Shaping the Future of the Business

Richard Pops
Chief Executive Officer

38th Annual J.P. Morgan Healthcare Conference

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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 mission of advancing patient-centered care and redefining what constitutes 'successful treatment'; the company's evolving research and development capabilities and focus, including the therapeutic areas that the company may pursue; the company's expectations with respect to its current and future financial and operating performance, business plans or prospects, including expectations relating to potential expansion of the company's product portfolio, continued growth of revenue from the company's commercial products, new potential elements of revenue, including royalty and manufacturing revenues for VUMERITY® and potential revenue from ALKS 3831 if approved, and the company's potential to deliver profitability; the real-world impact and potential therapeutic and commercial value of the company's marketed and development products; timelines, plans and expectations for development activities relating to the company's products and product development candidates in both central nervous system ("CNS") disorders and oncology, including ongoing enrollment and other progress across the ARTISTRY clinical development program for ALKS 4230 and emerging data from such program, and lead optimization and/or IND-enabling activities for the company's preclinical compounds, including the company's HDAC inhibitor platform and the company's IL-10 fusion protein platform; the company's expectations relating to regulatory actions by the U.S. Food and Drug Administration ("FDA") relating to the company's new drug application ("NDA") submission for ALKS 3831, including the adequacy of the data contained in the NDA to serve as the basis of approval of ALKS 3831 for both the treatment of schizophrenia and the treatment of bipolar I disorder; the company's growing commercial infrastructure and expectations concerning commercial activities relating to the company's products and product candidates, including preparations for the potential commercial launch of ALKS 3831; and the company's expectations regarding the duration of patent protection for VUMERITY. 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Alkermes' Distinctive Mission and Impact

Through our advocacy, we advance patient-centered care and seek to redefine what constitutes successful treatment.

Our science and medicines are making a real-world impact in the treatment of serious diseases.

Actively Shaping the Future of the Business

Expanding and driving growth of our **product portfolio**

Advancing a **diversified CNS and oncology pipeline**

Positioning the business to deliver **long-term growth** and profitability

Expanding and Driving Growth of Our Product Portfolio

Proprietary Commercial Products for Addiction and Schizophrenia

- Extended-release opioid antagonist provides therapeutic levels of naltrexone for a one-month period
- Only medication indicated for the prevention of relapse to opioid dependence, following opioid detoxification; Indicated for the treatment of alcohol dependence

Vivitrol®
(naltrexone for extended-release injectable suspension)

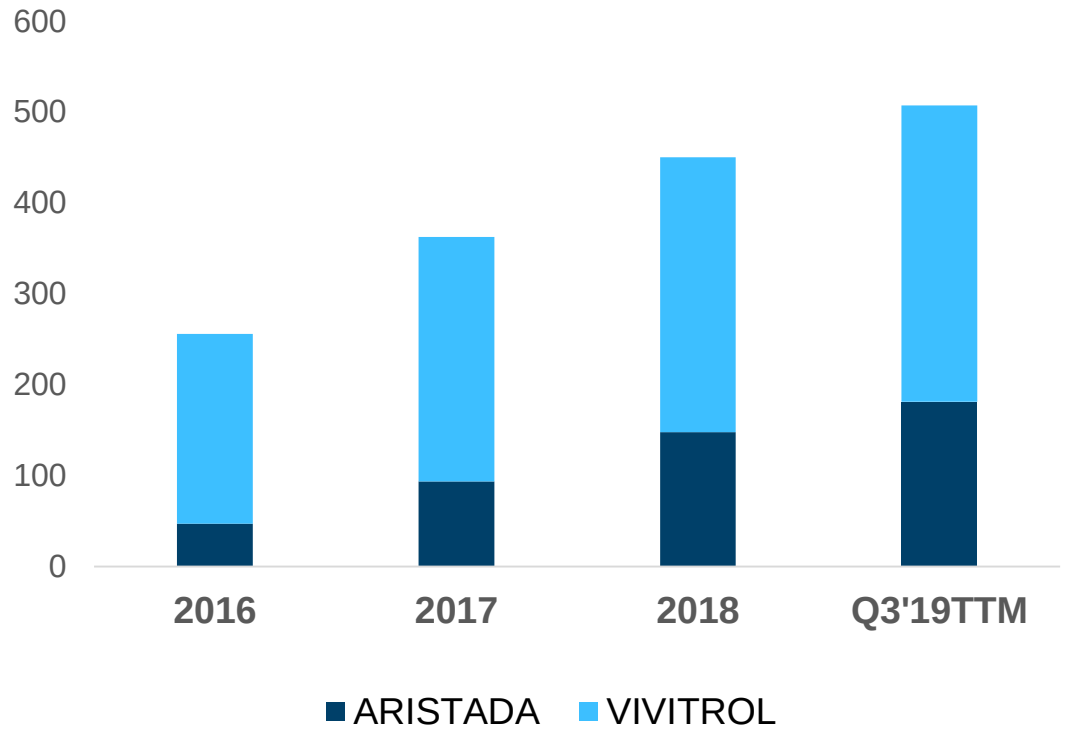
- Long-acting injectable (LAI) atypical antipsychotic indicated for the treatment of schizophrenia
- First and only LAI with ability to fully dose on day one* for up to two months with ARISTADA INITIO® regimen

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

*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.

$1 Billion Topline Commercial Enterprise Driven by Growth of Proprietary Products

Proprietary Product Net Sales *($M)*



2019

- Growing proprietary commercial products
  - **VIVITROL®**
  - **ARISTADA®**
- Financial foundation of license, royalty and manufacturing revenues

New potential revenue elements:

2020

- Royalty and manufacturing: **VUMERITY®**

2021

- Proprietary psychiatry portfolio: Potential launch of **ALKS 3831** (pending FDA approval)

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

- Novel oral fumarate with a distinct chemical structure for the treatment of relapsing forms of MS
- Discovered and developed by Alkermes
- Approved by FDA in October 2019
- Exclusive, worldwide license to commercialize held by Biogen
  - Launched by Biogen in late Q4 2019
- Composition of matter patent extends into 2033

Now Approved

~325K patients treated for multiple sclerosis in the U.S. (~75% RRMS*)[1]

- 15K MS patients new to therapy each year
- 60K MS patients change therapy each year

*RRMS: Relapsing Remitting Multiple Sclerosis

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

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

- Investigational antipsychotic designed to offer robust efficacy of olanzapine; addition of samidorphan intended to mitigate olanzapine-associated weight gain
- Single NDA for treatment of adults with schizophrenia and adults with bipolar I disorder submitted Nov. 2019
  - Conducted pre-NDA meeting to discuss contents of NDA and FDA requirements
- Fixed-dose combination
  - Bilayer tablet of samidorphan (10 mg) and olanzapine (5 mg, 10 mg, 15 mg, or 20 mg)

