Singular Company With Emerging Blockbusters

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Alkermes’ Four Pillars: Integrating Multiple Real-World Inputs Into Product Selection and Development

Science  
People Affected

Policy  
Economics
## Products and Pipeline Driving Growth

### Proprietary Commercial Products

- **Vivitrol®**
  - Naltrexone for extended-release injectable suspension, 380mg/ivial
- **Aristada™**
  - Aripiprazole lauroxil, extended-release injectable suspension, 441mg · 662mg · 882mg

### Key Products Using Alkermes Technology

- **Risperdal Consta®**
- **Invega Sustenna®**
- **Invega Trinza™**
- **Ampyra®/Fampyra®**
- **Bydureon®**

### Proprietary Pipeline

- **ALKS 5461**
  - Depression
- **ALKS 3831**
  - Schizophrenia
- **ALKS 8700**
  - Multiple Sclerosis
- **ALKS 6428**
  - Opioid Taper Kit
- **ALKS 7119**
  - Alzheimer’s Agitation
- **RDB 1450**
  - Immuno-oncology

*Products developed and sold by Janssen Pharmaceuticals Inc. using Alkermes technology*
VIVITROL®: Only Once-Monthly Treatment for Alcohol and Opioid Dependence
Breaking good: VIVITROL, a drug given as a monthly shot, is helping addicts stay clean.
Rates of the primary outcome of week 4 opioid relapse were lower among XR-NTX participants.
VIVITROL®: Accelerating Growth

Broader adoption in treatment systems for alcohol and opioid dependence

Expanding and diverse array of state and criminal justice programs provides platform for growth

Source: Alkermes data on file.
ARISTADA™ (aripiprazole lauroxil): Now Approved and Launching Into Dynamic Schizophrenia Market
Embodies key attributes important to patients, nurses and physicians

- Range of doses and dosing intervals
  - Three available doses
    - 441 mg, 662 mg, 882 mg
  - Additional six-week dosing interval approved for 882 mg dose

- Administration features
  - Ready-to-use pre-filled syringe
  - Deltoid and gluteal administration for 441 mg dose
  - Non-refrigerated
Launching Into High-Growth U.S. LAI Atypical Market

- Launch of INVEGA SUSTENNA® 8/09
- Launch of ZYPREXA® RELPREVV® 3/10
- Launch of ABILIFY MAINTENA® 3/13
- Launch of RISPERDAL CONSTA® 12/03
- Launch of ARISTADA™ 10/15

Source: IMS Health
Five Factors Are Coalescing to Grow LAI Market

1. Multiple entrants with a common message
2. Disappearance of promotion of orals
3. Decade of pharmacoeconomic and medical outcomes data
4. New imperative for focus on total costs
5. Elevated public interest in treatment
Targeting Well-Defined Physician Population at Launch

Majority of U.S. LAI* Volume Driven by Concentrated Group of Physicians

At Launch

- Low
  - 26,500 = All LAI Rx Volume

- High
  - 5,700 = 80% of Rxs
  - 1,700 = 50% of Rxs

Later

Commercial Priority

Sources: IMS XPO Plantrak June 2014
*INVEGA SUSTENNA®, RISPERALD CONSTA®, ZYPREXA® RELPREVV®, ABILIFY MAINTENA®
ARISTADA™: Commercial Launch Underway

- Approved by U.S. FDA on Oct. 5, 2015

- Launch ongoing
  - Leverages established specialty injectable commercial infrastructure
  - 175 seasoned field sales representatives with 16 years average industry experience

- Extended-durations study ongoing
  - Initiated Dec. 2014
  - Enrollment ~140 patients with stable schizophrenia
  - Testing new dose strength for two-month dosing interval

- Executing strategy for expansion of product family
ALKS 5461: Moving FORWARD in the Treatment of Depression
ALKS 5461: Designed for the Needs of Patients

- In phase 3 in patients with major depressive disorder and inadequate response to standard therapies
  - New mechanism of action
  - Balanced neuromodulator differentiated from traditional monoamine approach (SSRI/SNRI)
  - Once-daily, oral co-formulation of buprenorphine and samidorphan

- Compelling and statistically significant results
  - Phase 2 study: Significantly improved depression scores
  - Granted Fast Track status by FDA

