Developing Breakthrough Therapies for Rare Inflammatory and Fibrotic Diseases

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Overview

Focus on rare, chronic, serious inflammatory and fibrotic diseases

Anabasum | First-in-class oral synthetic endocannabinoid mimetic

Phase 3 SSc Study | Expected Start
Q4 2017

Positive Phase 2 data in 3 indications

Multiple value-driving milestones expected in Q4 2017

Intellectual Property | 2034

Expected Start | Q4 2017

Positive Phase 2 data in 3 indications

Multiple value-driving milestones expected in Q4 2017

Intellectual Property | 2034
### Anabasum Pipeline: Multiple Opportunities in Rare Autoimmune / Inflammatory / Fibrotic Diseases

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patient Population</th>
<th>Phase of Development</th>
<th>Orphan Designation</th>
<th>Fast Track Status</th>
<th>Open-Label Extension</th>
<th>Nondilutive Funding</th>
<th>Next Catalyst</th>
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<tbody>
<tr>
<td><strong>Autoimmune</strong></td>
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<tr>
<td>Systemic Sclerosis (SSc)</td>
<td>90,000 (US+EU)</td>
<td>Launch Phase 3</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Plan to commence Phase 3 study Q4 2017</td>
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<tr>
<td>Dermatomyositis (DM)</td>
<td>70,000 (US)</td>
<td>Positive Phase 2</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>Positive Topline Phase 2 data reported Q4 2017</td>
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<td>Systemic Lupus Erythematosus (SLE)</td>
<td>500,000 (US+EU)</td>
<td>Launch Phase 2</td>
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<td>✓</td>
<td>✓ NIH Funded₁</td>
<td>Plan to commence Phase 2 study Q4 2017</td>
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<td><strong>Genetic / Inflammatory</strong></td>
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<tr>
<td>Cystic Fibrosis (CF)</td>
<td>75,000 (worldwide)</td>
<td>Launch Phase 2b</td>
<td>✓</td>
<td>✓</td>
<td>✓ CF Foundation²</td>
<td></td>
<td>Plan to commence Phase 2b study by EoY 2017</td>
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</table>

1) NIH grants fund Phase 2 trials of anabasum in dermatomyositis and systemic lupus erythematosus; Corbus retains all rights to the product and owns the IND data
2) Awarded 2015; project completed
Normal Inflammatory Process vs. Chronic Inflammation

Normal Inflammation Process

- Activation
- Resolution

Immune System Returns to Homeostasis

Inflammatory / Fibrotic Disease

- Activation
- Chronic Inflammation / Fibrosis

Immune System is Unable to Return to Homeostasis, Leading to Fibrosis
Anabasum Promotes Resolution of Inflammation and Fibrotic Responses

Resolution of Chronic Inflammation and Fibrosis

Inflammation / Fibrosis

Activation

CB2

Homeostasis

Time

MOA Applicable to Multiple Inflammatory / Fibrotic Diseases
Endocannabinoids Play a Unique Role in Inflammation and Fibrosis

MOA of CB2 agonism: triggers resolution of inflammation

1 Shinohara 2012
The Endocannabinoid System Has a Dual Role

Central Nervous System

- CB1 receptors are mostly found in the brain
  - Pain
  - Nausea
  - Spasms
  - Appetite

Immune System

- CB2 receptors are mostly within the immune system
  - Immune modulation
Attractive Candidate for Rare + Chronic Inflammatory / Fibrotic Diseases

High
• CB2 Binding Affinity (Pro-resolution receptors in the immune system)

Low
• CB1 Binding Affinity (Analgesic receptors in the brain)
  • Blood Brain Barrier Penetration

Targeting Inflammation Without Immunosuppression and Limited CNS Activity
Diffuse Cutaneous Systemic Sclerosis:

- Positive Phase 2 data
- Ongoing open-label extension
- Phase 3 study planned for Q4 2017
- Potential approval in 2020
Systemic Sclerosis
Chronic systemic autoimmune disease causing fibrosis of skin and internal organs

90,000 Patients in U.S. + EU
80% Female patients
40-60 Years Average age of patients

Lung Fibrosis Common cause of death - 40%-60% mortality in 10 years

Key Takeaways
Life-threatening, rare disease
No SSc-specific drugs approved
Current therapy: Immunosuppressive agents (safety risk)
Need for proven safe and effective therapies
Design of Phase 2 Study

Positive Results of Double-blinded, Placebo-controlled Portion of Trial Reported in November 2016

Primary Endpoints:
- Safety and tolerability
- ACR CRISS

Secondary Endpoints:
- ACR-CRISS domains: mRSS; FVC % predicted; PtGA; MDGA; HAQ-DI
- Patient-reported outcomes

43 Adults
2:1 overall ratio of anabasum:placebo

9 clinical sites across the U.S.

