

**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 11, 2022**

**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 D04 C5Y6**  
(Address of principal executive offices)

**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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, \$0.01 par value	ALKS	Nasdaq Global Select Market

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.

**Item 7.01 Regulation FD Disclosure.**

On January 11, 2022, Alkermes plc (the "Company") made available a copy of the corporate presentation to be displayed during its presentation at the virtual J.P. Morgan Healthcare Conference on January 12, 2022. A copy of the presentation is furnished herewith as Exhibit 99.1 and is incorporated by reference in this Item 7.01.

The information in this Item 7.01, 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 8.01 Other Events.**

On January 11, 2022, the Company confirmed receipt of a notice from Sarissa Capital Offshore Master Fund LP of its intention to nominate two director candidates for election to the Company's board of directors at the Company's 2022 annual general meeting of shareholders. A statement issued by the Company in respect of the notice is filed herewith as Exhibit 99.2 and is incorporated by reference in this Item 8.01.

Important Additional Information and Where to Find It

The Company intends to file a definitive proxy statement, accompanying proxy card and other relevant documents with the U.S. Securities and Exchange Commission (the "SEC") in connection with the solicitation of proxies for the Company's 2022 annual general meeting of shareholders. BEFORE MAKING ANY VOTING DECISION, SHAREHOLDERS OF THE COMPANY ARE URGED TO READ ALL RELEVANT DOCUMENTS FILED WITH OR FURNISHED TO THE SEC, INCLUDING THE COMPANY'S DEFINITIVE PROXY STATEMENT AND ANY AMENDMENTS AND SUPPLEMENTS THERETO, BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION. Investors and shareholders will be able to obtain a copy of the definitive proxy statement and other documents filed by the Company with the SEC free of charge from the SEC's website at [www.sec.gov](http://www.sec.gov). In addition, copies will be available at no charge by visiting the "Investors" section of the Company's website at [www.alkermes.com](http://www.alkermes.com), as soon as reasonably practicable after such materials are filed with, or furnished to, the SEC.

Certain Information Regarding Participants in the Solicitation

The Company, its directors and certain of its executive officers are considered participants in the solicitation of proxies from shareholders in respect of the Company's 2022 annual general meeting of shareholders. Information regarding the names of such participants and their respective interests in the Company by security holdings or otherwise is set forth in the Company's Form 10-K for the year ended Dec. 31, 2020, filed with the SEC on Feb. 11, 2021; the Company's Form 10-K/A for the year ended Dec. 31, 2020, filed with the SEC on Apr. 29, 2021; the Company's definitive proxy statement for the Company's 2021 annual general meeting of shareholders, filed with the SEC on May 10, 2021; the Company's Current Reports on Form 8-K filed with the SEC from time to time; and in Initial Statements of Beneficial Ownership on Form 3 or Statements of Change in Ownership on Form 4 filed with the SEC from time to time. These documents can be obtained free of charge from the sources indicated above. Additional information regarding the direct and indirect interests of these participants, by security holdings or otherwise, will also be included in the definitive proxy statement for the Company's 2022 annual general meeting of shareholders and other relevant materials to be filed with the SEC, if and when they become available.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	<a href="#">Alkermes plc corporate presentation.</a>
99.2	<a href="#">Statement issued by Alkermes plc dated January 11, 2022.</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

**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 11, 2022

By: /s/ David J. Gaffin  
David J. Gaffin  
Secretary

# Alkermes: Advancing Key Business Priorities in 2022

Richard Pops  
Chief Executive Officer

40<sup>th</sup> Annual J.P. Morgan Healthcare Conference  
January 2022



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# 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 or prospects, including expected commercial growth drivers and development opportunities, and execution against 2022 financial expectations and long-term profitability goals; the potential therapeutic and commercial value of the company’s marketed products and development candidates, including nemvaleukin alfa (“nemvaleukin”) as a cancer immunotherapy when used as monotherapy or in combination and whether delivered intravenously or subcutaneously, and its potential utility across a range of tumor types, dosing options and potential combinations with other targeted therapies; expectations regarding patent life for nemvaleukin; expectations regarding the effectiveness and potential of the company’s research and development (“R&D”) objective, approach and capabilities, including its molecule design and engineering capabilities; timelines, plans and expectations for development activities relating to the company’s development candidates, including (i) for nemvaleukin, planned and ongoing clinical studies in the ARTISTRY development program, including plans to evaluate potential dosing flexibility, and plans to pursue strategic collaborations, (ii) for ALKS 1140, plans to advance the phase 1 program, (iii) for ALKS 2680, plans to complete IND-enabling activities and prepare for initiation of a first-in-human study, and (iv) for the engineered cytokine program, plans to advance the IL-12 and IL-18 preclinical programs to key decision points; and expectations concerning commercial activities relating to the company’s products, including plans for the ongoing commercial launch of LYBALVI® and the company’s ability to leverage its existing commercial infrastructure. The company cautions that forward-looking statements are inherently uncertain. 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: whether LYBALVI will be commercialized successfully; the impacts of the ongoing COVID-19 pandemic and continued efforts to mitigate its spread on the company’s business, results of operations or financial condition; the unfavorable outcome of litigation, including so-called “Paragraph IV” litigation or other patent litigation which may lead to competition from generic drug manufacturers, or other disputes related to the company’s products or products using the company’s proprietary technologies; clinical development activities may not be completed on time or at all; the results of the company’s development activities may not be positive or predictive of real-world results, and preliminary data from ongoing studies may not be predictive of future or final data from such studies, results of future studies or real-world results; the U.S. Food and Drug Administration (“FDA”) or other regulatory authorities may not agree with the company’s regulatory approval strategies or components of the company’s marketing applications, including clinical trial designs, conduct and methodologies, manufacturing processes and facilities, or the adequacy of the data or other information included in the company’s regulatory submissions to support their requirements for approval, and may make adverse decisions regarding the company’s products; the company and its licensees may not be able to successfully commercialize their products or support growth of revenue from such 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 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 Annual Report on Form 10-K for the year ended Dec. 31, 2020 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.

**Note Regarding Trademarks:** The company and its affiliates are the owners of various U.S. federal trademark registrations (®) and other trademarks (™), including ARISTADA®, ARISTADA INITIO®, VIVITROL® and LYBALVI®. VUMERITY® is a registered trademark of Biogen MA Inc., used by Alkermes under license. 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.

