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Delivering powerful new treatment approaches

Our lead asset, itolizumab, is unique, modulating both the activity and trafficking of $T_{eff}$ cells.

Focused on immuno-inflammatory diseases with high unmet need

Initial clinical programs are targeting diseases with limited or no treatment options.

Driven by an accomplished team rapidly delivering key milestones

Successful 2018 IPO; launching multiple clinical PoC studies in 2019.
Accomplished Management Team

Dan Bradbury  
Chairman & Chief Executive Officer

Bruce Steel, CFA  
President & Chief Business Officer

Steve Connelly, PhD  
Chief Scientific Officer

Krishna Polu, MD  
Chief Medical Officer

Jason Keyes  
Chief Financial Officer

Christine Zedelmayer  
Vice-President of Operations
**CD6/ALCAM Role in Immuno-inflammatory Disease**

- **Teff cells** play an important role in the pathogenesis of T cell mediated diseases driving autoimmune and allergic inflammation.

**Initial Indications**

- **Acute Graft-Versus-Host Disease**
- **Chronic Graft-Versus-Host Disease**
- **Uncontrolled Asthma**
- **Interstitial Lung Diseases**
- **Chronic Obstructive Pulmonary Disease**
- **Multiple Sclerosis**
- **Neuromyelitis Optica**
- **Transplant Science**
- **Psoriasis**
- **Uveitis**
- **Lupus/Lupus Nephritis**
- **Vasculitis**
- **Scleroderma**
- **Behcet’s Disease**
- **Rheumatoid Arthritis**
- **Psoriatic Arthritis**
- **Ulcerative Colitis**
- **Lupus**
- **Optica**
- **Solid Organ Rejection**
- **Crohn’s Disease**
- **Dermatological**
- **Gastrointestinal**
- **Systemic Autoimmunity**

**Research implicates CD6/ALCAM pathway in disease pathogenesis**

**T cell mediated diseases**
Itolizumab (EQ001) – First-in-class Lead Program

First-in-class anti-CD6 mAb that inhibits the activity and trafficking of T_{eff} cells by selectively targeting the CD6/ALCAM pathway

- Unique, multi-modal mechanism with potential disease modifying utility

- Broad potential ‘pipeline in a product’ - launching multiple clinical studies during 2019

- Demonstrated clinical tolerability and efficacy - approved for the treatment of psoriasis in India

Equillium acquired exclusive rights to itolizumab for the U.S. & Canada from Biocon - partnership provides clinical & commercial product, commercial scale production at FDA regulated facility
Itolizumab Development Strategy

Equillium is well-capitalized and staffed to execute on key programs

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<td>• Data to inform further development in GVHD, e.g. GVHD prevention, cGVHD</td>
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The CD6/ALCAM Pathway
CD6 is a co-stimulatory receptor expressed on T cells, differentially expressed on subsets of innate lymphoid (ILC) and natural killer (NK) cells, but not on T regulatory cells (T_{reg}).

Activated leukocyte cell adhesion molecule (ALCAM), is expressed on both antigen-presenting cells and endothelial/epithelial tissue including the blood-brain-barrier, skin, gut, lung and kidney.

The binding of CD6/ALCAM is important for:
- Immune synapse formation
- Optimal co-stimulation and activation
- Trafficking into tissues

The CD6/ALCAM pathway modulates T cell activity and trafficking and is central to the pathogenesis of multiple immuno-inflammatory diseases.
Itolizumab Modulates CD6/ALCAM Pathway

**Itolizumab**
- Humanized IgG1 Kappa
- Binds to domain 1 of human CD6 with 1.3 nM affinity
- Inhibits ALCAM binding to CD6
- Non-depleting, modulatory action

**Manufacturing and formulation**
- Manufactured in CHO cells at commercial scale
- IV and SC formulations available

**Dosing**
- Half-life IV/SC @ 20/24 days respectively; target dosing of bi-weekly to monthly with potential for quarterly maintenance
CD6 – Central Role in Effector Cell Development

Highest levels of CD6 are found on activated T effector cells (T\textsubscript{eff}) and associated with amplification of the auto-reactive cascade.

- **CD6 Low/-**: T\textsubscript{reg} with weak signalling.
- **CD6 +**: T\textsubscript{naive} with strong signalling.
- **CD6 Hi**: T\textsubscript{eff} with Th\textsubscript{1}, Th\textsubscript{2}, Th\textsubscript{17}.

Immune Regulatory “Tolerance”

Autoreactive “Autoimmunity”
CD6/ALCAM Pathway Central to Immuno-inflammation

**ACTIVITY**

- Increased proinflammatory cytokine secretion
  - TNF-α, IL-6, IL-13, IL-17, IL-5
- Suppression of regulatory pathways
  - Treg

**TRAFFICKING**

- Increased trafficking of T_{eff} cells into target tissues
  - T_{eff} T_{1}, T_{2}, T_{17}

Optimal immune synapse formation, activation and proliferation

Suppression of regulatory pathways
Itolizumab Inhibits Pathogenic T Cell Activity & Trafficking

**ACTIVITY**
- Decreased proinflammatory cytokine secretion
- Restored regulatory pathways
- Inhibits optimal synapse formation co-stimulation, activation and proliferation

**TRAFFICKING**
- Decreased trafficking of $T_{eff}$ cells into target tissues
- Restoration of regulatory pathways
Itolizumab acts upstream and selectively targets autoreactive effector T cells, while sparing regulatory T cells to promote immune tolerance and durable disease remission.