Double-blind randomized, placebo-controlled

16 week study – 12 week active dosing

Weeks 1-4
- 5 mg QD
- 20 mg QD
- 20 mg BID
- Placebo

Weeks 5-12
- 20 mg BID
- Placebo
Safety and Tolerability Summary

• Anabasum was well tolerated

• No serious or severe anabasum-related TEAEs noted

• Most common adverse events were mild/moderate:
  - Dizziness (22% in anabasum-treated subjects vs. 13% in placebo-treated subjects)
  - Fatigue (19% in anabasum-treated subjects vs. 7% in placebo-treated subjects)
mRSS: Skin Thickening Improved

Primary Endpoint in Planned Phase 3 Study

![Graph showing mRSS Change from Baseline]

- mRSS Change from Baseline: Anabasum vs Placebo
- Change in mRSS, LS means ±SE
- Week: 0, 4, 8, 12, 16
- P = 0.085
- Minimal Important Improvement
- Reduction = improvement
Improved Patient Reported Skin Symptoms

• Greater improvement in skin symptoms than placebo-treated subjects
• Improvements were seen as early as 4 weeks with anabasum treatment

2: Efficacy population, least squares means ± SE, analysis of covariance model, one-sided p-value.
Additional Efficacy Outcomes Favor Anabasum

1: P-values are based on LS mean difference, one-sided p-values shown if P ≤ 0.10 (pre-specified)
Improvements in ACR-CRISS Scores

**Median ACR CRISS Score**

\[ P^1 = 0.044 \]

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Anabasum (n=26)</th>
<th>Placebo (n=15)</th>
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<tbody>
<tr>
<td>4</td>
<td>3.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>8</td>
<td>19.0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>12</td>
<td>27.5%</td>
<td>1.0%</td>
</tr>
<tr>
<td>16</td>
<td>33.0%</td>
<td>1.0%</td>
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</tbody>
</table>

1: LOCF, 1 sided mixed model using rank transformed data; 2: 25th percentile, 75th percentile
On Target Effect: Anabasum Reduces *Inflammation* in Skin (Histology Analysis)

Change in *inflammation* after only 12 weeks of treatment

**Placebo**
- 69% Worsened
- 16% Unchanged
- 15% Improved

$\Delta mRSS = -1.2$

**Anabasum**
- 48% Worsened
- 38% Unchanged
- 14% Improved

$\Delta mRSS = -5.1$

$P = 0.008$ Fisher’s exact test two-sided
On Target Effect: Anabasum Reduces \textit{Fibrosis} in Skin (Histology Analysis)

Change in \textit{fibrosis} after only 12 weeks of treatment

- **Placebo**:
  - Worsened: 46%
  - Unchanged: 15%
  - Improved: 39%
  - $\Delta mRSS = -1.8$

- **Anabasum**:
  - Worsened: 9%
  - Unchanged: 48%
  - Improved: 43%
  - $\Delta mRSS = -4.0$

$P = 0.049$ (Fisher’s exact test two-sided)
Planned Design of Upcoming Phase 3 Study

Phase 3 Study Scheduled to Commence Q4 2017

~ 350 Subjects
1:1:1 overall ratio of anabasum:placebo

Multinational

Double-blind randomized, placebo-controlled

52 week study

Dosing

20 mg BID or 5 mg BID or placebo

Primary Endpoint:
• Change from baseline in mRSS

Secondary Endpoints:
• Change from baseline in HAQ-DI
• ACR CRISS
• Change from baseline in FVC % predicted
• Safety and Efficacy of Anabasum (JBT-101) in Diffuse Cutaneous Systemic Sclerosis (dcSSc) Subjects Treated in An Open-Label Extension of Trial JBT101-SSc-001

• Prospective Validation of the Scleroderma Skin Patient-reported Outcome (SSPRO) in a Phase 2 Trial of Anabasum (JBT-101) in Diffuse Cutaneous Systemic Sclerosis (dcSSc)

• Anabasum (JBT-101) Enhances Resolution of Inflammation in Humans

• Effect of Anabasum (JBT-101) on Gene Expression in Skin Biopsies from Subjects with Diffuse Cutaneous Systemic Sclerosis (dcSSc) and the Relationship of Baseline Molecular Subsets to Clinical Benefit in the Phase 2 Trial

• A Phase 2 Study of Safety and Efficacy of Anabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist in Diffuse Cutaneous Systemic Sclerosis
Cystic Fibrosis:

- Positive Phase 2 data
- Support from the Cystic Fibrosis Foundation
- Expect to commence Phase 2b study in Q4 2017
Cystic Fibrosis
CF is a life-threatening, genetic disease that primarily affects the lungs and digestive system. CF is characterized by chronic lung inflammation that leads to lung damage and fibrosis.