# Three Strategic Priorities Grounded in Strong Culture of Responsibility

**Commercial**  
Grow commercial portfolio of proprietary products



**Development Pipeline**  
Advance pipeline of neuroscience and oncology candidates



**Profitability**  
Drive long-term profitability



Patient-focused ethos and strong commitment to corporate responsibility and governance

# 2021 Key Achievements Advanced Core Business Objectives

## Commercial Execution

- LYBALVI®: Approved and commercially launched
- ARISTADA®: Drove TRx growth that outpaced the aLAI market
- VIVITROL®: Advanced alcohol dependence strategy to drive next phase of growth



## Development Pipeline

- Initiated nemvaleukin alfa studies in mucosal melanoma and platinum-resistant ovarian cancer to support potential registration
- Initiated ALKS 1140 phase 1 FIH study
- Nominated ALKS 2680 and commenced IND-enabling activities



## Profitability

- Focused on disciplined capital allocation and optimized cost structure
- Restructured commercial organization to support launch of LYBALVI



## Patient-focused ethos and strong commitment to corporate responsibility and governance

- Supported research, education and patient advocacy programs to benefit people affected by serious mental illness, addiction or cancer
- Introduced new Diversity, Inclusion and Belonging employee resource groups
- Continued commitment to sustainability
- Continued Board of Directors refreshment efforts
  - Appointed two new independent Directors
  - Announced retirement of two longer-serving Directors
- Initiated declassification of Board of Directors

# Diversified Biopharmaceutical Company With Proven Drug Development and Commercialization Capabilities

Significant, diverse revenues with new growth opportunities

**LYBALVI**  
olanzapine and samidorphan  
5 mg/10 mg - 10 mg/10 mg - 15 mg/10 mg  
20 mg/10 mg tablets

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

**Vivitrol**  
(naltrexone for extended-release  
injectable suspension) 380 mg/vial

**VUMERITY**  
(diroximel fumarate) delayed-release  
capsules 23 mg  
Licensed to and commercialized by Biogen  
(royalty & manufacturing revenue)

Pipeline of novel development candidates designed to target significant unmet needs

## Oncology

- |                         |  |
|-------------------------|--|
| <b>Nemvaleukin Alfa</b> | <ul style="list-style-type: none"> <li>Phase 2/3</li> <li>Advanced solid tumors</li> </ul> |
| <b>IL-12</b>            | <ul style="list-style-type: none"> <li>Discovery</li> <li>Advanced solid tumors</li> </ul> |

## Neuroscience

- |                  |   |
|------------------|---|
| <b>ALKS 1140</b> | <ul style="list-style-type: none"> <li>Phase 1</li> <li>Neurodegenerative and neurologic disorders</li> </ul> |
| <b>ALKS 2680</b> | <ul style="list-style-type: none"> <li>Preclinical</li> <li>Narcolepsy</li> </ul>                             |



## Current Growth Drivers

# Commercial Growth Drivers

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**LYBALVI**<sup>®</sup>  
olanzapine and samidorphan  
5 mg/10 mg - 10 mg/10 mg - 15 mg/10 mg  
20 mg/10 mg tablets



**ARISTADA**<sup>®</sup>  
aripiprazole lauroxil  
extended-release injectable suspension  
4.41 mg 6.62 mg 8.82 mg 10.64 mg



**Vivitrol**<sup>®</sup>  
(naltrexone for extended-release  
injectable suspension) 380 mg/vial



**VUMERITY**<sup>®</sup>  
(diroximel fumarate) delayed-release  
capsules 23 mg

# LYBALVI®: Oral Treatment Option for Adults With Schizophrenia or Bipolar I Disorder



- Once-daily, oral atypical antipsychotic composed of olanzapine, an established antipsychotic agent, and samidorphan, a new chemical entity
- Commercially launched in U.S. Q4 2021
- Indicated for the treatment of:
  - Schizophrenia in adults
  - Bipolar I disorder (BD-1) in adults
    - Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate
    - Maintenance monotherapy treatment

Boxed Warning: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. LYBALVI is not approved for the treatment of patients with dementia-related psychosis. Full prescribing information may be found at [www.lybalvi.com/lybalvi-prescribing-information.pdf](http://www.lybalvi.com/lybalvi-prescribing-information.pdf)

# LYBALVI®: Offers Proven Efficacy With a Differentiated Weight Gain Profile in Adult Patients with Schizophrenia



## LYBALVI offers proven efficacy\* and was associated with less weight gain versus olanzapine in patients with schizophrenia in the ENLIGHTEN-2 clinical trial\*\*

- ENLIGHTEN-1: LYBALVI demonstrated a statistically significant improvement in the change from baseline in PANSS total score versus placebo in patients with schizophrenia at week 4<sup>†</sup>
- ENLIGHTEN-2: LYBALVI was associated with less weight gain versus olanzapine in patients with schizophrenia at week 24<sup>†</sup>

\*Inclusion of samidorphan in LYBALVI did not appear to negatively impact the efficacy of olanzapine.

\*\*Inclusion of samidorphan in LYBALVI appeared to result in less weight gain than was seen with olanzapine alone.<sup>1</sup>

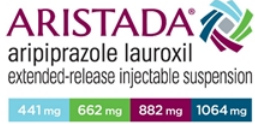
<sup>†</sup> Increased weight was the most common adverse reaction in patients treated with LYBALVI in ENLIGHTEN-1 and ENLIGHTEN-2. Other common adverse reactions were somnolence, dry mouth and headache.

**Boxed Warning:** Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. LYBALVI is not approved for the treatment of patients with dementia-related psychosis. Full prescribing information may be found at [www.lybalvi.com/lybalvi-prescribing-information.pdf](http://www.lybalvi.com/lybalvi-prescribing-information.pdf)

<sup>1</sup>Correll CU, Newcomer JW, Silverman B, et al. Effects of olanzapine combined with samidorphan on weight gain in schizophrenia: a 24-week phase 3 study. *Am J Psychiatry*. 2020. doi.org/10.1176/appi.ajp.2020.19121279.



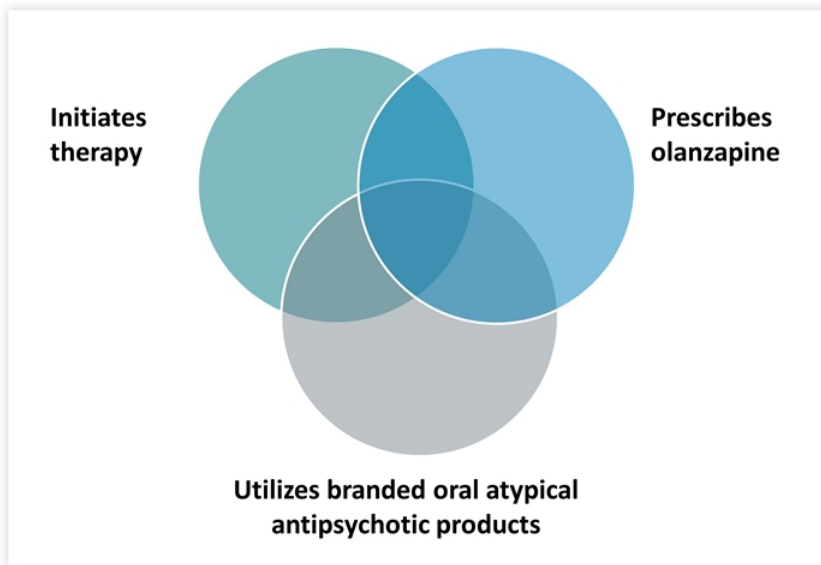
# LYBALVI®: Sophisticated Commercial Presence in Psychiatry Creates Operating & Financial Leverage