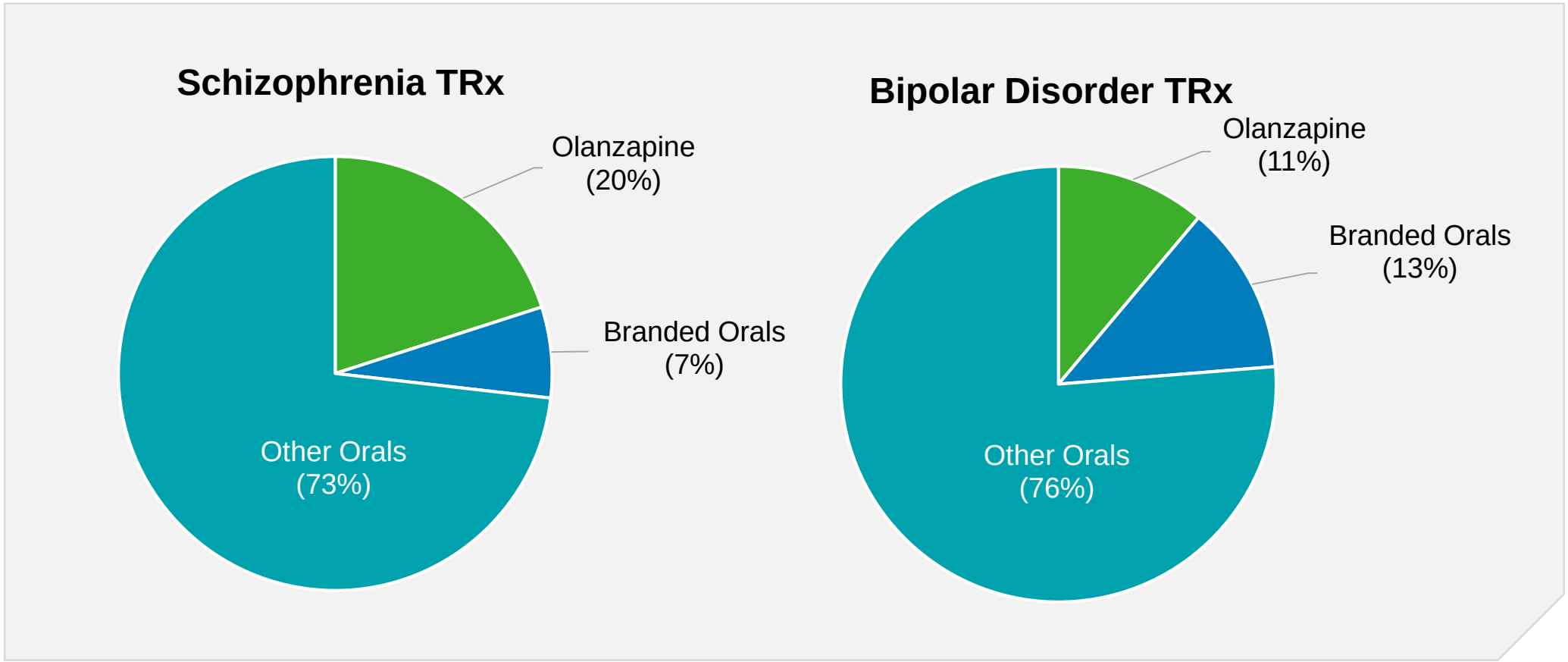
ALKS 3831 Launch Preparations

Disease State Awareness

Payer Engagement

Building on existing commercial infrastructure and capabilities in schizophrenia

Olanzapine: Atypical Antipsychotic Treatment Driven by Efficacy



Source: IQVIA R12M as of Nov. 2019
Branded orals include: LATUDA®, REXULTI®, VRAYLAR®, SAPHRIS®, FANAPT®

Advancing a Diversified Pipeline

CNS and Oncology

Alkermes

Alkermes' Evolving Research and Development Capabilities

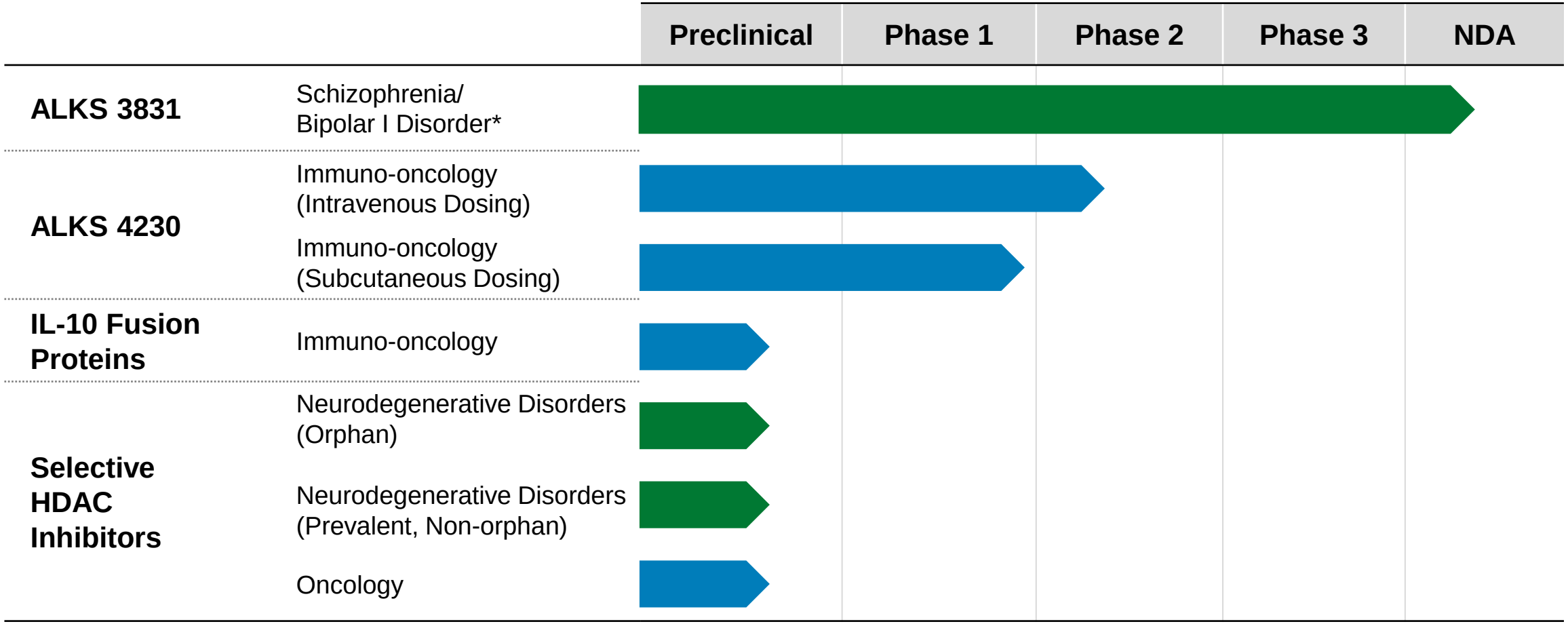
	2000s	2010s	2020
R&D Focus	Formulation & Drug Delivery	New Molecular Entities	New Biology in CNS & Oncology
Capabilities	Modifying Existing Small Molecules, Proteins, Peptides	Prodrug & NCE Chemistry, Cytokine Engineering	Small Molecule Chemistry, Protein Fusion
Approved Medicines, Drug Candidates & Therapeutic Areas	LAI Atypical Antipsychotics VIVITROL® BYDUREON®	ARISTADA® VUMERITY® ALKS 3831 ALKS 4230	Psychiatry Neurodegeneration Oncology

Building Fully-Integrated Capabilities Across CNS and Oncology

	CNS	Oncology
Research & Discovery	✓	✓
Formulation & CMC	✓	✓
Clinical Trial Operations	✓	✓
Regulatory Affairs	✓	✓
Medical Affairs	✓	✓
Commercial	✓	
Patient Engagement	✓	✓

- Expanding ex-U.S. trial network
- Evaluating strategic development and commercial partnerships

Research and Development Pipeline: Novel Molecules in High-Potential Therapeutic Areas