- FORWARD: Comprehensive pivotal program underway
  - Designed to replicate results from previous studies
  - FORWARD-1: Confirmed positive data through eight-week study
  - Data from three core efficacy studies expected in 2016
Majority of MDD Market is for Second Line Therapy Due to Inadequate Response

Drug-Treated MDD Patients in U.S.\textsuperscript{1,2}

- 10.9 Million
- 6.9 Million
- 4.8 Million

- 63% treated with 2\textsuperscript{nd} line therapy
- 44% treatment resistant after 2\textsuperscript{nd} line

2. Decision Resources (PatientBase 2014)
Standard Algorithm for Treatment-Resistant Depression (TRD)

Better

SSRI/SNRI: First Line
4-6 weeks

SSRI/SNRI: Second Line
4-6 weeks

SSRI/SNRI: Third Line
4-6 weeks

Worse

ECT

Antipsychotics

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Better

**ALKS 5461**

SSRI/SNRI: First Line
4-6 weeks

SSRI/SNRI: Second Line
4-6 weeks

Elapsed Time

Tolerability

Decreased Tolerability/ Increased Clinical Complexity

Worse

ECT

Antipsychotics
ALKS 5461: Executing FORWARD Pivotal Program in 2015

FORWARD-1 Titration

FORWARD-2 Long-Term Safety

Core Efficacy

FORWARD-3

FORWARD-4

FORWARD-5

Supporting Studies

Human Abuse Liability (HAL)

Special Populations

Standard Clin/Pharm Package

2014  2015  2016
Primary endpoint: Safety and tolerability of two titration schedules of ALKS 5461
- Double-blind, eight-week study
- Administered once daily as adjunctive treatment
- One- and two-week titration schedules
- 66 patients randomized

Exploratory endpoint: Efficacy measured by change in Montgomery-Åsberg Depression Rating Scale (MADRS) total score from baseline
FORWARD-1 Results: MADRS Reduction From Baseline Continued Through Week 8

1. ALKS 5461 phase 2 study, stage 1. Results announced April 17, 2013.
2. ALKS 5461 FORWARD-1 phase 3 titration study. Results announced Jan. 6, 2015.
FORWARD Program Enrollment Update: Progress Driving Earlier-Than-Expected Readouts

<table>
<thead>
<tr>
<th>Study</th>
<th>Initiation</th>
<th>Active Study Sites</th>
<th>Current Projections for Topline Results</th>
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</thead>
<tbody>
<tr>
<td>FORWARD-4</td>
<td>May 2014</td>
<td>44</td>
<td>Q1 2016</td>
</tr>
<tr>
<td>FORWARD-3</td>
<td>May 2014</td>
<td>48</td>
<td>Q1 2016</td>
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<tr>
<td>FORWARD-5</td>
<td>July 2014</td>
<td>37</td>
<td>Q3 2016</td>
</tr>
</tbody>
</table>

- Core efficacy phase 3 enrollment ahead of schedule
- High level of patient and data quality
- High retention and rollover into open-label extension
ALKS 3831: Blockbuster Opportunity in Schizophrenia Moving Into Pivotal Program
Another Mechanism for Affecting Outcomes is Through Improved Tolerability

Source: Decision Resources Pharmacor Report, Nov. 2010, "Schizophrenia"; Based on multiple sources, including manufacturer package inserts, clinical trials and review articles.
ALKS 3831: Designed to Advance the Treatment of Schizophrenia

- Novel, oral, broad-spectrum antipsychotic drug candidate
  - Designed to provide powerful efficacy and favorable metabolic profile
  - Expands pharmacologic spectrum of olanzapine
  - Adds proprietary mu-antagonist to address specific unmet needs of patients
  - ALKS 3831 demonstrated antipsychotic efficacy equivalent to olanzapine with statistically significant lower weight gain in phase 2 study

- Straightforward pivotal program to begin in Q4 2015
  - Program designed to evaluate attenuating effects of ALKS 3831 on olanzapine-associated weight gain in patients with schizophrenia
  - Pivotal program design based on positive phase 2 results and productive End-of-Phase 2 meeting with FDA