<b>Commercial Support Infrastructure</b>
<ul style="list-style-type: none"><li>• Marketing</li><li>• Managed markets</li><li>• Patient support services</li><li>• Commercial operations</li><li>• State and Federal policy efforts</li></ul>
<b>Commercial Field Organization</b>
<ul style="list-style-type: none"><li>• Psychiatry field sales organization calling on highly synergistic prescriber universe</li></ul>
<b>Hybrid Promotional Approach</b>
<ul style="list-style-type: none"><li>• Increased reach and efficiency utilizing digital channels and virtual interactions</li></ul>



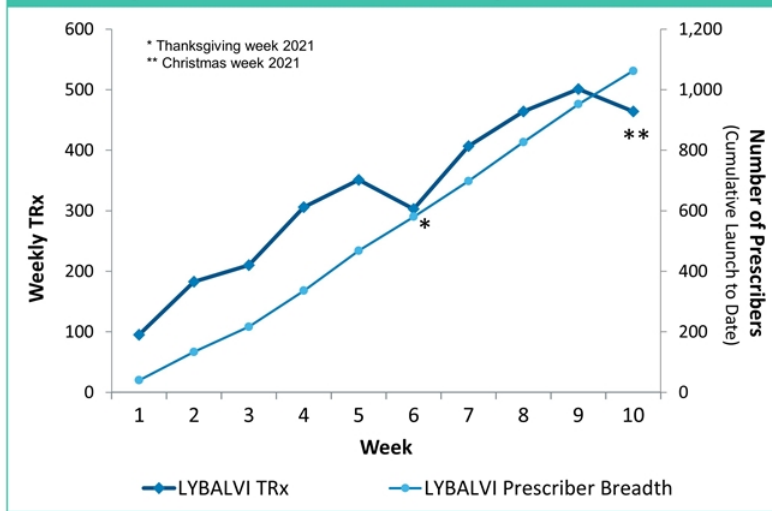
# LYBALVI®: Launch Targeting Focused on Three Prescriber Characteristics Across Schizophrenia and BD-1



Alkermes field organization calls on focused healthcare provider universe, prioritized for high-potential prescribers of branded oral antipsychotics

# LYBALVI®: Commercial Launch Off to Strong Start

Prescription and Prescriber Growth by Week Post Launch†



† Source: IQVIA NPA and IQVIA XPO

## U.S. Oral Atypical Antipsychotic Market

- ~63M oral atypical antipsychotics TRx<sup>1</sup>
  - ~15M in schizophrenia/schizoaffective<sup>2</sup>
  - ~13M in bipolar I disorder
- ~8M TRx for olanzapine<sup>1</sup>
  - 22% market share in schizophrenia
  - 12% market share in bipolar I disorder
- ~5.7M branded oral atypical antipsychotic TRx<sup>1,3</sup>

<sup>1</sup> IQVIA reported TRxs (NPA Audit Nov'21 R12M). Unlike olanzapine, LYBALVI contains an opioid antagonist and is contraindicated in persons using opioids.

<sup>2</sup> Due to data limitations, schizophrenia data includes schizoaffective disorder (for which LYBALVI is not indicated).

<sup>3</sup> Branded market includes: LATUDA®, REXULTI®, VRAYLAR®, CAPLYTA®, FANAPT®, SAPHRIS®

# Commercial Growth Drivers

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**LYBALVI**  
olanzapine and samidorphan  
5 mg/10 mg - 10 mg/10 mg - 15 mg/10 mg  
20 mg/10 mg tablets



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



**Vivitrol**  
(naltrexone for extended-release  
injectable suspension) 380 mg/vial



**VUMERITY**  
(diroximel fumarate) delayed-release  
capsules 23 mg

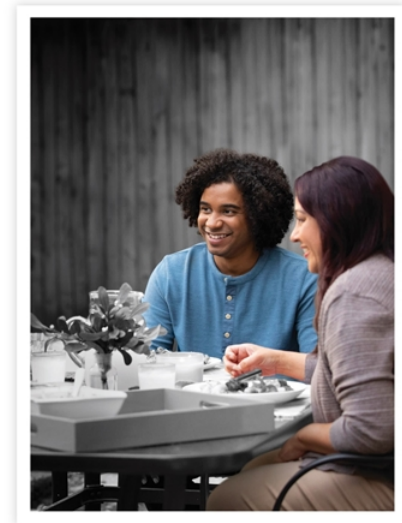
# ARISTADA®: LAI for Schizophrenia With Dosing Flexibility

- Long-acting injectable (LAI) atypical antipsychotic indicated for the treatment of schizophrenia
- Novel molecular entity designed to address the real-world needs of patients and providers
- Ability to fully dose on day one for up to two months with ARISTADA INITIO® regimen\*



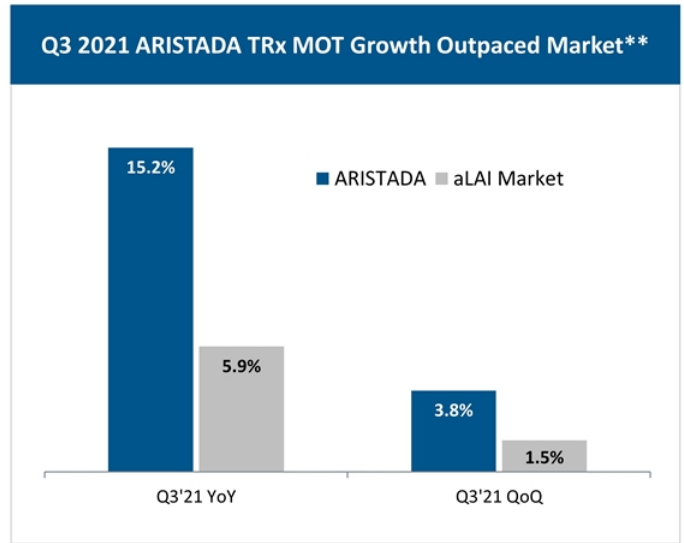
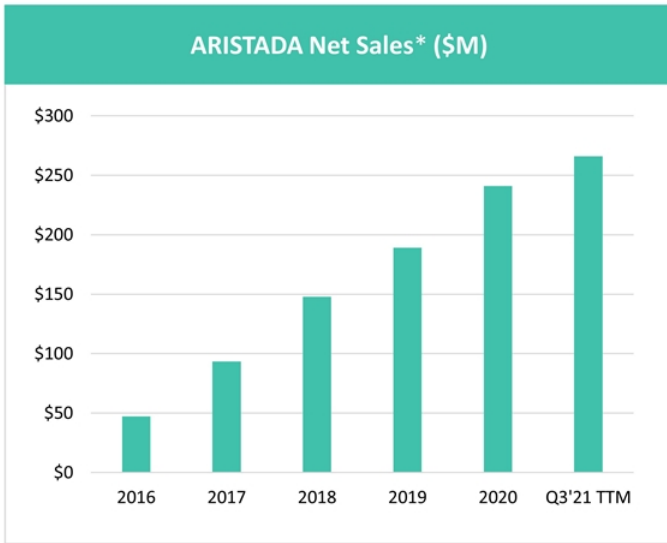
**ARISTADA**  
aripiprazole lauroxil  
extended-release injectable suspension