*NDA submitted to FDA in Nov. 2019

Advancing a Diversified Pipeline

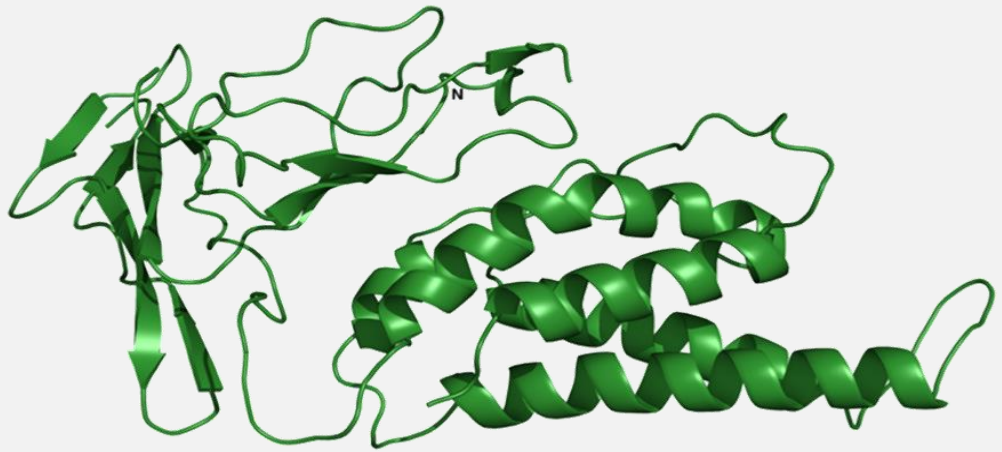
Cytokine Platform

Alkermes

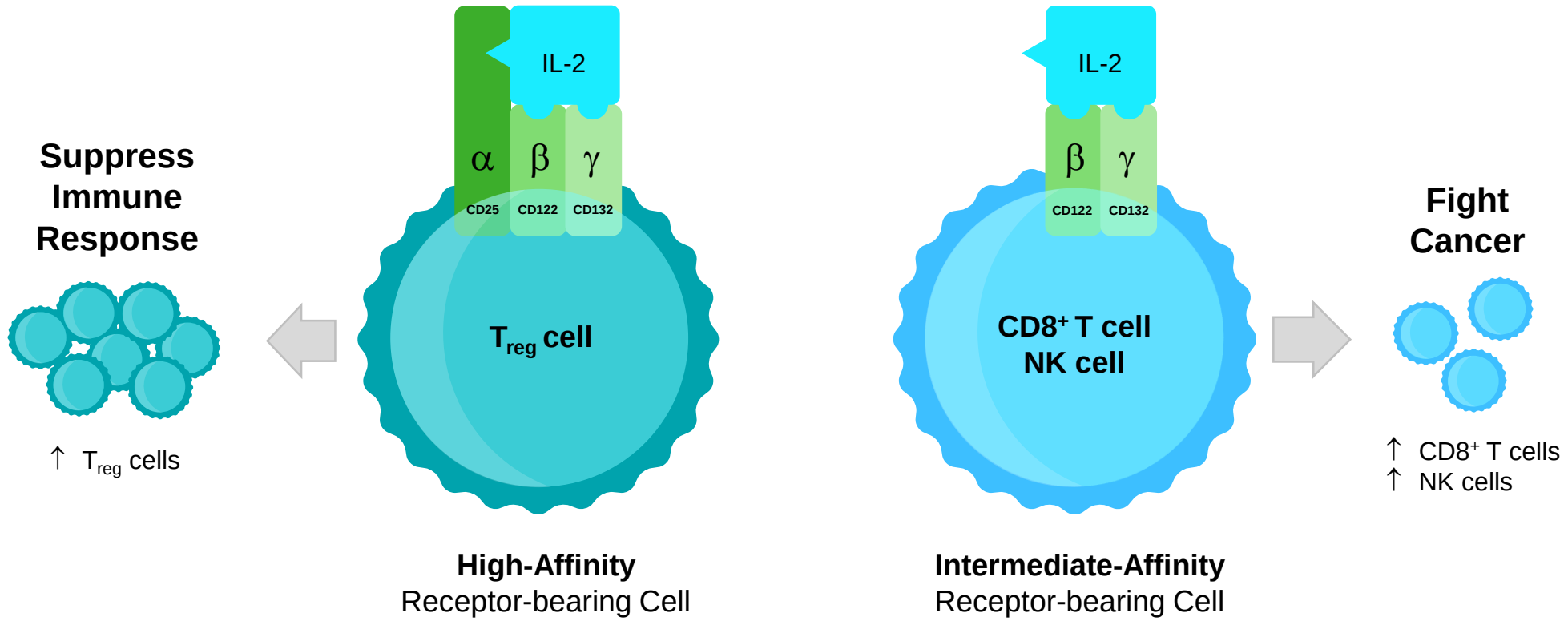
ALKS 4230: Selective IL-2 Fusion Protein

- Novel investigational drug designed to leverage proven anti-tumor effects of interleukin-2 (IL-2) pathway
- Stable, single polypeptide designed to selectively bind to intermediate-affinity IL-2 receptor and expand tumor-killing $CD8^+$ and Natural Killer (NK) T cells, and have negligible effects on T_{reg} expansion
- ARTISTRY-1 and ARTISTRY-2 phase 1/2 studies ongoing
- Data presented at Society of Immunotherapy of Cancer meeting in Nov. 2019

ALKS 4230



IL-2 Activates and Expands Immune Suppressive Regulatory T Cells That Dampen Anti-Cancer Immune Responses

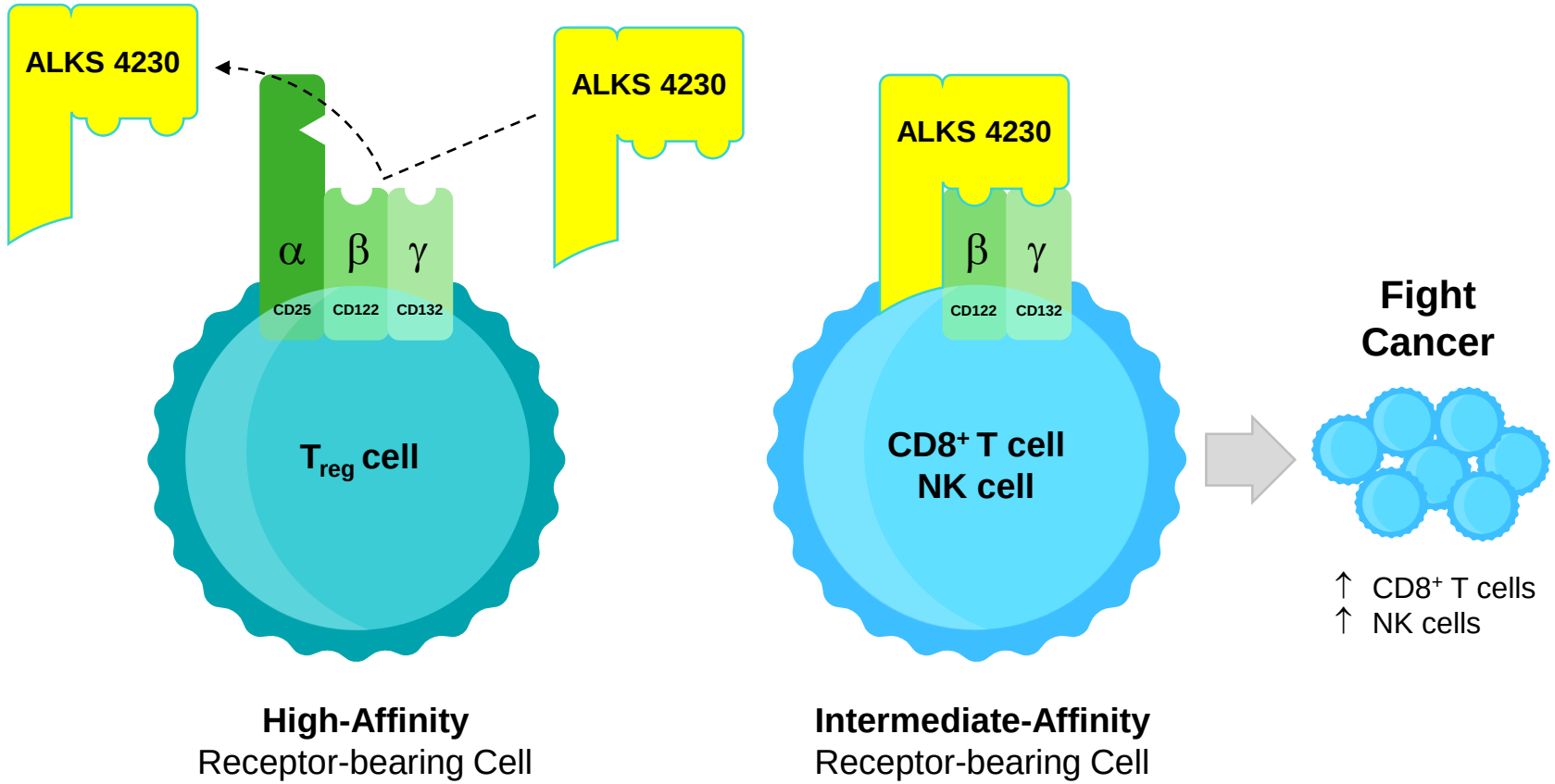


Graphics for illustrative purposes only.

ALKS 4230 Designed to Selectively Activate Intermediate-Affinity Receptor

ALKS 4230
Design Intention:

- Preferentially expand cancer-fighting CD8⁺ T cells and NK cells to potentially improve anti-tumor efficacy
- Prevent IL-2-derived expansion of T_{reg} cells to minimize inhibition of immune response
- Mitigate certain side effects of IL-2, including vascular leak syndrome



Graphics for illustrative purposes only.

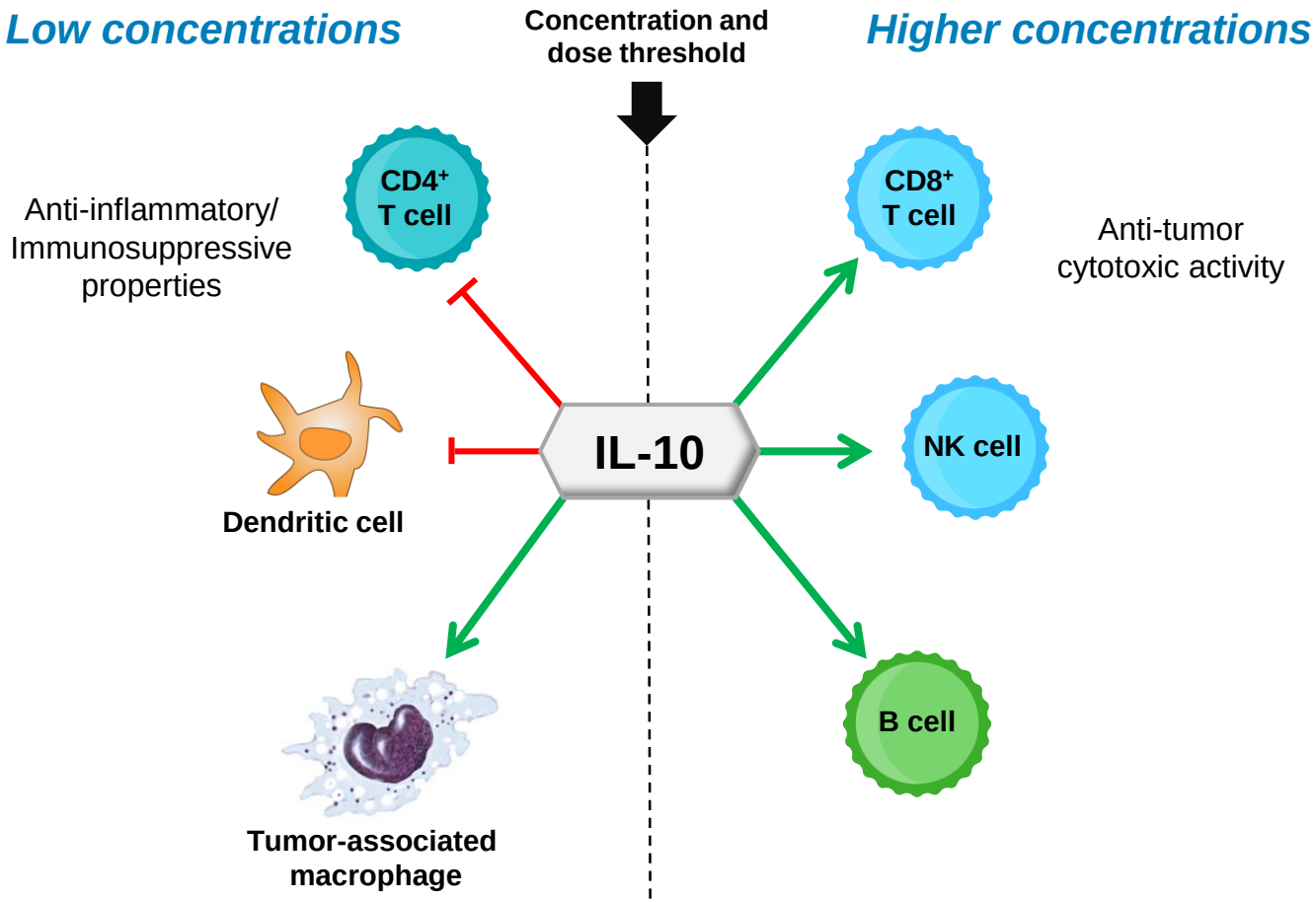
Overview of ALKS 4230 Clinical Development Program

