Evolving the Business: Expanding the Product Portfolio and Scientific Platform

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Chief Executive Officer

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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; the expected timeline for closing of the company’s acquisition (the “Acquisition”) of Rodin Therapeutics, Inc. ("Rodin"); the therapeutic and commercial value of the company’s marketed and development products and Rodin’s development candidate portfolio; timelines, plans and expectations for clinical development activities relating to the company’s products and development candidates, including details and expected timing of the ION-01, ARTISTRY-1 and ARTISTRY-2 clinical studies for ALKS 4230 and the anticipated expansion of the company’s presence and development efforts in central nervous system (“CNS”) diseases to include neurodegenerative disorders and synaptopathies; the company’s plans for development of Rodin’s development candidate portfolio, including preclinical activities related to FTD-GRN and exploratory work in hematological disorders and oncology; the company’s expected timelines relating to actions by the U.S. Food and Drug Administration (“FDA”) relating to the company’s new drug application (“NDA”) submission for ALKS 3831; expected continued growth in the market for treatments for multiple sclerosis; and the potential financial benefits that may be achieved under the license and collaboration agreement between the company and Biogen for VUMERITY®. 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These risks, assumptions and uncertainties include, among others: the company’s clinical development activities, including those relating to the Rodin development candidate portfolio, may not be completed on time or at all; the results of the company’s development activities, including those relating to Rodin’s development candidate portfolio, may not be positive; preliminary or interim results from preclinical and clinical studies, including preliminary, interim or final data from preclinical and early clinical studies of ALKS 4230 as a monotherapy or in combination with pembrolizumab, may not be predictive of final results of such trials, results of future clinical trials or real-world results; preclinical and early clinical data relating to Rodin’s development candidate portfolio may not be predictive of results of future preclinical or clinical trials or real-world results; our products and/or development candidates and Rodin’s development candidates could be shown to be unsafe or ineffective; regulatory submissions may not occur or be submitted in a timely manner; data from clinical trials, including the clinical studies for ALKS 4230, may be interpreted by the FDA in different ways than the company interprets it; the FDA may not agree with the company’s regulatory approval strategies, including its clinical study designs and conduct, or the sufficiency of the results thereof to support approval; 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 and commercial benefits of collaboration with Biogen under the license and collaboration agreement between the company and Biogen may not be achieved; the Acquisition may involve unexpected costs, liabilities or delays; a condition to the closing of the Acquisition may not be satisfied or waived in a timely manner or at all and may result in closing being delayed or not occurring; the anticipated benefits of the Acquisition, including the anticipated expansion of the company’s development efforts and presence in CNS, 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. 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Alkermes’ Diversified Business Platform

### Royalty & Manufacturing

Revenue streams provide a financial foundation to further advance Alkermes’ proprietary development candidates.

### Proprietary Products

- Medicines for people with serious mental illness and addiction;
- Specialized commercial capabilities to address complex treatment systems

### Development Pipeline

Specific areas of high-interest within CNS and oncology:
- ALKS 4230 - Phase 1/2
- Preclinical assets
  - Oncology – cytokine therapy
  - CNS – neurodegenerative disorders*  

- ALKS 3831
  - NDA submitted;
  - Launch preparations underway

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* Pending closing of acquisition of Rodin Therapeutics, Inc.
VUMERITY® (Diroximel Fumarate) for Multiple Sclerosis
VUMERITY® (Diroximel Fumarate) for Multiple Sclerosis (MS)

• Novel oral fumarate with a distinct chemical structure for the treatment of relapsing forms of MS
  – Administered in oral, micro pellet, controlled-release dosage form

• Approved by FDA in October 2019
  – Composition of matter patent extends into 2033

• Announced positive topline results of EVOLVE-MS-2 elective head-to-head gastrointestinal (GI) tolerability study in July 2019

• Biogen holds the exclusive, worldwide license to commercialize VUMERITY
VUMERITY®: Clinical Development Program

**EVOLVE-MS-1**

- Phase 3 two-year, open-label safety study in ~1000 patients with relapsing-remitting multiple sclerosis
- Designed to assess safety and tolerability of diroximel fumarate and support regulatory approval

**EVOLVE-MS-2**

- Elective, phase 3 study in 506 patients with relapsing-remitting multiple sclerosis
- Designed to assess GI tolerability profile of diroximel fumarate compared to TECFIDERA® (dimethyl fumarate) based on self-reported GI symptoms
Multiple Sclerosis is a Large and Growing Market

- Approximately 325K patients are 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
- Total market growth of 17% from 2013-2016\(^2\)
  - Orals make up ~45% of this growth
- Potential for additional indications and ex-U.S. opportunities\(^3\)