441 mg	662 mg	882 mg	1064 mg
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\*ARISTADA INITIO + single 30 mg oral dose of aripiprazole replaces need for concomitant three weeks of oral aripiprazole for initiation of ARISTADA. The first ARISTADA dose may be administered on the same day as ARISTADA INITIO or up to 10 days thereafter. Full prescribing information for ARISTADA, including Boxed Warning, may be found at [www.aristada.com/downloadables/ARISTADA-PI.pdf](http://www.aristada.com/downloadables/ARISTADA-PI.pdf)

# ARISTADA®: Growth has Outpaced the aLAI Market



\*Inclusive of ARISTADA INITIO®  
TTM (trailing 12 month) data include Q4'20 through Q3'21 net sales results.

\*\*TRx Data: IQVIA NPA data Q3'21; aLAI Market data inclusive of ARISTADA; MOT: Months of therapy

# Commercial Growth Drivers

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olanzapine and samidorphan  
5 mg/10 mg -10 mg/10 mg -15 mg/10 mg  
20 mg/10 mg tablets



**ARISTADA**  
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4.41 mg 6.62 mg 8.82 mg 10.64 mg



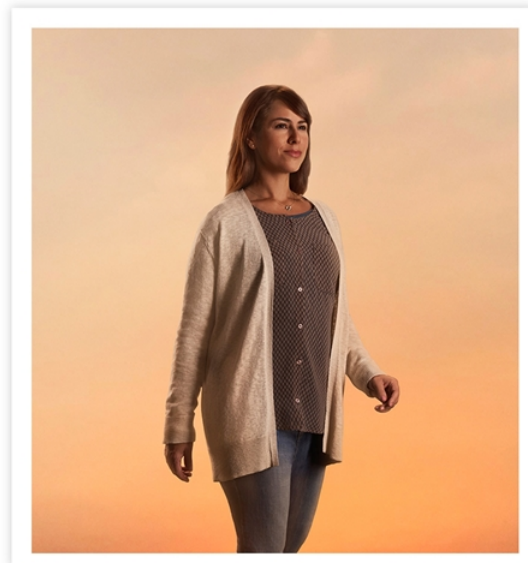
**Vivitrol**  
(naltrexone for extended-release  
injectable suspension) 380 mg/vial



**VUMERITY**  
(diroximel fumarate) delayed-release  
capsules 23 mg

# VIVITROL®: LAI for the Treatment of Opioid Dependence and Alcohol Dependence

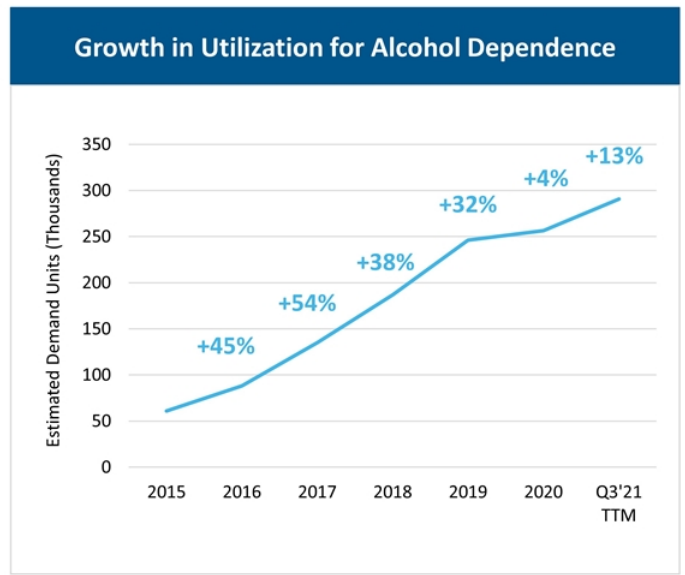
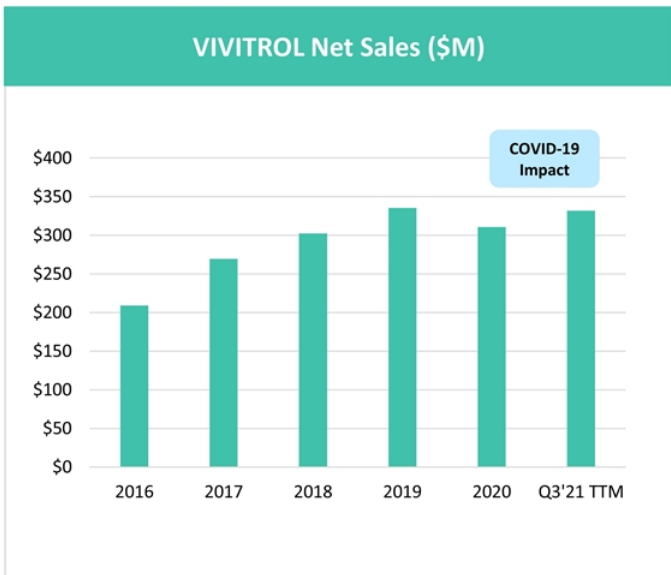
- Extended-release opioid antagonist provides therapeutic levels of naltrexone for a one-month period
- Indicated for the treatment of alcohol dependence (AD) in patients able to abstain from alcohol in an outpatient setting prior to initiation of treatment with VIVITROL
- Indicated for the prevention of relapse to opioid dependence (OD), following opioid detoxification



Full prescribing information for VIVITROL may be found at [www.vivitrol.com/content/pdfs/prescribing-information.pdf](http://www.vivitrol.com/content/pdfs/prescribing-information.pdf). Treatment with VIVITROL should be part of a comprehensive management program that includes psychosocial support.