- Ongoing phase 2 program in patients with schizophrenia and alcohol use disorder
ALKS 3831 Phase 2 Study Assessed Efficacy and Attenuation of Olanzapine-Associated Weight Gain

300-patient, multicenter, double-blind, active-controlled, dose-ranging study

- One-week oral olanzapine lead-in enabled stratification and data analysis by early weight gain
- Patients randomized to olanzapine or three different doses of ALKS 3831 for 12 weeks
  - Olanzapine + 5 mg, 10 mg or 20 mg samidorphan
  - Followed by 12-week extension period in which all patients received ALKS 3831: results extended findings from first 12 weeks and demonstrated beneficial weight effect for patients switching from olanzapine to ALKS 3831

Primary endpoint: PANSS total score at Week 12, compared to olanzapine

Secondary endpoints focused on impact of ALKS 3831 on weight gain, compared to olanzapine
ALKS 3831 Phase 2 Primary Endpoint: Equivalent Antipsychotic Efficacy to Olanzapine

PANSS Total Scores +/- SEM (Points)

- Olanzapine
- ALKS 3831 Combined Treatment Groups

*95% CI: (-1.2 – 2.5)
## ALKS 3831 showed significant reduction in mean % weight gain vs. Olanzapine at Week 12

<table>
<thead>
<tr>
<th>Study Population</th>
<th>Mean (SE) % Change From Baseline in Body Weight at Week 12</th>
<th>Olanzapine</th>
<th>ALKS 3831†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full Study Population</strong></td>
<td></td>
<td>4.1% (0.5)</td>
<td>2.6% (0.3)</td>
</tr>
<tr>
<td>Reduction in Mean % Weight Gain</td>
<td></td>
<td></td>
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<tr>
<td>ALKS 3831 vs. Olanzapine</td>
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<td>37%</td>
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<tr>
<td><strong>P-value</strong></td>
<td></td>
<td>p=0.006*</td>
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<tr>
<td><strong>Early Weight Gain Population</strong></td>
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<td>5.3% (0.6)</td>
<td>2.6% (0.3)</td>
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<tr>
<td>Reduction in Mean % Weight Gain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALKS 3831 vs. Olanzapine</td>
<td></td>
<td>51%</td>
<td></td>
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<tr>
<td><strong>P-value</strong></td>
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<td>p&lt;0.001*</td>
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</tr>
</tbody>
</table>

†ALKS 3831 combined treatment groups.

*Results based on Mixed-Effect Model Repeated Measure (MMRM) model.
Most Common Reasons for Changing Atypical Antipsychotic Therapy

- **Risperidone**
  - Efficacy: 38%
  - Weight Gain/Metabolic: 12%
  - Extrapyramidal: 22%

- **Aripiprazole**
  - Efficacy: 45%
  - Weight Gain/Metabolic: 3%
  - Extrapyramidal: 11%

- **Quetiapine**
  - Efficacy: 49%
  - Weight Gain/Metabolic: 18%
  - Extrapyramidal: 3%

- **Olanzapine**
  - Efficacy: 17%
  - Weight Gain/Metabolic: 68%
  - Extrapyramidal: 1%

- **Ziprasidone**
  - Efficacy: 59%
  - Weight Gain/Metabolic: 3%
  - Extrapyramidal: 17%

2. Decision Resources, 2009 (n=75), U.S.-based psychiatrists
Olanzapine Market Share 20% Despite Significant Metabolic Side Effects

U.S. Atypical Antipsychotic TRxs for Schizophrenia

- Other Atypical Antipsychotics: 75%
- Long-Acting Injectables: 5%
- ZYPREXA®/Olanzapine: 20%

Sources: IMS Health MAT Nov. 2014; Encuity 2014
ALKS 3831: Straightforward Pivotal Program

- Four-week efficacy study evaluating antipsychotic properties of ALKS 3831 in patients with acute schizophrenia
  - Primary endpoint: Reduction in PANSS total score compared to placebo
  - Study will include active olanzapine comparator
  - Expected to enroll ~390 patients, planned to begin in Q4 2015

- Six-month study evaluating weight-attenuating effects of ALKS 3831 compared to olanzapine, similar to highly successful phase 2 program
  - Primary endpoint: Change in percent bodyweight from baseline
  - Expected to enroll ~500 patients with stable schizophrenia, planned to begin Q1 2016