ARTISTRY-1 Phase 1/2	**Intravenous dosing** *Refractory advanced solid tumors*	• Part A: Monotherapy dose escalation • Part B: Monotherapy dose expansion • Part C: ALKS 4230 + pembrolizumab combination
ARTISTRY-2 Phase 1/2	**Subcutaneous dosing** *Refractory advanced solid tumors*	• 6-week monotherapy lead-in phase • Followed by ALKS 4230 + pembrolizumab combination – Evaluating once-weekly and once every three weeks dosing • Efficacy expansion phase planned
ION-01 Phase 2	**Intravenous dosing** *Anti-PD-1 pre-treated HNSCC* patients*	• Collaboration with Fred Hutchinson Cancer Research Center • ALKS 4230 + pembrolizumab combination • Assessment of tumor microenvironment from paired biopsies • Predictive biomarker assessments

HNSCC*: Head and neck squamous cell carcinoma

Interleukin-10: Concentration-Dependent, Immuno-Regulatory Cytokine

- **Low concentrations:** Activates innate immune cells to provide anti-inflammatory and immunosuppressive activities
- **Higher concentrations:** Activates anti-tumor $CD8^+$ T cells and Natural Killer cells
- Short half-life of native IL-10 limits ability to achieve and maintain higher concentrations

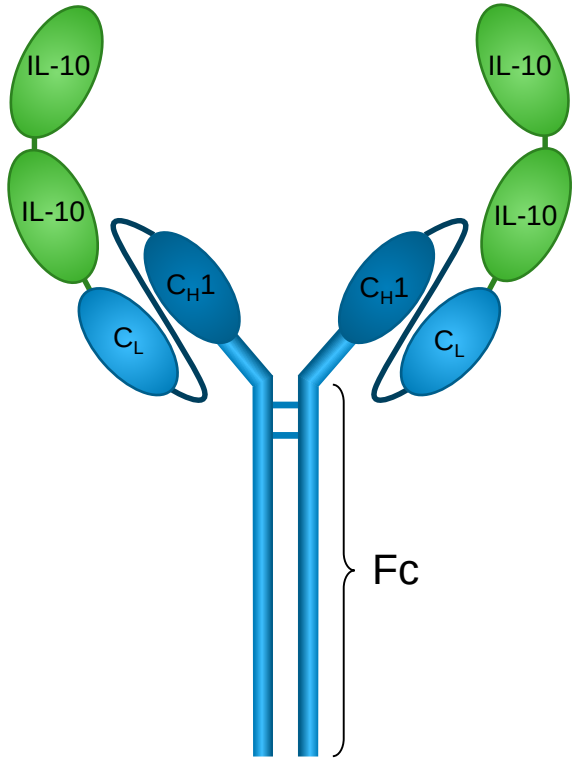


Mannino MH et al. Cancer *Lett*. 2015.

Expanding Investigational Cytokine Therapy Portfolio: IL-10 Fusion Proteins

Protein engineering expertise yields differentiated molecular design

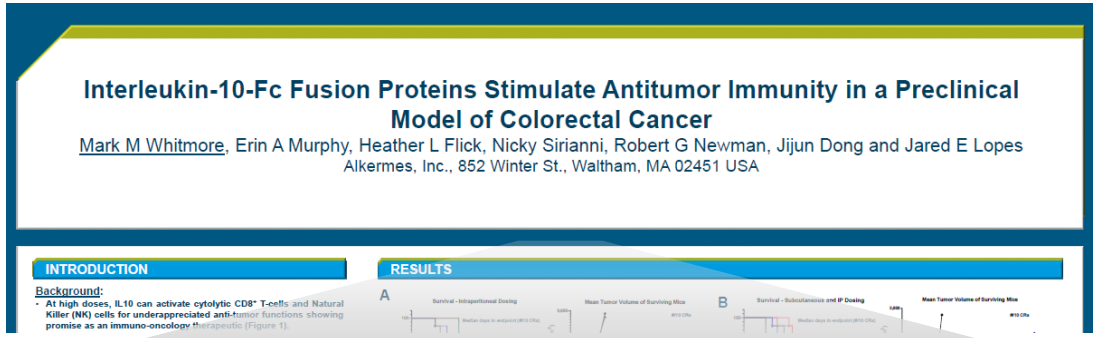
- Alkermes' design objectives:
  - Antibody scaffolding to extend circulating half-life
    - Achieve higher concentrations
    - Reduce dosing frequency
  - Retain anti-tumor functions of IL-10
  - Fc-mediated activities to provide potential additional effects
- Lead evaluation underway

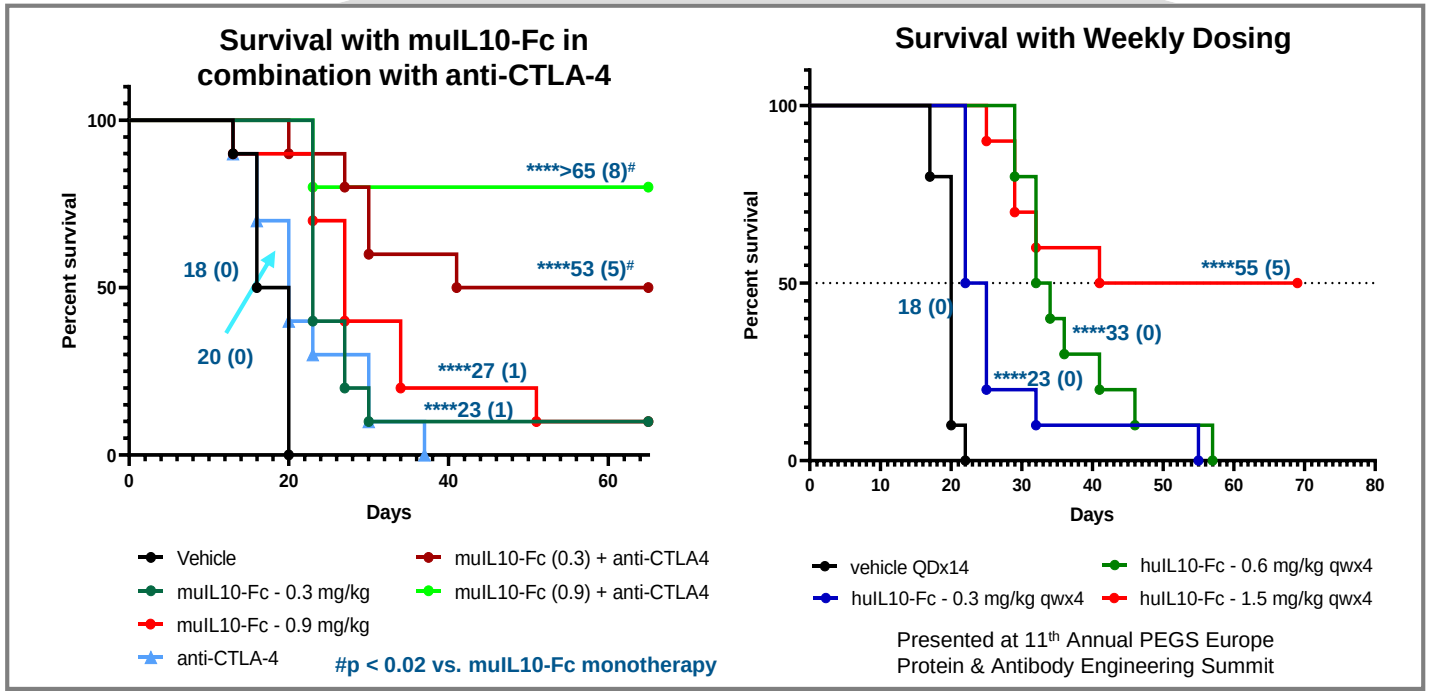


Preclinical Data Demonstrated Anti-Tumor Activity and Potential for Weekly Dosing