# VIVITROL®: Sales Fueled Increasingly by Alcohol Dependence Indication



TTM (trailing 12 month) data include Q4'20 through Q3'21 VIVITROL net sales results.

# Commercial Growth Drivers

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**LYBALVI**  
olanzapine and samidorphan  
5 mg/10 mg -10 mg/10 mg -15 mg/10 mg  
20 mg/10 mg tablets



**ARISTADA**  
aripiprazole lauroxil  
extended-release injectable suspension  
4.41 mg 6.62 mg 8.82 mg 10.64 mg



**Vivitrol**  
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injectable suspension) 380 mg/vial



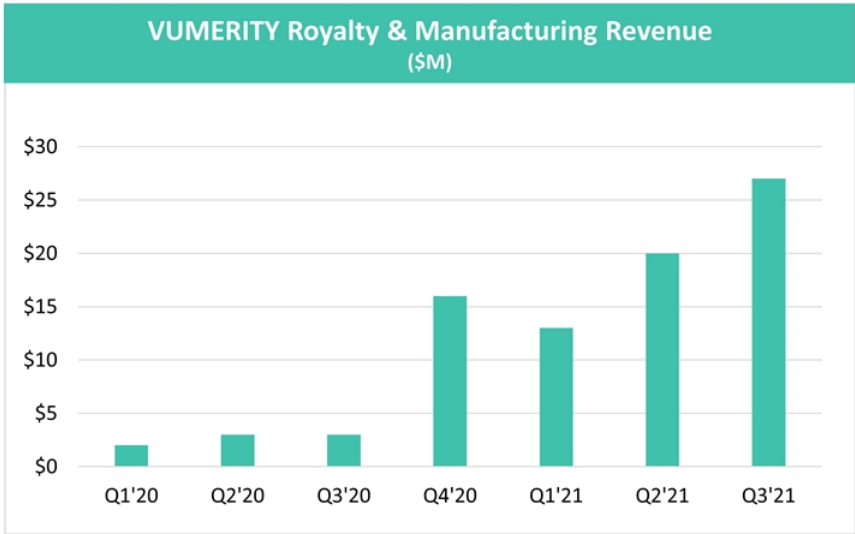
**VUMERITY**  
(diroximel fumarate) delayed-release  
capsules 25 mg

# VUMERITY® (Diroximel Fumarate) for Multiple Sclerosis (MS)

- Novel oral fumarate for the treatment of relapsing forms of multiple sclerosis
- Discovered and developed by Alkermes
- Composition of matter patent extends into 2033



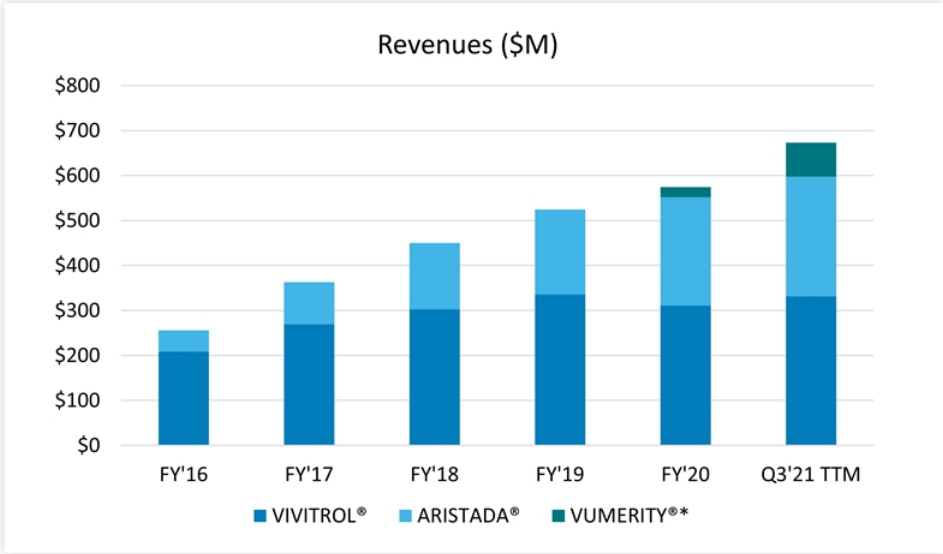
# VUMERITY® Offers Long-Term Revenue Growth Opportunity



- Novel oral fumarate for the treatment of relapsing forms of multiple sclerosis (MS)
  - Approved in U.S. Q4 2019
- Biogen holds exclusive, worldwide license to commercialize
  - **15%** royalty to Alkermes on worldwide net sales
- ~\$7B oral U.S. MS market\*
- Multiple recent regulatory approvals in Europe


\*IQVIA NPA data as of Nov 2021 TTM (trailing 12 month)

# Topline Growth and Diversification Reflect Evolving Business



- Key product revenues drove 21% 5-year CAGR
- Commercial launch of LYBALVI® in Q4 2021 provides additional revenue stream

TTM (trailing 12 month) data include Q4'20 through Q3'21 net sales results.  
\*Licensed product (royalty & manufacturing revenue)



Innovation Focused on Unmet Patient Need  
in Neuroscience and Oncology

# R&D Objective: Novel Drug Development With Differentiated and Disciplined Approach

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Employ integrated approach to target selection, development and lifecycle management with **continuous evaluation of potential medical and economic value**