30,000 Patients in the U.S.
75,000 Patients worldwide
40 Years Average life expectancy of CF patients

Key Takeaways
- Life-threatening, rare disease
- Inflammation and fibrosis play key role in CF morbidity and mortality
- Need for safe and effective drugs that target chronic inflammation and fibrosis is unmet and recognized
- Pharmacoeconomics are proven and favorable
PEx
PULMONARY EXACERBATIONS

Cost
$95,000 per episode

Annual rate
~17,000

Multiple PEx per year

Frequency, severity increase with age and FEV1 impairment*

* (Rubin-Cahill et al. 2015)

Dangerous manifestation of lung disease

Shortness of breath, cough, sputum production and reduced FEV1

Increased inflammation precedes PEx

Irreversible lung function loss, including FEV1
Design of Completed Phase 2 Study

Positive Data Announced March 2017

85 Adults 21 clinical sites across the U.S. and Europe

5:2 overall ratio of anabasum:placebo

Double-blind randomized, placebo-controlled

16 week study – 12 week active dosing

Primary Objectives:
- Evaluate safety and tolerability
  - Pulmonary exacerbations are an event of special interest

Secondary Objectives:
- FEV1 % predicted, lung clearance index and CFQ-R
- Blood and sputum biomarkers
- Microbiome in sputum
- Metabolipidomic profile
- Pharmacokinetics

58 Adults

21 clinical sites across the U.S. and Europe

5:2 overall ratio of anabasum:placebo

Double-blind randomized, placebo-controlled

16 week study – 12 week active dosing

Primary Objectives:
- Evaluate safety and tolerability
  - Pulmonary exacerbations are an event of special interest

Secondary Objectives:
- FEV1 % predicted, lung clearance index and CFQ-R
- Blood and sputum biomarkers
- Microbiome in sputum
- Metabolipidomic profile
- Pharmacokinetics
Safety and Tolerability Summary

- Anabasum was well tolerated
- No serious or severe anabasum-related TEAEs noted
- Most common anabasum-related mild adverse event:
  - Dry mouth (mild, 13% vs 0% in placebo)
- FEV-1 remained stable throughout the study across all cohorts
Clear reduction in rate of PEx treated with IV antibiotics for anabasum
Clear reduction in rate of PEx treated with any new antibiotic for anabasum

Rate of Pulmonary Exacerbations Requiring New Antibiotics

### Weeks 1-4

- **Placebo**: 0.77
- **1 mg**: 0.35
- **5 mg**: 0.38

- **Placebo**: 0.46
- **20 mg**: 0.25
- **20 mg bid**: 0.21
Consistent Reduction in Key Inflammatory Biomarkers (Sputum)

Reduction with anabasum 20 mg BID compared to placebo ($\log_{10}$)

- Neutrophils, cells/ml: $-0.70, p = 0.043$
- Eosinophils, cells/ml: $-0.61, p = 0.07$
- Lymphocytes, cells/ml: $-1.34, p = 0.033$
- Macrophages, cells/ml: $-0.23, p = 0.037$
- Neutrophil elastase, cells/ml: $-0.19, p = 0.033$
- IL-8, pg/ml: $-0.19, p = 0.033$
- IgG, mg/dl

Least squares mean difference from placebo (SE), $\log_{10}$
Presenting Three Abstracts at NACFC - November 2-4, in Indianapolis, IN

• A Double-Blind, Placebo Controlled Phase 2 Study in Adults with Cystic Fibrosis of Anabasum, A Selective Cannabinoid Receptor Type 2 Agonist

• Anabasum Reduces Excessive Inflammatory Responses in Cystic Fibrosis Patient-Derived Lung Macrophages

• Anabasum Enhances Resolution of Bacterial-Induced Inflammation in Healthy Humans
Dermatomyositis:

- Positive Topline Phase 2 data
- Late-breaking data to be presented at ACR
- Ongoing open-label extension
**Dermatomyositis**
Chronic systemic autoimmune disease characterized by inflammation of skin and muscles

70,000
Patients in the U.S. + EU

**Skin & Muscle**
Involvement can cause significant morbidity and mortality from interstitial lung disease

**No FDA**
Approved therapies for overall disease activity

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**Key Takeaways**

- Treated with immunosuppressive therapies, but with significant toxicities
- Single center study underway at University of Pennsylvania
- Collaborating with NIH
Dermatomyositis Phase 2 Clinical Study

Positive Topline Data Announced October 2017

22 Adults

1 Site - University of Pennsylvania Perelman School of Medicine

1:1 overall ratio of anabasum:placebo

Double-blind randomized, placebo-controlled

16 week study – 12 week active dosing

Primary Endpoints:
- Safety/tolerability
- Change in skin activity using CDASI

Secondary Endpoints:
- Quality of life and disease activity outcomes
- Biomarkers of inflammation and disease activity in blood and skin
- Metabolipidomic profile

22 Adults randomly assigned

1 Site - University of Pennsylvania Perelman School of Medicine

1:1 overall ratio of anabasum:placebo

Double-blind randomized, placebo-controlled

16 week study – 12 week active dosing

Primary Endpoints:
- Safety/tolerability
- Change in skin activity using CDASI

Secondary Endpoints:
- Quality of life and disease activity outcomes
- Biomarkers of inflammation and disease activity in blood and skin
- Metabolipidomic profile

20 mg QD or placebo

20 mg BID or placebo
Safety and Tolerability Summary

• Anabasum was well tolerated and demonstrated a favorable safety profile
• No evidence of immunosuppression
• No serious or severe side effects related to anabasum
• No subjects dropped out of the study
CDASI was developed to measure multiple inflammatory elements in the skin\(^1\)

Disease Severity

\[0 \quad \text{CDASI SCALE} \quad 48\]

4-5 Point Decrease in score is considered clinical improvement
Anabasum improved CDASI by 9.3 vs. 3.7 for placebo; p = 0.04, 2-sided MMRM
Additional Efficacy Outcomes Favor Anabasum

Patient Skin Global

- Mean change from Day 1 (SE)
- Weeks Completed: 0, 4, 8, 12, 16
- Placebo vs. Anabasum
- Improvement: Placebo vs. Anabasum
- P-values: 0.06, 0.04, 0.04
- 20 mg QD, 20 mg BID, Post

Skindex-29 Symptoms

- Mean change from Day 1 (SE)
- Weeks Completed: 0, 4, 8, 12, 16
- Placebo vs. Anabasum
- Improvement: Placebo vs. Anabasum
- P-values: 0.09, 0.03, 0.10, 0.09
- 20 mg QD, 20 mg BID, Post

PROMIS-29 Pain Interference

- Mean change from Day 1 (SE)
- Weeks Completed: 0, 4, 8, 12, 16
- Placebo vs. Anabasum
- Improvement: Placebo vs. Anabasum
- P-values: 0.05, 0.07, 0.02
- 20 mg QD, 20 mg BID, Post

PROMIS-29 Physical Function

- LS Mean change from Day 1 (SE)
- Weeks Completed: 0, 4, 8, 12, 16
- Anabasum
- Improvement: Anabasum
- P-values: 0.005, 0.02
- 20 mg QD, 20 mg BID, Post

CDASI Damage Index

- LS Mean change from Week 4 (SE)
- Weeks Completed: 4, 8, 12, 16
- Anabasum 20 mg BID
- Improvement: Anabasum 20 mg BID
- P-values: 0.09, 0.23, 0.04
- 20 mg BID, Post

P-values = 1-sided, MMRM, anabasum vs. placebo, change from end of Week 4

P-values = 1-sided, MMRM, anabasum vs. placebo, change from Day 1

P-values = 1-sided, MMRM, anabasum vs. placebo, change from Week 4
Strong Evidence of Clinical Benefit Merits Further Development in Dermatomyositis

• First potential treatment for skin-predominant dermatomyositis to show clinical benefit in a double-blind, randomized, placebo-controlled trial

• Data selected for Late-Breaking Presentation at ACR on November 7, 2017
  - A Phase 2 Study of Safety and Efficacy of Anabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist, in Refractory Skin-Predominant Dermatomyositis
  - Additional ACR abstract: Comparison of Patients with Dermatomyositis in a Specialty Clinic Versus Clinical Trial with Anabasum (JBT-101), a Cannabinoid Receptor Type 2 Agonist