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**Biogen License and Collaboration Agreement**

- Granted Biogen exclusive, worldwide license to commercialize VUMERITY®
- NDA transferred to Biogen post-approval
- $150M milestone payment received following approval by FDA
- Mid-teens percentage royalty to Alkermes on worldwide net sales of VUMERITY

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1. Decision Resources MS Disease Landscape (Nov. 2016)
2. IMS SMART Solutions (% of sales in MS factored using InVentiv Health Research & Insights TreatmentAnswers\(^\text{TM}\) Generator).
3. Under License and Collaboration Agreement, Biogen controls the pursuit of any additional indications and/or ex-U.S. opportunities.
Proprietary Commercial Products for Addiction and Schizophrenia

**Vivitrol®**
(naltrexone for extended-release injectable suspension)

Long-acting injectable extended-release naltrexone for the prevention of relapse to opioid dependence following detoxification and alcohol dependence

**ARISTADA®**
(aripiprazole lauroxil extended-release injectable suspension)

441mg · 662mg · 882mg · 1064mg

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

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### Evolving Research and Development Focus in High-Potential Opportunities

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<th>CNS</th>
<th>Oncology</th>
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<td>• Schizophrenia</td>
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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

• ARTISTRY-1 and ARTISTRY-2 phase 1/2 studies ongoing

• Data presented at Society of Immunotherapy of Cancer meeting in November 2019
IL-2 Activates and Expands Immune Suppressive Regulatory T Cells That Dampen Anti-Cancer Immune Responses

- Recombinant human IL-2, PROLEUKIN® (aldesleukin) approved for metastatic renal cell carcinoma and metastatic melanoma based on complete and durable remissions
- IL-2 potently activates the high-affinity IL-2 receptor found on vascular endothelial cells, resulting in poor tolerability and toxicities
- Toxicity profile of IL-2 significantly limits broad use, despite established anti-tumor efficacy

Graphics for illustrative purposes only.
ALKS 4230 is ‘Sterically Occluded’ From Binding to the High-Affinity Receptor

**ALKS 4230 Design Intention:**

- Selectively expand cancer-fighting CD8\(^+\) T cells and NK cells to potentially improve anti-tumor efficacy
- Prevent IL-2-derived expansion of T\(_{\text{reg}}\) 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

**IV 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

**IV dosing**
*Anti-PD-1 pre-treated HNSCC patients*

- ALKS 4230 + pembrolizumab combination
- Assessment of tumor microenvironment from paired biopsies
- Predictive biomarker assessments

HNSCC: Head and neck squamous cell carcinoma
**ALKS 4230: ARTISTRY-1 Phase 1/2 Study Design**

**Part A: Monotherapy Dose Escalation**
*Inpatient*

- Identified RP2D of 6 µg/kg
- Ongoing to determine MTD

**Part B: Monotherapy Dose Expansion**
*Outpatient*

- Renal Cell Carcinoma Cohort
- Melanoma Cohort

**Part C: ALKS 4230 + Pembrolizumab Combination Therapy**
*Outpatient*

- 1 µg/kg combo safety run in
- 3 µg/kg combo safety run in
- 6 µg/kg combo safety run in

- PD-1/L1 approved tumor types (treatment naïve)
- PD-1/L1 approved tumor types (pretreated)
- PD-1/L1 unapproved tumor types*
- Monotherapy rollover
- 1st line melanoma
- 2nd line NSCLC
- 2nd line head and neck squamous cell carcinoma

RP2D: Recommended phase 2 dose
MTD: Maximum tolerated dose
NSCLC: Non-small cell lung cancer

*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
ARTISTRY-1 Part A Monotherapy Dose Escalation:
Dose-Dependent, Selective Expansion of NK and CD8+ T Cells

Identified 6 µg/kg/day administered intravenously as recommended phase 2 dose (RP2D)
ARTISTRY-1 Part C Combination Stage With Pembrolizumab:
Overall Response: PD-1/L1 Unapproved Tumor Types & Monotherapy Rollover Patient

- 12 of 18 patients with evaluable scans had stable disease or better over the course of their treatment
- 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

Duration of Treatment by Overall Response

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<th>Evaluation of SD</th>
<th>Evaluation of PR</th>
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Time on Study (weeks)

SD: Stable Disease; PR: Partial Response; PD: Progressive Disease

Data as of cutoff date of Aug. 2, 2019

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

Phase 1: Dose Escalation, 6-Week Monotherapy Lead-in
- Cohort 1: 0.3 mg SC q7d
- Cohorts q7d SC
- Cohorts q21d SC