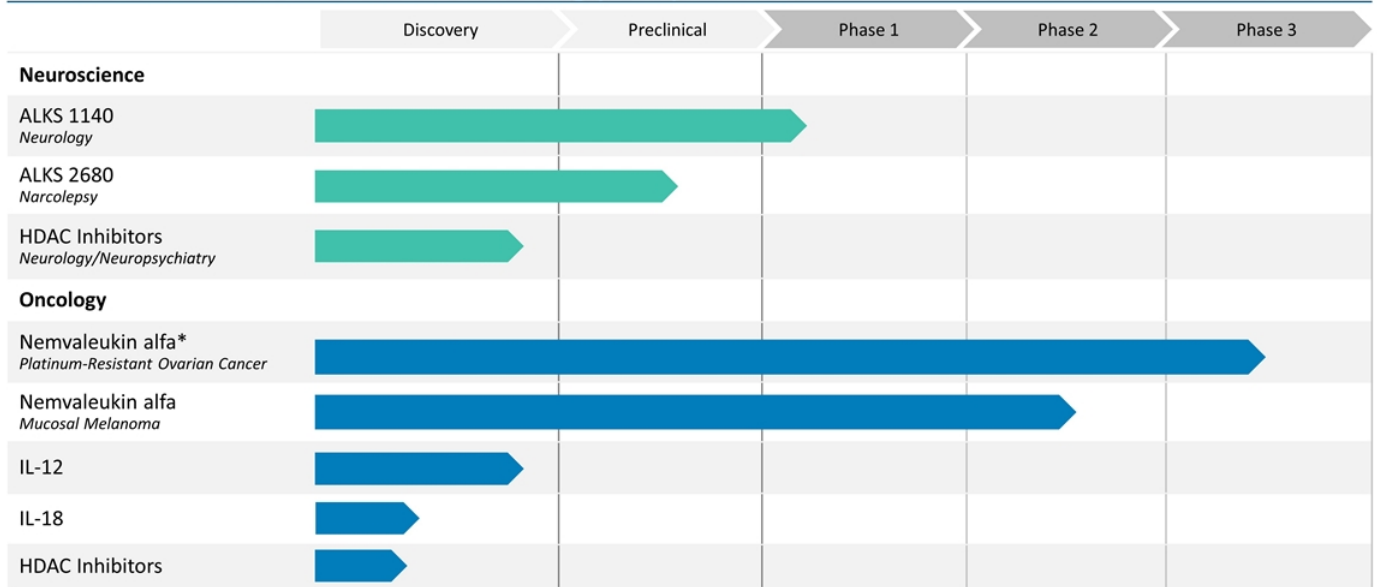


**Leverage advanced medicinal chemistry and protein engineering capabilities** to develop novel molecular entities with strong intellectual property protection



**De-risk programs** early by accelerating time to data and decision milestones and adhering to clear go/no-go criteria

# Neuroscience and Oncology Pipeline



\*In combination with pembrolizumab



# Nemvaleukin Alfa: Accumulating Data Support Critical Design Criteria

Design

Inherently active, stable fusion protein

PD Profile

Dose-dependent expansion of NK and CD8+ T cells, with minimal effects on T<sub>regs</sub>

Clinical Benefit

Anti-tumor activity observed both as a single agent and with checkpoint inhibitors (CPI);  
Anti-tumor activity observed in CPI-unapproved tumor types and post-CPI settings

Dosing Flexibility

Multiple potential routes of administration and dosing schedules being investigated in the clinic

Strategy

Clinical strategy focused on difficult-to-treat cancers with clear unmet need;  
FDA Fast Track Designation granted in mucosal melanoma\* and platinum-resistant ovarian cancer\*\*

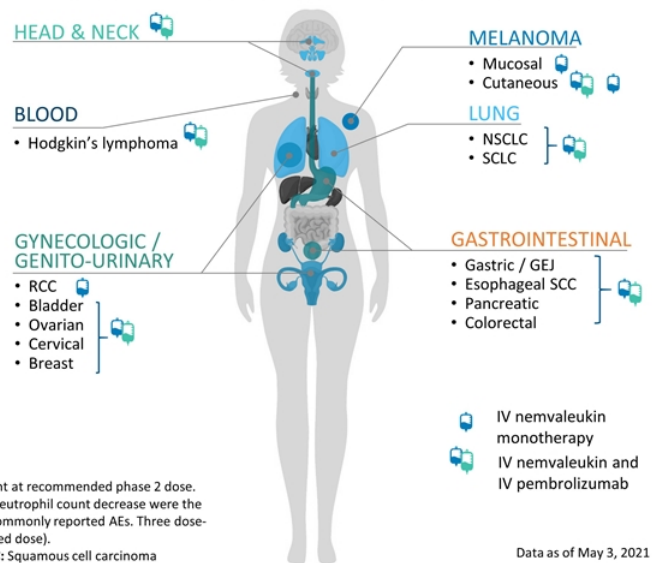
\* Also granted FDA Orphan Drug Designation; \*\*In combination with pembrolizumab

T<sub>reg</sub>: Regulatory T cell; NK cell: Natural killer cell

# Nemvaleukin: Durable and Deepening Responses Observed

- Demonstrated **durable and deepening responses** in high unmet need populations
  - **Monotherapy activity** (IV) in prior anti-PD-(L)1 treated melanoma and renal cell carcinoma
  - **Combination activity** (IV) with pembrolizumab in a range of tumor types
- Designed to avoid hallmark toxicities of high-dose IL-2
  - Treatment-related adverse events (AEs) in ARTISTRY-1 and ARTISTRY-2 have been consistent with expectations based on nemvaleukin's mechanism of action and were mostly transient and manageable\*\*

## Monotherapy and Combination Responses\*



IV: Intravenous; SC: Subcutaneous

\*Includes one response from ARTISTRY-2 study evaluating SC nemvaleukin. ARTISTRY-2 expansion cohorts open for enrollment at recommended phase 2 dose.

\*\*ARTISTRY-1: Pyrexia, chills and nausea were the most commonly reported AEs. Transient and asymptomatic neutropenia/neutrophil count decrease were the most commonly reported events of grade  $\geq 3$ ; ARTISTRY-2: Pyrexia, fatigue, chills and injection site reactions were the most commonly reported AEs. Three dose-limiting toxicities were reported, all in the highest doses evaluated in each dosing regimen (declared as the maximum tolerated dose).

NSCLC: Non-small cell lung cancer; SCLC: Small cell lung cancer; RCC: Renal cell carcinoma; GEJ: Esophagogastric junction; SCC: Squamous cell carcinoma

# Nemvaleukin: Evaluating Multiple Potential Dosing Options to Provide Flexibility and Support Broader Clinical Utility

## Daily IV x5

- Achieved proof-of-concept
- Demonstrated anti-tumor activity as monotherapy and in combination with pembrolizumab in a range of tumor types
- Established safety and tolerability profile
- Advanced into potential registrational studies for difficult-to-treat tumor types with high unmet need



## Less frequent IV dosing

- Extensive PK/PD modeling supports evaluation of once every three-week and twice every three-week dosing intervals
- Advancement into clinic expected Q1'22











## Subcutaneous once-weekly dosing

- Initial PK/PD, safety and tolerability profile observed
- Identified recommended phase 2 dose
- Evaluating anti-tumor activity



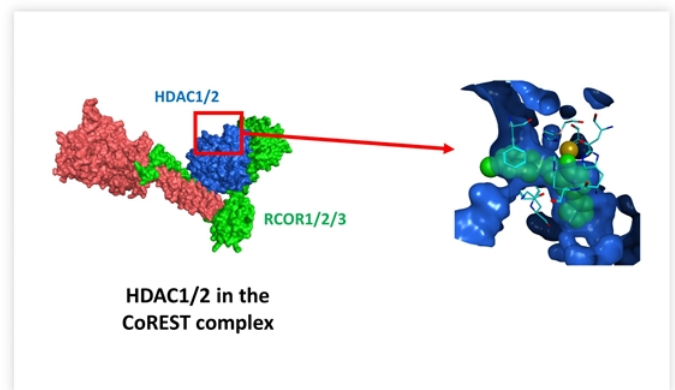
# Nemvaleukin: Focused Clinical Program in 2022