- IL-10-Fc fusion proteins* delayed tumor growth and provided a number of complete responses in a murine model of colorectal cancer
- IL-10-Fc fusion proteins activated $CD8^+$ T cells and reduced regulatory T cells in tumor microenvironment
- Weekly dosing of human IL-10-Fc achieved similar efficacy to daily dosing
- Enhanced potency relative to IL-10 on select immune cells mediated by Fc receptor interaction

*Murine and human



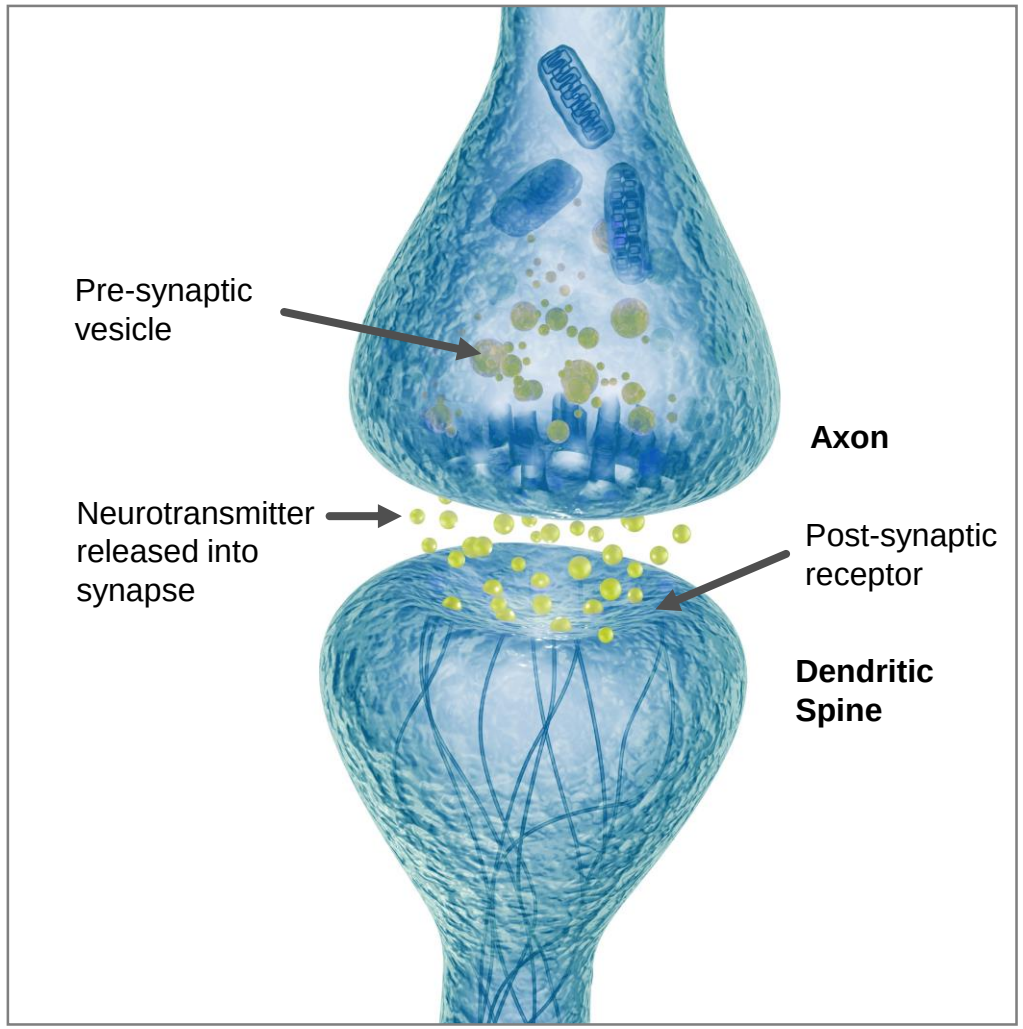


Advancing a Diversified Pipeline

Selective HDAC Inhibitors

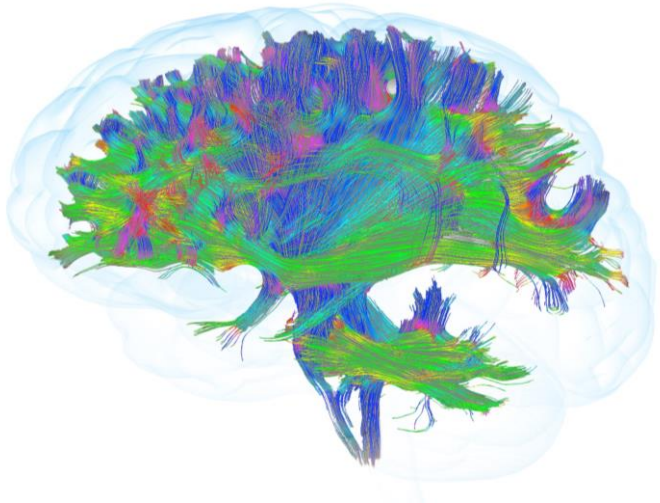
Synapses Play a Vital Role in Brain Function

- Synapses are the points of communication within the network of neurons that make up the brain
- Synaptic function is critical to brain development, learning and memory
- Synaptogenesis is the formation of synapses between neurons in the nervous system that occurs throughout a healthy person's lifespan



Synaptopathies Span Multiple Neurological Diseases Independent of Underlying Pathology

- Synaptic loss and dysfunction occur across a wide range of disorders and are associated with clinical symptoms[1]
- Increased synaptic density and function strengthen neuronal connectivity, potentially leading to clinically relevant benefits[2], independent of underlying disease pathology

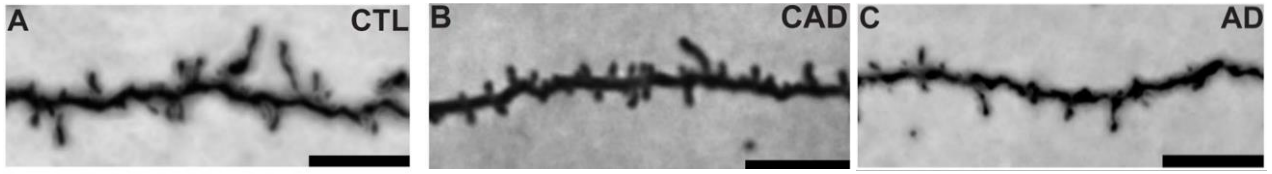


Neuropsychiatric	Neurodegenerative		Neurodevelopment
Bipolar spectrum disorder	Frontotemporal dementia	Parkinson's	Autism spectrum disorder
Schizophrenia	Huntington's	Cochlear	Fragile X syndrome
Major depressive disorder	Alzheimer's	Retinal	Epilepsy

[1]Lepeta, K et al. *J Neurochem*. 2016.
[2]Verstraelen, P et al. *Front. Neurosci*. 2018.

Loss of Synapses Correlated to Cognitive Decline in Neurodegenerative Patients

- Preserved synaptic density observed in cognitively normal patients with underlying Alzheimer's Disease pathology (CAD)
- Spine density was similar among control and CAD cases but was reduced significantly in patients with Alzheimer's Disease (AD) that demonstrated clinical dementia



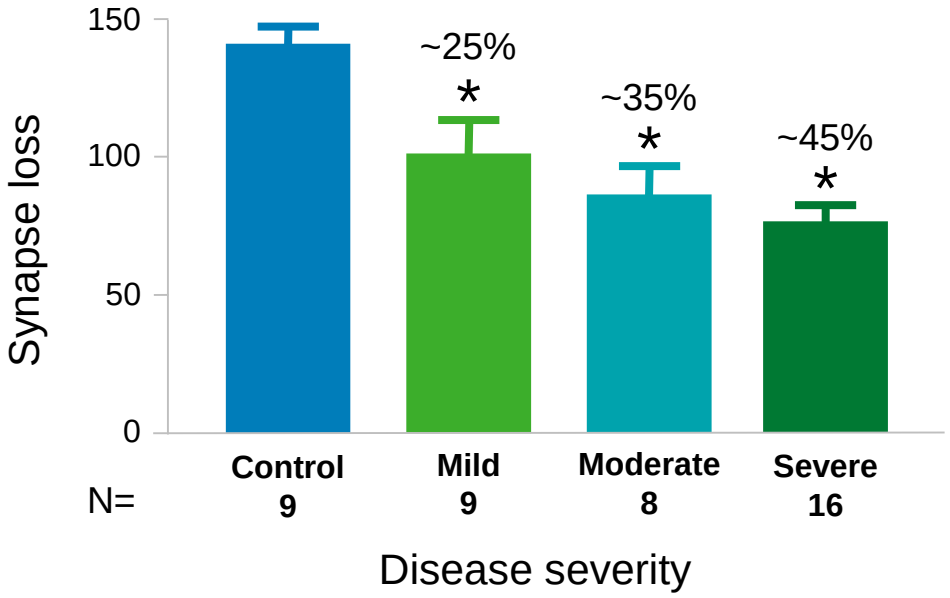
Control

Cognitively normal patient with underlying AD pathology

AD patient that demonstrated clinical dementia

Boros et al. *Annals of Neurology*. 2017.