• Will meet with regulatory authorities to review data and determine next steps in clinical development plan
Management Team

Yuval Cohen, PhD
*Chief Executive Officer, Director*

Co-founder and former President of Celsus Therapeutics (CLTX). Expertise in developing anti-inflammatory drugs including for CF

Sean Moran, CPA, MBA
*Chief Financial Officer*

Former CFO: InVivo (NVIV), Celsion (CLSN), Transport Pharma, Echo Therapeutics (ECTE) & Anika Therapeutics (ANIK)

Mark Tepper, PhD
*President & Chief Scientific Officer*

Former VP U.S. Research & Operations, EMD Serono; Sr. Investigator, Bristol-Myers Squibb

Barbara White, MD
*Chief Medical Officer*

Board-certified Rheumatologist and clinical immunologist. Previously SVP and Head, R&D Stiefel, a GSK company, VP and Head of Immunology Therapeutic Area for UCB, VP and Senior Director of Clinical Development for MedImmune, and Director of Medical Affairs, Inflammation Therapeutic Area for Amgen
Board of Directors

Amb. Alan Holmer Ret.- Chairman of the Board
- Former CEO of PhRMA (1996-2005)
- Over two decades of public service in Washington, D.C. including Special Envoy to China (2007-2009)
- Former board member of Inspire Pharma
- Chairman of the Board of the Metropolitan Washington, D.C. Chapter of the Cystic Fibrosis Foundation

Avery W. (Chip) Catlin
- CFO Celldex Therapeutics (CLDX) since 2000
- Over 20 years experience in industry: Repligen (CFO) and Endogen (CFO)

David Hochman
- Managing Partner of Orchestra Medical Ventures
- Over 19 years of venture capital and investment banking experience
- Former Managing Director of Spencer Trask Ventures, Inc.

Renu Gupta, MD
- Over 25 years of R&D, regulatory and senior management experience in the biopharma industry
- Former EVP, and CMO of Insmed, a specialty CF company
- Former VP and Head of U.S. Clinical Research and Development, Novartis
- Senior Advisor to CEOs and Boards of biopharma

Paris Panayiotopoulos
- Former President and Chief Executive Officer and a member of the Board of Directors of ARIAD Pharmaceuticals, Inc., which was acquired by Takeda Pharmaceuticals for $5.2 billion
- Former President of EMD Serono, Inc., President of the Serono Research and Development Institute and President of Merck Serono, Tokyo, Japan
- Has led multiple partnerships, including those with Pfizer Inc., Bristol-Myers Squibb Company, Eli Lilly and Company, Sumitomo Dainippon Pharma Co., Ltd., Mitsubishi Tanabe Pharma Corporation, Otsuka Pharmaceutical Co. Ltd. and Incyte Corporation
<table>
<thead>
<tr>
<th>Scientific Advisors</th>
<th>Principal Investigators</th>
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<tbody>
<tr>
<td>Michael Knowles, MD</td>
<td>Robert Spiera, MD</td>
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<tr>
<td>Charles Serhan, PhD</td>
<td>Christopher Denton, PhD, FRCP</td>
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<td></td>
<td>James Chmiel, MD</td>
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<td></td>
<td>Stuart Elborn, MD, FRCP</td>
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<td>Victoria Werth, MD</td>
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<td>Meggan Mackay, MD</td>
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Expected Milestones in Q4 2017

**SSc**
- Launch Phase 3 study
- Interim data from open-label study
- Phase 2 Data to be presented at ACR-17

**CF**
- Expected launch of Phase 2b study
- Phase 2 data to be presented at NACFC-17

**DM**
- Reported positive topline Phase 2 data

**SLE**
- Start Phase 2 study
Financial Profile: CRBP (NASDAQ)

- $346MM Market cap*
- 50.2MM Common shares outstanding (59.3MM fully diluted)**
- $78MM Raised to-date + $20MM non-dilutive funding from N.I.H. and CF Foundation
- 596K 3 month average daily volume*
- $43MM Cash balance**

* Based on October 24, 2017 closing price of $6.90 per share
** As of June 30, 2017
Focused on rare diseases with no current approved therapies

First-in-class drug targeting inflammation + fibrosis

Positive Phase 2 data in 3 indications

Solid execution with multiple milestones expected in Q4 2017
Corbus Pharmaceuticals Holdings, Inc.

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