<p><b>Potential Registration Supporting</b></p>	<p><b>ARTISTRY-6</b> </p> <p>Evaluating efficacy, safety and tolerability as monotherapy</p> <p><b>Tumor Type:</b> Advanced cutaneous and mucosal melanoma: previously treated with checkpoint inhibitor</p> <p><i>FDA granted nemvaleukin both Orphan Drug Designation and Fast Track Designation for treatment of mucosal melanoma.</i></p>	<p><b>ARTISTRY-7</b> </p> <p>Evaluating efficacy, safety and tolerability; as monotherapy and in combination with pembrolizumab, compared to investigator choice chemotherapy</p> <p><b>Tumor Type:</b> Platinum-resistant ovarian cancer</p> <p><i>FDA granted nemvaleukin in combination with pembrolizumab Fast Track Designation for treatment of platinum-resistant ovarian cancer</i></p>	<p><b>Administration:</b></p> <ul style="list-style-type: none"> <li> Subcutaneous injection</li> <li> Intravenous infusion</li> </ul>
<p><b>Dose Options</b></p>	<p><b>ARTISTRY-2</b> </p> <p>Evaluating safety, SC RP2D, and ORR; as monotherapy and in combination with pembrolizumab</p> <p><b>Tumor Type:</b> Advanced solid tumors that have progressed after at least one line of treatment</p>	<p><b>ARTISTRY-3</b> </p> <p>Evaluating efficacy, safety and tolerability of less frequent IV dosing and PK/PD in TME, as monotherapy and in combination with pembrolizumab</p> <p><b>Tumor Type:</b> Advanced solid tumors that progressed after treatment or intolerant to at least one established, indication-specific therapy</p>	<p>In collaboration with MSD. Partnership with the GOG Foundation and ENGOT to conduct the study</p>
<p><b>Potential Strategic Collaboration</b></p>	<p><b>Next phase of development</b></p> <p>Scientific rationale for combinations with multiple targeted treatment approaches</p> <p><b>Tumor Type:</b> Opportunity to enable broad utility across a number of solid tumor types</p>		<p><b>Region:</b></p> <ul style="list-style-type: none"> <li> Global</li> <li> USA</li> </ul>

IV: Intravenous; SC: Subcutaneous; RP2D: Recommended phase 2 dose; ORR: Overall response rate; TME: Tumor microenvironment; MSD: A tradename of Merck & Co., Inc. Kenilworth, NJ, USA

# ALKS 1140: Novel CoREST-Selective HDAC Inhibitor Candidate

- HDAC inhibitors increase accessibility of DNA for transcription of genes associated with synaptogenesis
- Many neurological disorders are characterized by synaptic pathology
- Targeting the synapse may slow progression and preserve cognitive and functional abilities in a range of diseases
- ALKS 1140 selectively targets HDAC1/2 bound in the CoREST complex, which is directly involved in repression of prosynaptic genes
- ALKS 1140 increased dendritic spines and synapses; improved synaptic function in areas associated with memory and cognition in preclinical models



Fuller et al. *ACS Chem. Neurosci.* 2019;10(3):1729-1743

CoREST: Co-repressor of repressor element-1 silencing transcription factor; HDAC: Histone deacetylase

# ALKS 1140: First-in-Human Study Underway and Clinical Strategy Focused on Early Validation of Biology

- ALKS 1140 clinical development program includes early evaluation of prosynaptic mechanism of action
- First-in-human (FIH), single-ascending dose study underway
- Phase 0 biomarker research underway and intended to inform indication priorities and biomarker strategy for future clinical development

## Phase 1 Biomarkers Assess Target Engagement and Pharmacodynamic (PD) Response

- **Assess target engagement:** histone acetylation in PBMCs
- **Assess PD response:**
  - Synaptic proteins (e.g., neurogranin) in blood and CSF
  - Synaptic density and structure in brain: SV2A PET and microstructural MRI
  - Functional synaptic biomarkers, such as qEEG endpoints, associated with cognition

## Phase 0 Biomarker Research Objective

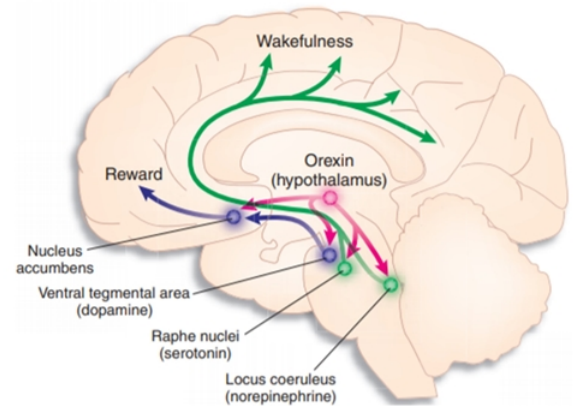
Characterize synaptopathy in patients using fluid, neuroimaging and electrophysiological biomarkers to prioritize indications based on robust, measurable changes in synaptic integrity, density and function

**PBMCs:** Peripheral blood mononuclear cells; **CSF:** Cerebrospinal fluid;  
**PET:** Positron emission tomography; **qEEG:** Quantitative electroencephalogram

# Leveraging Alkermes' Molecular Design Capabilities to Target Orexin Dysfunction in Narcolepsy

- In narcolepsy and other sleep disorders, low orexin levels lead to inconsistent neurotransmitter release, resulting in sleep lapses and poor regulation of REM sleep
- Narcolepsy affects ~200,000 people in U.S. and 3M people globally<sup>1</sup>
- 70% of people with narcolepsy have narcolepsy type 1<sup>2</sup>, distinguished by:
  - Cataplexy, a sudden muscle weakness triggered by strong emotions
  - Low or no orexin in the brain
- Orexin 2 receptor agonists may have utility as replacement therapy by stimulating downstream release of wake-promoting neurotransmitters

## Orexin neurons promote wakefulness and modulate reward pathways



<sup>1</sup> Global Narcolepsy Drugs Market, Forecast 2019-2025. Allied Market Research

<sup>2</sup> Swick TJ. Treatment paradigms for cataplexy in narcolepsy: past, present, and future. *Nat Sci Sleep*. 2015;7:159-169

Figure from: Scammell, T E, and Saper, C B. *Nature medicine*. 2007;13:126-8



# ALKS 2680: Orexin 2 Receptor Agonist

ALKS 2680 molecular design objectives for optimization of PK/PD relationship:

- Mimic potency and performance of endogenous peptide OX2R agonist
  - Increased wakefulness duration
  - Improved cataplexy control
- Provide convenient dosing
  - Once-daily, oral medication
  - Dose to allow for 8-12 hours wakefulness with no later insomnia
- Demonstrate favorable tolerability
  - Reduced risk of heart rate and blood pressure effects than seen with stimulants