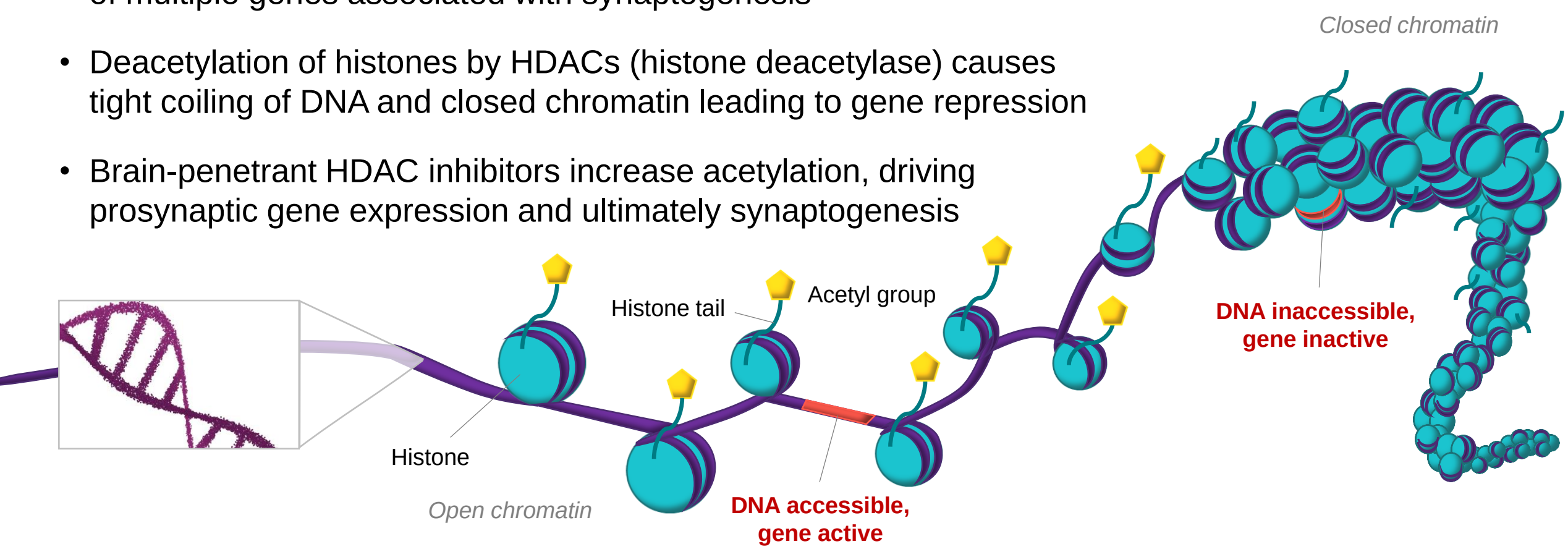
Synapse loss tracked disease progression



Masliah E. et al. *J Alzheimers Dis.* 2001.

Epigenetic Control of Synaptogenesis

- Acetylation of histones increases accessibility of DNA for transcription of multiple genes associated with synaptogenesis
- Deacetylation of histones by HDACs (histone deacetylase) causes tight coiling of DNA and closed chromatin leading to gene repression
- Brain-penetrant HDAC inhibitors increase acetylation, driving prosynaptic gene expression and ultimately synaptogenesis



Extensive Literature Discussing Prosynaptic Effects of HDAC Inhibitors

Molecular Gene and/or protein modification	**Structural** Synapse formation	**Functional** Increased long-term potentiation

nature

An epigenetic blockade of cognitive functions in the neurodegenerating brain

Neuro pharmacology

Crebinostat: A Novel Cognitive Enhancer that Inhibits Histone Deacetylase Activity and Modulates Chomatin-Mediated Neuroplasticity

Neurobiology of Learning and Memory

Basolateral amygdala activity is required for enhancement of memory consolidation produced by histone deacetylase inhibition in the hippocampus

PLOS ONE

Detection of Histone Acetylation Levels in the Dorsal Hippocampus Reveals Early Tagging on Specific Residues of H2B and H4 Histones in Response to Learning

Neuropsychopharmacology (2015) 40, 2307–2316
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www.neuropsychopharmacology.org

Pharmacological Selectivity Within Class I Histone Deacetylases Predicts Effects on Synaptic Function and Memory Rescue

LEARNING & MEMORY

The Class I HDAC inhibitor RGFP963 enhances consolidation of cued fear extinction

THE JOURNAL OF BIOLOGICAL CHEMISTRY
© 2004 by The American Society for Biochemistry and Molecular Biology, Inc.

Regulation of Histone Acetylation during Memory Formation in the Hippocampus*

nature

HDAC2 negatively regulates memory formation and synaptic plasticity

PLOS ONE

SAHA Enhances Synaptic Function and Plasticity *In Vitro* but Has Limited Brain Availability *In Vivo* and Does Not Impact Cognition

PNAS

Modulation of long-term memory for object recognition via HDAC inhibition

Neuropsychopharmacology (2013), 1–8
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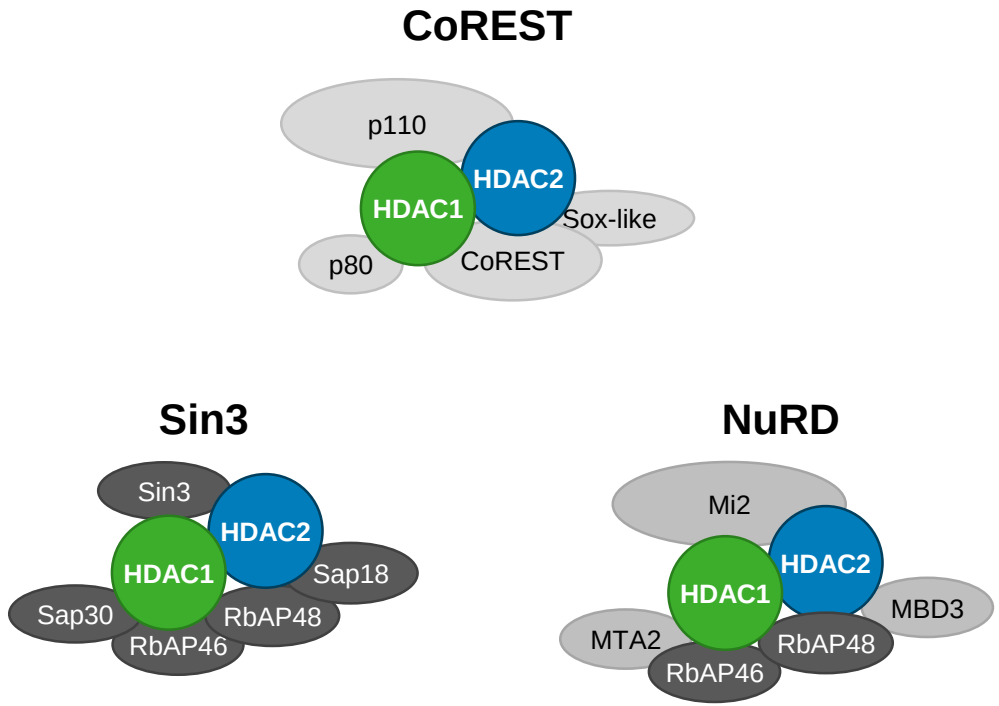
www.neuropsychopharmacology.org

Exercise and Sodium Butyrate Transform a Subthreshold Learning Event into Long-Term Memory via a Brain-Derived Neurotrophic factor-Dependent Mechanism

New Chemistry Targets Selective HDAC Complexes

- Approved HDAC inhibitor compounds have been limited by hematological toxicities, precluding application to chronic neurologic conditions
- HDACs function in association with multi-protein complexes which determine their activity
- Alkermes' proprietary compounds target specific subsets of HDAC complexes
- **CoREST** (co-repressor of repressor element-1 silencing transcription factor) is directly involved in repression of prosynaptic genes in neuronal tissue