Determine RP2D and dosing frequency

Safety Expansion
ALKS 4230 + pembrolizumab

Phase 2: Efficacy Expansion in Solid Tumors
Combination ALKS 4230 + pembrolizumab
- Cohorts of specific tumors TBD

- In phase 1 dose escalation: Patients receive 42 days of monotherapy lead-in ALKS 4230 SC q7d or q21d, followed by combination of q21d pembrolizumab (200 mg) and either ALKS 4230 SC q7d or q21d
- Cohort 1 dosing of 0.3 mg was chosen as the starting dose based on predictive modeling

SC: subcutaneous; q7d: Administered once weekly; q21d: Administered once every three weeks
Acquisition of Rodin Therapeutics Announced This Week

- Builds on Alkermes’ expertise and capabilities in CNS, and broadens R&D efforts into a wide range of neurogenerative disorders

- Rodin compounds: Designed to be first-in-class, brain-permeable therapeutics for synaptopathies, targeting specific histone deacetylase (HDAC) complexes
  - HDACs are involved in chromatin remodeling and gene expression; have been shown to regulate synaptogenesis and synaptic plasticity
  - Currently available HDAC inhibitors with known prosynaptic effects are associated with dose-limiting hematological toxicities, precluding their use in the treatment of chronic neurologic conditions

- Expected to close by end of November 2019

Selective inhibition of HDAC-CoREST complex believed to:

- Reactivate neuronal gene expression
- Strengthen existing synapses and promote creation of new synapses
- Minimize known class-based hematologic safety concerns
Synaptopathies Span Multiple Diseases

- Synapses are the points of communication within the network of neurons that make up the brain.
- Impaired synaptic function and synaptic loss disrupt neuronal communication and lead to clinical symptoms.
- Synaptic loss and dysfunction are associated with certain clinical symptoms across a wide range of neurodegenerative, neuropsychiatric, and neurodevelopment disorders, regardless of the underlying pathology.

- Bipolar spectrum disorder
- Schizophrenia
- Major depressive disorder
- Frontotemporal dementia
- Huntington’s
- Alzheimer’s
- Parkinson’s
- Cochlear
- Retinal
- Autism spectrum disorder
- Fragile X syndrome
- Epilepsy
Decades of Literature Discussing Prosynaptic Effects of HDAC Inhibitors

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

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

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

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

Regulation of Histone Acetylation during Memory Formation in the Hippocampus

An epigenetic blockade of cognitive functions in the neurodegenerating brain

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

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

Historical HDAC Challenges

**Brain PK**
Common HDAC inhibitors have shown low brain exposure.

**Toxicity**
Approved HDAC inhibitors have suffered from dose-limiting hematopoietic toxicity in the clinic.

**Selectivity**
Drug discovery efforts focused on hard-to-achieve HDAC subtype selectivity.

Novel approach to address challenges

- Novel chemotypes designed to enable good brain PK and ADME properties.
- Use predictive *in vitro* toxicity assays to derive SAR:
  - Demonstrated significantly improved hematological safety *in vitro*.
  - Studied in 28-day preclinical GLP toxicity studies.
- Activity assay to confirm selective HDAC-CoREST modulation:
  - Demonstrated potent *in vitro* and *in vivo* activity.

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

**SAR:** Structure-activity relationship; **GLP:** Good Laboratory Practice

*ACS Chem. Neurosci. 2019, 10, 1729-1743*
Plans for Advancement of Preclinical Research and IND-Enabling Activities

• **HDAC Co-REST inhibitors**
  Pursue IND-enabling activities for lead preclinical compounds

• **FTD-GRN**
  Advance preclinical research program focused on subset of frontotemporal dementia (FTD) patients with inherited mutation of the progranulin gene

• **Translational development and biomarkers**
  Continue development of biomarker and translational tools to demonstrate potential target engagement and efficacy

• **Hematological disorders and oncology**
  Continue exploratory work to assess the potential utility of selective HDAC modulation
Positioning Alkermes for Long-Term Growth and Success

- Appointed two new directors
  - Expertise in oncology and strategic value creation

- Implemented strategic reorganization
  - Streamlined cost structure and increased flexibility to pursue business development activities

- Received FDA approval for VUMERITY®
  - Transferred NDA to Biogen

- Presented ALKS 4230 data at SITC
  - Preliminary safety and efficacy data from ARTISTRY-1

- Submitted ALKS 3831 NDA
  - Twelve-month review expected; launch preparations underway

- Agreed to Acquire Rodin Therapeutics
  - Expands R&D efforts into neurodegenerative disorders