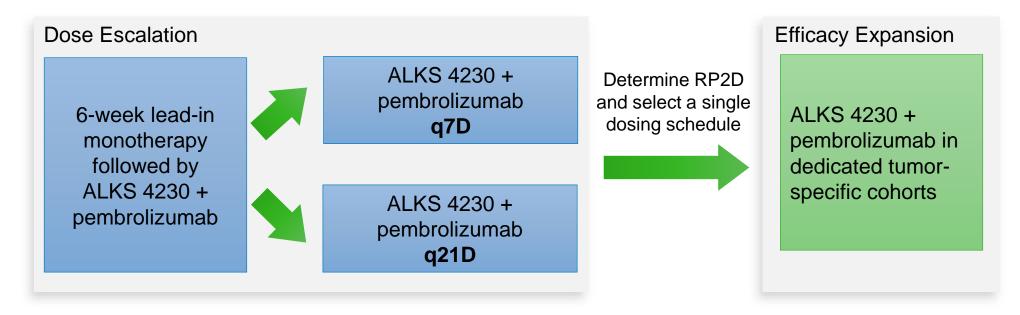
## ALKS 4230: Recommended Phase 2 Monotherapy Dose Identified and Initial Signals of Efficacy Observed Across ARTISTRY-1

- Initiated monotherapy dose expansion stage to evaluate efficacy, safety and tolerability of ALKS 4230 in patients with renal cell carcinoma or melanoma
  - Followed identification of 6 μg/kg/day administered intravenously as recommended phase 2 dose (RP2D)
  - Dose escalation data demonstrated effector T-cell expansion in line with recombinant human IL-2, with minimal activation of immunosuppressive regulatory T cells
- Initial signs of clinical benefit (as of June 14, 2019)
  - Monotherapy dose-escalation stage: At the 3 and 6 μg/kg/day doses, 8 of the 14 patients who completed on-study first scans demonstrated stable disease; Majority of these 8 patients continued to demonstrate stable disease upon their second scan
  - Combination therapy stage: 5 of the 9 patients who completed on-study first scans demonstrated stable disease or better in their initial scans; All 5 patients had PD-1 unapproved tumor types
  - Demonstrated side effect profile across completed cohorts consistent with cytokine therapy: Fever and chills were most common treatment-related adverse events; No capillary leak syndrome observed
- Plan to present initial efficacy data from program at medical meeting this fall, pending conference acceptance



## ALKS 4230: ARTISTRY-2 Phase 1/2 Study Subcutaneous Dosing Summary Design and Preliminary Findings

 Designed to explore the safety, tolerability and efficacy of ALKS 4230 administered subcutaneously as monotherapy and in combination with the PD-1 inhibitor KEYTRUDA® (pembrolizumab) in patients with advanced solid tumors



- Initial signals of efficacy observed in first dosing cohort
  - Observed disease stabilization on initial scan during the 6-week monotherapy lead-in period

### News Flow Expected in 2019

Schizophrenia	ARISTADA®  ✓ Report topline results for ALPINE phase 3b study (Q2)
	ALKS 3831  ✓ Present ENLIGHTEN-2 data at medical meeting (Q2)  □ Submit NDA for schizophrenia and bipolar I disorder (Q4)
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® (Q3)  □ Expected FDA regulatory action (Q4)
Immuno-oncology	<ul> <li>ALKS 4230</li> <li>✓ Initiate monotherapy expansion stage of ARTISTRY-1 study (Q2)</li> <li>□ Complete monotherapy dose-escalation stage of ARTISTRY-1 study</li> <li>✓ Initiate ARTISTRY-2 subcutaneous dosing study (Q1)</li> <li>□ Present initial efficacy data at medical meeting, pending acceptance (H2)</li> </ul>

#### Alkermes: 2019 Financial Expectations\*

(in millions, except per share amounts)	Financial Expectations for Year Ending Dec. 31, 2019 <sup>†</sup>
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<sup>†</sup>
- ARISTADA® net sales of \$200M - \$210M<sup>††</sup>
- License revenues: \$150M milestone anticipated upon FDA approval of DRF (expected Q4'19)

<sup>\*</sup> 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; change in the fair value of contingent consideration; change in the fair value of warrants and equity method investments; 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.



<sup>†</sup>This financial guidance was initially provided by the Company in its Current Report on Form 8-K filed with the SEC on Feb. 14, 2019. This financial guidance was reiterated by the Company in its Current Report on Form 8-K filed with the SEC on July 25, 2019 and is effective only as of such date.

<sup>††</sup> Revised from previous guidance in the range of \$210 - \$230M provided by the Company in its Current Report on Form 8-K filed with the SEC on Feb. 14, 2019. This revised guidance was provided by the Company in its Current Report on Form 8-K filed with the SEC on July 25, 2019 and is effective only as of such date.

<sup>\*</sup>The Company expressly disclaims any obligation to update or reaffirm this guidance. The Company only provides guidance in a Regulation FD compliant manner.

#### Diverse Commercial Portfolio With Long Patent Lives

	Description	Patent Life
Vivitrol® (natrexone for extended-release injectable suspension) 300 mg/val	Once-monthly medication for treatment of alcohol and opioid dependence	<b>2029</b> in U.S.*
ARISTADA aripiprazole lauroxil extended-release injectable suspension 441mg · 662 mg · 882 mg · 1064 mg	Long-acting atypical antipsychotic for treatment of schizophrenia with once-monthly, six-week and two-month dosing	<b>2035</b> in U.S.
RISPERDAL CONSTA® (A Janssen product)	Long-acting atypical antipsychotic for treatment of schizophrenia and bipolar I disorder	<b>2023</b> in U.S. <b>2021</b> in EU
INVEGA SUSTENNA® / XEPLION® (Janssen products)	Long-acting atypical antipsychotic for treatment of schizophrenia and schizoaffective disorder	<b>2031</b> in U.S. <b>2022</b> in EU
FAMPYRA® (An Acorda product)	Treatment to improve walking in patients with multiple sclerosis	<b>2025</b> in EU

FAMPYRA® (prolonged-release fampridine tablets) is being developed and marketed outside the U.S. by Biogen, under a licensing agreement with Acorda Therapeutics.

RISPERDAL CONSTA® and INVEGA SUSTENNA® are trademarks of Johnson & Johnson, and are products developed and sold by Janssen Pharmaceuticals Inc. using Alkermes technology.

<sup>\*</sup> Pursuant to a settlement agreement entered into on July 26, 2019, Amneal Pharmaceuticals LLC was granted a non-exclusive right to market a generic formulation of VIVITROL in the U.S. beginning sometime in 2028 or earlier under certain circumstances.



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

	Description	Patent Life (U.S.)
ALKS 3831	Investigational, novel, once-daily, oral atypical antipsychotic drug candidate for the treatment of schizophrenia and bipolar I disorder	2031
Diroximel fumarate (BIIB098)	Novel oral fumarate candidate in development for the treatment of relapsing forms of MS	2033
ALKS 4230	Novel, engineered fusion protein designed to selectively expand tumor-killing immune cells while avoiding activation of immunosuppressive cells by preferentially binding to the intermediate-affinity IL-2 receptor complex	2033



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