HDAC Complexes



Adapted from Seto & Yoshida. *Cold Spring Harb Perspect Biol*. 2014

Progress Across Three Key Areas of Optimization of HDAC Inhibitors for Synaptopathies

Brain Penetration	CoREST Selectivity	Toxicity
☑ Novel chemotypes designed to enable good brain PK and ADME properties	☑ Selective HDAC-CoREST modulation* activity observed	☑ Demonstrated significantly improved hematological safety*

PK: Pharmacokinetic; ADME: Absorption, distribution, metabolism and excretion

*Fuller et al. *ACS Chem. Neurosci*. 2019, 10, 1729-1743

CoREST Complex-Selective HDAC Inhibitors Showed Prosynaptic Effects and Improved Safety Profile

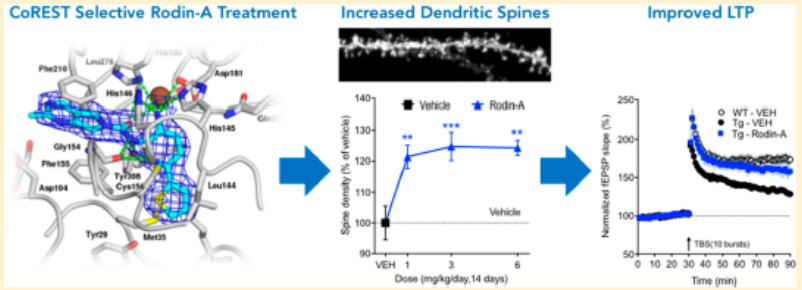
ACS Chemical Neuroscience
Research Article
Cite This: *ACS Chem. Neurosci.* XXXX, XXX, XXX–XXX
pubs.acs.org/chemneuro

CoREST Complex-Selective Histone Deacetylase Inhibitors Show Prosynaptic Effects and an Improved Safety Profile To Enable Treatment of Synaptopathies

Nathan O. Fuller, Antonella Pirone, Berkley A. Lynch, Michael C. Hewitt, Maria S. Quinton, Timothy D. McKee, and Magnus Ivarsson*

Rodin Therapeutics, 300 Technology Square, Cambridge, Massachusetts 02139, United States

Supporting Information



ABSTRACT: Synaptic dysfunction is a pathological feature in many neurodegenerative disorders, including Alzheimer's disease, and synaptic loss correlates closely with cognitive decline. Histone deacetylases (HDACs) are involved in chromatin remodeling and gene expression and have been shown to regulate synaptogenesis and synaptic plasticity, thus providing an attractive drug discovery target for promoting synaptic growth and function. To date, HDAC inhibitor compounds with prosynaptic effects are plagued by known HDAC dose-limiting hematological toxicities, precluding their application to treating chronic neurologic conditions. We have identified a series of novel HDAC inhibitor compounds that selectively inhibit the HDAC−co-repressor of repressor element-1 silencing transcription factor (CoREST) complex while minimizing hematological side effects. HDAC1 and HDAC2 associate with multiple co-repressor complexes including CoREST, which regulates neuronal gene expression. We show that selectively targeting the CoREST co-repressor complex with the representative compound Rodin-A results in increased spine density and synaptic proteins, and improved long-term potentiation in a mouse model at doses that provide a substantial safety margin that would enable chronic treatment. The CoREST-selective HDAC inhibitor Rodin-A thus represents a promising therapeutic strategy in targeting synaptic pathology involved in neurologic disorders.

"…novel HDAC inhibitor compounds that selectively inhibit the HDAC−co-repressor of repressor element-1 silencing transcription factor (CoREST) complex while **minimizing hematological side effects**…selectively targeting the CoREST co-repressor complex…results in **increased spine density and synaptic proteins**, and **improved long-term potentiation** in a mouse model at doses that provide a **substantial safety margin that would enable chronic treatment."**

Fuller et al. CoREST Complex-Selective Histone Deacetylase Inhibitors Show Prosynaptic Effects and an Improved Safety Profile To Enable Treatment of Synaptopathies. *ACS Chem. Neurosci.* 2019, 10, 3, 1729-1743.

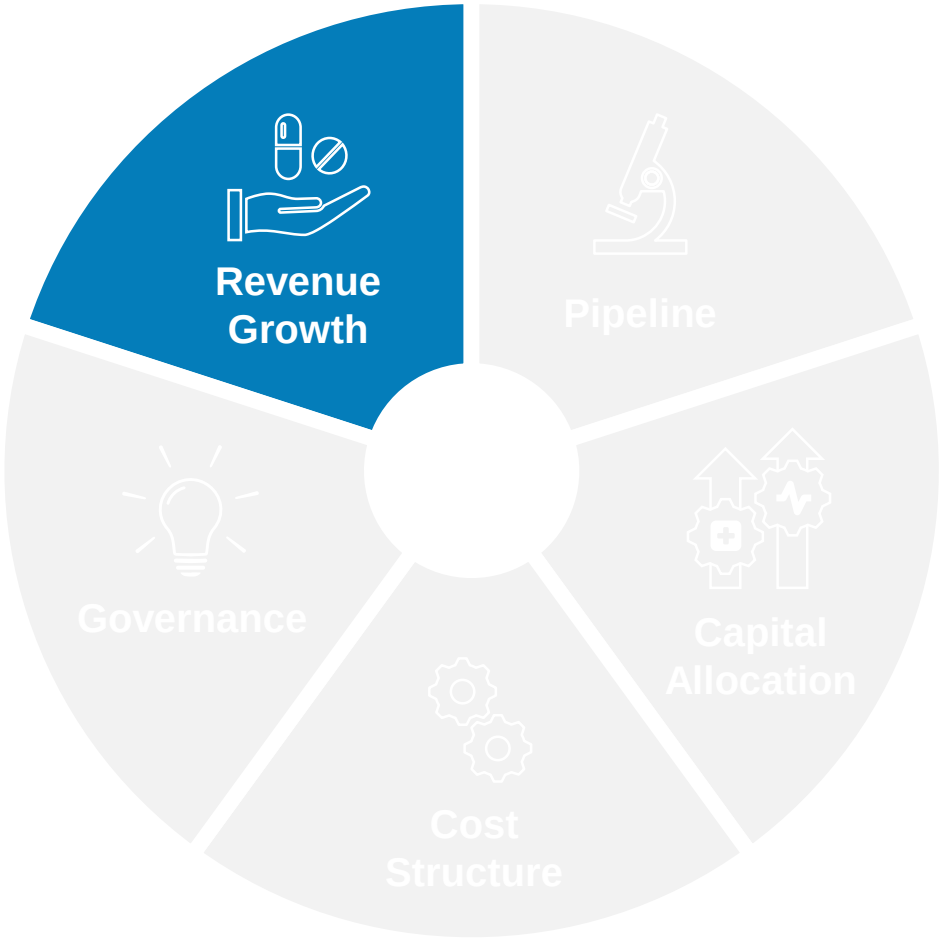
Advancing Preclinical Research and IND-Enabling Activities

- **HDAC CoREST inhibitors for synaptopathies**
  Pursue IND-enabling activities for lead preclinical compounds
  - Potential utility across highly-prevalent neurodegenerative diseases such as Alzheimer's Disease as well as orphan diseases such as frontotemporal dementia and Huntington's Disease
- **Oncology and other disease areas**
  Continue exploratory work to assess the potential utility of selective HDAC modulation
- **Translational development and biomarkers**
  Continue development of biomarker and translational tools to help demonstrate potential target engagement and efficacy