- Each will roll over into longer-term safety studies
ALKS 8700: A Novel Entrant in a Growing MS Market
12.3 Pharmacokinetics

After oral administration of TECFIDERA, dimethyl fumarate undergoes rapid presystemic hydrolysis by esterases and is converted to its active metabolite, monomethyl fumarate (MMF). Dimethyl fumarate is not quantifiable in plasma following oral administration of TECFIDERA. Therefore all pharmacokinetic analyses related to TECFIDERA were performed with plasma MMF concentrations. Pharmacokinetic data were obtained in subjects with multiple sclerosis and healthy volunteers.

Source: TECFIDERA prescribing information
ALKS 8700: Novel, oral, twice-daily molecule designed to metabolize into monomethyl fumarate (MMF) with differentiated features vs. TECFIDERA® (DMF)

Initial pharmacokinetic (PK) bridging data met criteria for bioequivalence to TECFIDERA announced Oct. 2015

- Randomized, double-blind, crossover study evaluated plasma MMF levels of single doses of ALKS 8700 and TECFIDERA in 35 healthy volunteers
- Most common adverse events:
  - ALKS 8700: Flushing, dizziness and constipation
  - TECFIDERA: Flushing, nausea and diarrhea
Following FDA meeting, agreement that 505(b)(2) strategy referencing TECFIDERA® is appropriate regulatory pathway; registration program will include:

- PK bridging studies to demonstrate bioequivalence of ALKS 8700 to TECFIDERA
- Two-year, phase 3 safety study
  - ~600 patients with MS
  - Planned to begin in Q4 2015

Will conduct additional head-to-head gastrointestinal tolerability study comparing ALKS 8700 and TECFIDERA

- ~420 patients
- Planned to begin in mid-2016

Alkermes expects to complete these studies and file NDA in 2018
ALKS 7119: Multivalent NCE for the Treatment of Multiple Psychiatric Indications
ALKS 7119: Informed by Molecular and Clinical Precedents

- Oral, small-molecule NCE for treatment of agitation in Alzheimer’s disease (AD), treatment-resistant depression (TRD) and other psychiatric conditions

- Based on clinical observations of effects of “NMDA antagonism” and SSRIs
  - Dextromethorphan + Quinidine: Agitation in AD, TRD
  - Ketamine (and analogs): TRD
  - Citalopram (SSRI): Agitation in AD

- Designed for optimized pharmacology and favorable ADME properties
  - “Low-trapping” NMDA antagonist with serotonin reuptake inhibition
  - 10-fold increased oral bioavailability in rats and dogs vs. dextromethorphan
Alzheimer’s disease: A large and growing medical issue

- Approximately 5.2 million patients in the U.S. in 2014\(^1\)
- Growing with the aging of baby boomer generation

Psychiatric symptoms, not cognitive decline, are the leading source of morbidity and caregiver burden in Alzheimer’s disease\(^2\)

Major unmet need expressed by physicians and caregivers

- Physicians reluctantly use antipsychotics to sedate patients despite safety concerns, including black box warning

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ALKS 7119: Advancing Into the Clinic

- IND-enabling studies completed
- Manufacture of GMP clinical supplies ongoing
- Plan to initiate phase 1 program in Q1 2016
  - First studies: Single- and multiple-dose safety studies in normal volunteers and healthy elderly
  - Extensive neuropsychiatric assessments to provide early indications of activity
- Target indications: Agitation in Alzheimer’s disease and treatment-resistant depression
Key Value-Creating Inflection Points Expected in 2015

CNS Pipeline
✓ ALKS 8700: Phase 1 data
☐ ALKS 8700: Start registration program
✓ ALKS 3831: Phase 2 six-month data in weight attenuation
☐ ALKS 3831: Start pivotal program
☐ ALKS 5461: FORWARD progress and data readouts
✓ Disclose new candidate (ALKS 7119)
☐ Data presentations at medical and scientific forums

Proprietary Commercial Portfolio
✓ ARISTADA™: FDA approval and launch
☐ VIVITROL®: Expansion of criminal justice and state programs