IND-enabling activities underway with potential to initiate first-in-human study by year-end 2022

PK: pharmacokinetic; PD: pharmacodynamic

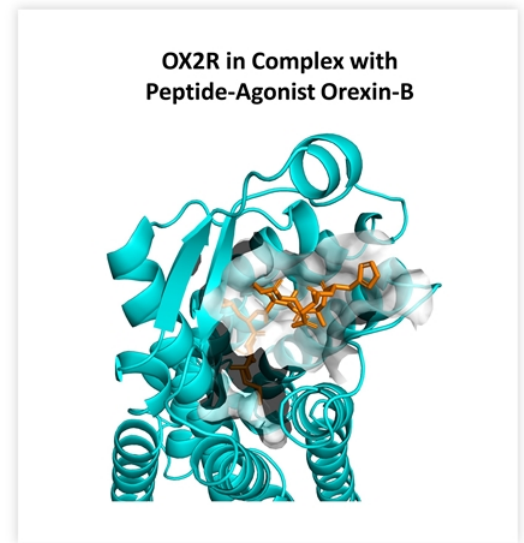


Figure adapted from: Hong, Chuan, et al. *Nature communications*. 2021:12; 3. PDB ID: 7L1U



## Looking Ahead: 2022 Strategic Priorities

### Commercial Portfolio

- Execute successful LYBALVI® launch and continue to establish payer access profile
- Drive growth of VIVITROL® in AD and increase ARISTADA® share of aLAI market

### Nemvaleukin

- Advance enrollment of ARTISTRY-6 & ARTISTRY-7
- Execute clinical evaluation of subcutaneous and less frequent IV dosing
- Pursue strategic collaborations to expand development program

### Early-stage Pipeline

- ALKS 1140: Advance phase 1 program
- ALKS 2680: Complete IND-enabling activities and prepare for initiation of FIH study
- Engineered cytokines: Advance IL-12 and IL-18 preclinical programs to key decision points

### Financial

- Provide and execute against 2022 financial expectations and long-term profitability goals

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



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**Alkermes' Statement Regarding Notice of Director Nominations from Sarissa**

Alkermes plc (Nasdaq: ALKS) confirmed that affiliates of Sarissa Capital Management ("Sarissa") submitted a notice of its intention to nominate two director candidates for election to the company's Board of Directors (the "Board") at the company's 2022 Annual General Meeting of Shareholders. The company issued the following statement regarding Sarissa's notice:

Alkermes is committed to creating value for its shareholders and values their feedback. We have had constructive discussions with Sarissa and will continue to engage with them, along with our other shareholders.

Over the past three years, our Board has appointed six new, independent and highly qualified directors, including a director designated by Sarissa in November 2021, a director designated by Elliott Investment Management L.P. (together with its affiliates, "Elliott") in May 2021, and two directors appointed with the support of Elliott in December 2020. In addition, three of our longer-serving directors retired from the Board during this time period, and the company has initiated the declassification of our Board.

Shareholders are not required to take any action at this time. The Board will carefully evaluate Sarissa's nominees and present its recommendations regarding all director nominees for election at the company's 2022 Annual General Meeting of Shareholders in the company's definitive proxy statement to be filed with the U.S. Securities and Exchange Commission (the "SEC"). The company's 2022 Annual General Meeting of Shareholders has not yet been scheduled.

**About Alkermes**

Alkermes plc is a fully-integrated, global biopharmaceutical company developing innovative medicines in the fields of neuroscience and oncology. The company has a portfolio of proprietary commercial products focused on addiction, schizophrenia and bipolar I disorder, and a pipeline of product candidates in development for neurodegenerative disorders and cancer. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, Ohio. For more information, please visit Alkermes' website at [www.alkermes.com](http://www.alkermes.com).

**Note Regarding Forward-Looking Statements**

Certain statements set forth in this press release 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 engagement with Sarissa and other shareholders of the company; future actions that may be taken by Sarissa in connection with the company's 2022 Annual General Meeting of Shareholders; and the company's commitment to creating value for its shareholders. The company cautions that forward-looking statements are inherently uncertain. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to various risks and uncertainties, including, among others, the company's ability to create value for its shareholders and to continue to engage with Sarissa and other shareholders; and those risks and uncertainties described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2020 and in subsequent filings made by the company with the SEC, which are available on the SEC's website at [www.sec.gov](http://www.sec.gov). 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 press release.

**Important Additional Information and Where to Find It**

The company intends to file a definitive proxy statement, accompanying proxy card and other relevant documents with the SEC in connection with the solicitation of proxies for the company's 2022 Annual General Meeting of Shareholders. BEFORE MAKING ANY VOTING DECISION, SHAREHOLDERS OF THE COMPANY ARE URGED TO READ ALL RELEVANT DOCUMENTS FILED WITH OR FURNISHED TO THE SEC, INCLUDING THE COMPANY'S DEFINITIVE PROXY STATEMENT AND ANY AMENDMENTS AND SUPPLEMENTS THERETO, BECAUSE THEY WILL CONTAIN

IMPORTANT INFORMATION. Investors and shareholders will be able to obtain a copy of the definitive proxy statement and other documents filed by the company with the SEC free of charge from the SEC's website at [www.sec.gov](http://www.sec.gov). In addition, copies will be available at no charge by visiting the "Investors" section of the company's website at [www.alkermes.com](http://www.alkermes.com), as soon as reasonably practicable after such materials are filed with, or furnished to, the SEC.

**Certain Information Regarding Participants in the Solicitation**

The company, its directors and certain of its executive officers are considered participants in the solicitation of proxies from shareholders in respect of the company's 2022 Annual General Meeting of Shareholders. Information regarding the names of such participants and their respective interests in the company by security holdings or otherwise is set forth in the company's Form 10-K for the year ended Dec. 31, 2020, filed with the SEC on Feb. 11, 2021; the company's Form 10-K/A for the year ended Dec. 31, 2020, filed with the SEC on Apr. 29, 2021; the company's definitive proxy statement for the company's 2021 Annual General Meeting of Shareholders, filed with the SEC on May 10, 2021; the company's Current Reports on Form 8-K filed with the SEC from time to time; and in Initial Statements of Beneficial Ownership on Form 3 or Statements of Change in Ownership on Form 4 filed with the SEC from time to time. These documents can be obtained free of charge from the sources indicated above. Additional information regarding the direct and indirect interests of these participants, by security holdings or otherwise, will also be included in the definitive proxy statement for the company's 2022 Annual General Meeting of Shareholders and other relevant materials to be filed with the SEC, if and when they become available.