Positioning the Business to Deliver Long-Term Growth and Profitability

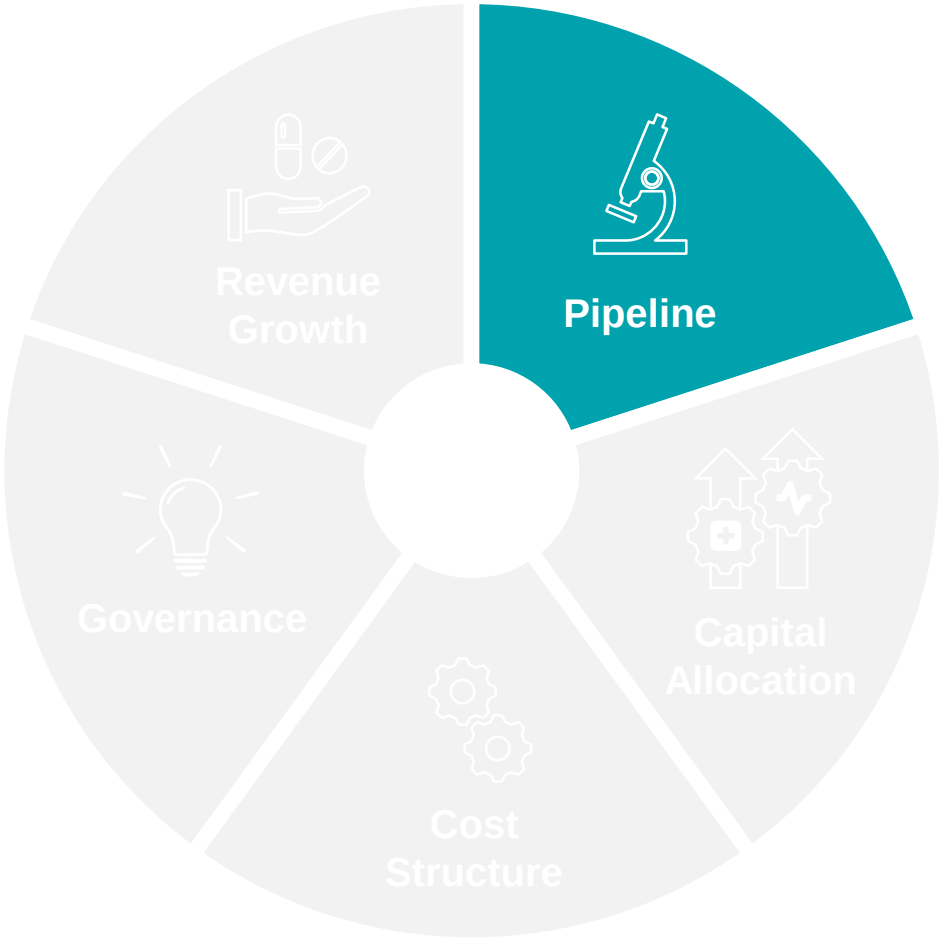
Positioning Alkermes for Long-Term Growth

Positioning Alkermes for Long-Term Growth



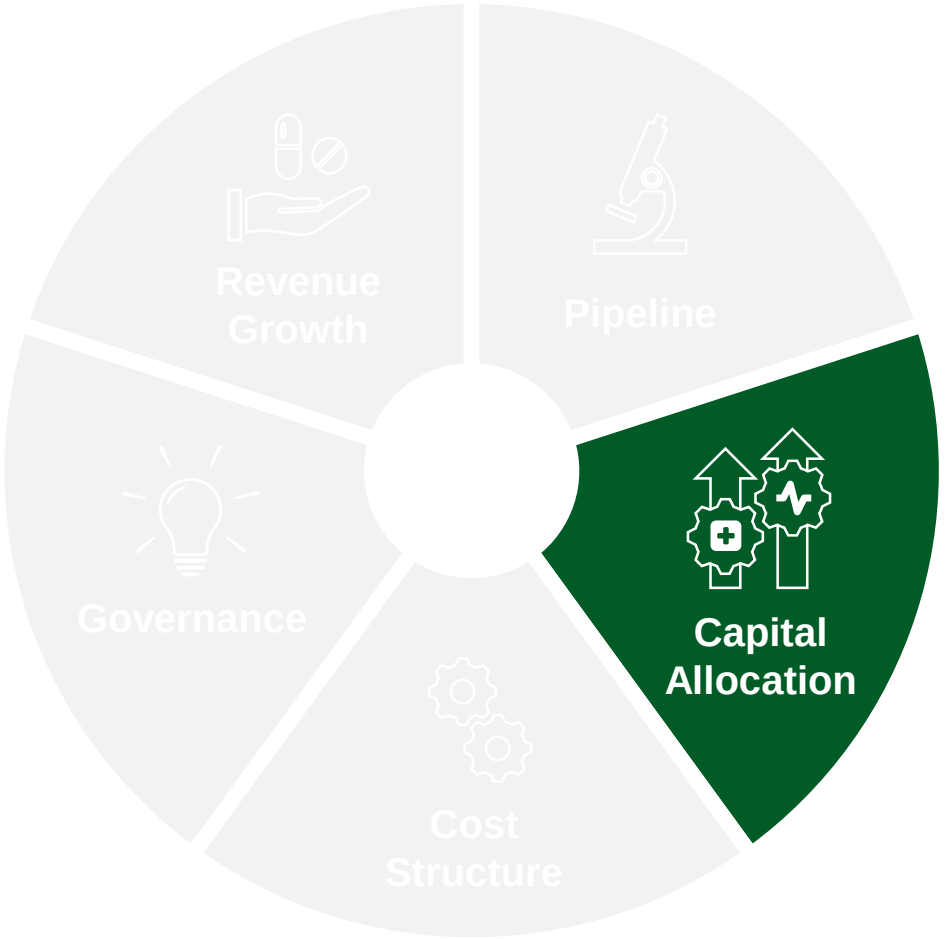
- **VIVITROL® & ARISTADA® : Executing commercial plans**
- **VUMERITY®: Received FDA approval; Launched by Biogen**
- **ALKS 3831: Submitted NDA and preparing for launch**

Positioning Alkermes for Long-Term Growth



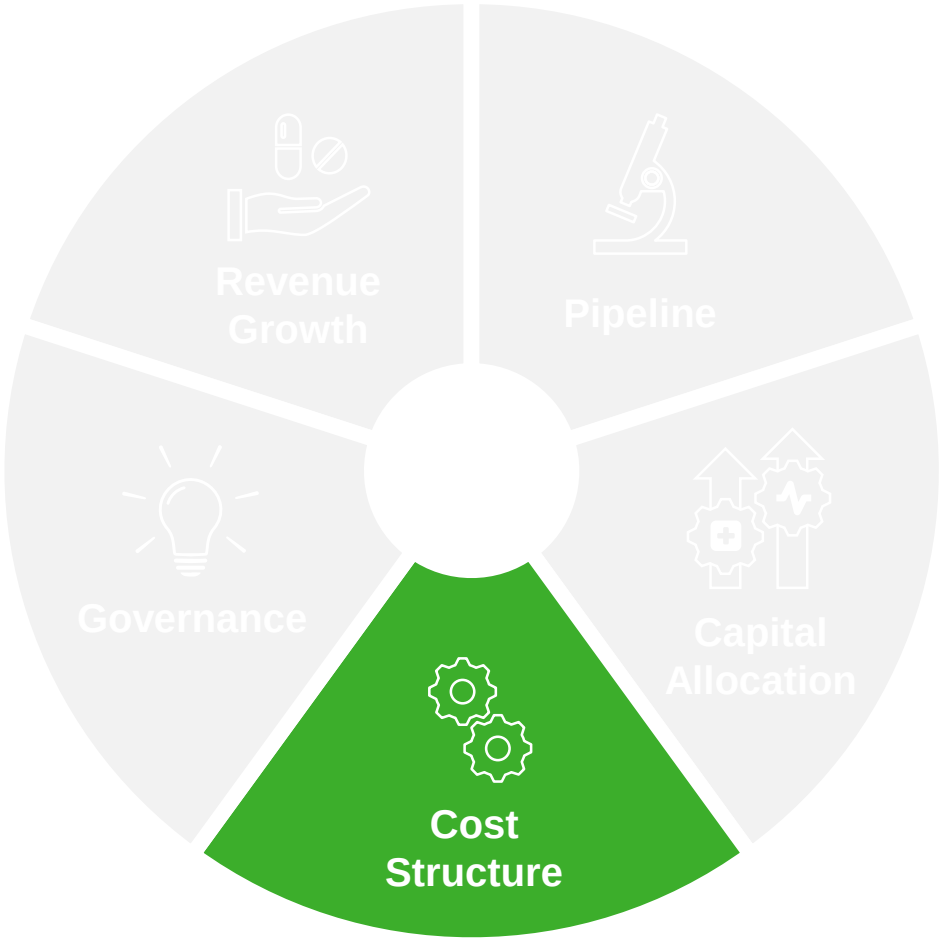
- VIVITROL® & ARISTADA® : Executing commercial plans
- VUMERITY®: Received FDA approval; Launched by Biogen
- ALKS 3831: Submitted NDA and preparing for launch
- **Expanded ALKS 4230 program driven by emerging data**
- **Introduced IL-10-Fc program and HDAC inhibitor platform**

Positioning Alkermes for Long-Term Growth



- VIVITROL® & ARISTADA® : Executing commercial plans
- VUMERITY®: Received FDA approval; Launched by Biogen
- ALKS 3831: Submitted NDA and preparing for launch
- Expanded ALKS 4230 program driven by emerging data
- Introduced IL-10-Fc program and HDAC inhibitor platform
- **Acquired Rodin Therapeutics**
- **Focusing investment in highest-potential R&D programs**

Positioning Alkermes for Long-Term Growth



- VIVITROL® & ARISTADA® : Executing commercial plans
- VUMERITY®: Received FDA approval; Launched by Biogen
- ALKS 3831: Submitted NDA and preparing for launch
- Expanded ALKS 4230 program driven by emerging data
- Introduced IL-10-Fc program and HDAC inhibitor platform
- Acquired Rodin Therapeutics
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Actively Shaping the Future of the Business

Expanding and driving growth of our **product portfolio**

Advancing a **diversified CNS and oncology pipeline**

Positioning the business to deliver **long-term growth** and profitability

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