- Synergistic inhibition of multiple T_{eff} cells and cytokines*
- Inhibition of T_{eff} trafficking into key target organs
- Restoration of immune regulation without immunosuppression

*including but not limited to IFN-γ, TNF-α, IL-4, IL-5, IL-6, IL-13 and IL-17
Clinical Strategy
Acute graft-versus-host disease (aGVHD)

A multisystem complication of allogeneic hematopoietic stem cell transplants, or allo-HSCT, caused by T_{eff} cells, recognizing and attacking the recipient’s body.

- 8,500 Allo-HSCT’s performed in 2016
- 4% procedural growth year-over-year
- 30-70% Allo-HSCT patients will develop aGVHD
- 53% Survival rate for steroid responders
- 95% Mortality rate for steroid non-responders
- 0 Number of approved treatments
- 2 Number of products in development for first-line aGVHD
- 1 Product in development that modulates both the activity and trafficking of T_{eff} cells - itolizumab

All numbers are approximate and based on published reports.
Itolizumab is a Differentiated aGVHD Treatment Option

**Acute GVHD**
0-100 days post-transplant

- **Prevention**
  - Takeda: ENTYVIO® (Phase 3)
  - CSL Behring: ZEMAIRA® (Phase 3 ready)
  - Jazz Pharmaceuticals: DEFITELIO® (Phase 2)
  - Kalytera: Cannabidiol (Phase 2a)

- **First-line**
  - equillium: Itolizumab (Phase 1b/2)
  - Incyte: Itacitinib (Phase 3)

- **Steroid-Refractory**
  - JAKARI® + sNDA
  - Imesoblast® + PROCYMAL® + BLA
  - T-Guard™ + Xenikos

**First line positioning**

- **Dual mode of action** inhibits the activity and trafficking of T_{eff} cells
- Potential disease-modifying therapy with **durable benefit**
- **Immunomodulatory** and not immunosuppressive
- **No cytopenias** seen in Biocon Phase 3 psoriasis studies
- Positive Phase 1b data will inform lifecycle opportunity in GVHD prevention and cGVHD
Strong Scientific Rationale for Itolizumab in aGVHD

**Scientific Rationale**
- $T_{h,17}$ cells expressing CD6 play a critical role in the pathogenesis of aGVHD
- $T_{h,17}$ cells are **steroid resistant**
- ALCAM expressed on target organs facilitates infiltration of CD6+ T$_{eff}$ cells
- Studies have shown a high $T_{h,17}$:$T_{reg}$ ratio indicative of a loss of tolerance in aGVHD patients

**Translational Validation**
- Itolizumab shown to be effective in animal models of GVHD and inflammatory bowel disease (IBD)
- *Ex vivo* depletion of CD6+ T$_{eff}$ cells from donor bone marrow prior to allogeneic transplant effectively reduced GVHD incidence
- CD6+ T cells in drive $T_{h,1}/T_{h,17}$ immune responses and mucosal inflammation in IBD

**Clinical Development**
- FDA Fast Track for treatment of aGVHD and Orphan Drug Designations for both the prevention and treatment of aGVHD
- Phase 1b/2 aGVHD trial initiated in Q1 2019
- Data to inform further development in GVHD, e.g. GVHD prevention, cGVHD

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EQUATE Study for First-line Treatment of aGVHD Patients

Study Population: First-line treatment of newly diagnosed aGVHD patients

Study Design
- Phase 1b N~24 (high-risk MacMillan criteria)
  - Open-label, 3x3, dose escalation
  - Cohort 1: 0.4 mg/kg
  - Cohort 2: 0.8 mg/kg
  - Cohort 3: 1.4 mg/kg
  - Cohort 4: 2.4 mg/kg
- Phase 2 N~60 (Grade II – IV)
  - Randomized, double-blind, placebo controlled

Primary Objectives
- Assess the safety and tolerability of intravenous (IV) dosing of itolizumab
- Determine optimal IV dose level(s) of itolizumab

Secondary Objectives
- Characterize the pharmacokinetics (PK) and pharmacodynamics (PD) of itolizumab
- Assess the clinical activity of itolizumab (GVHD ORR, NRM, cGVHD, durability)
- Further characterize the safety, tolerability and PD of intravenous (IV) dosing of itolizumab

Phase 1b topline expected Q1 2020
Phase 1b informs Phase 2 study as well as lifecycle strategy that may include GVHD prevention and cGVHD
Uncontrolled moderate to severe asthma

A heterogeneous disease characterized by different $T_{eff}$ cell subtypes and other innate immune cells driving both allergic and autoimmune mechanisms, leading to chronic airway inflammation.

2.6mm

Uncontrolled moderate to severe asthma

1.3mm

~50%

Severe asthma patients in the U.S.

Patients uncontrolled by standard-of-care treatments (long-acting beta-agonists, inhaled corticosteroids, oral corticosteroids)

Of uncontrolled patients do not respond to existing biologic treatments

Approved products that cover the full spectrum of disease ($T_{h,2}$ High – Non-$T_{h,2}$ asthma)

Products in development that target Non-$T_{h,2}$ asthma

Product in development that modulates both the activity and trafficking of $T_{eff}$ cells – itolizumab

All numbers are approximate and based on published reports.
Itolizumab May Address The Full Spectrum of Uncontrolled Asthma

- **T_{h}2**
  - TH2-High Eosinophils

- **T_{h}17**
  - TH17-Low Eosinophils

Reciprocally regulated

**Response to steroids**

- Current therapies target downstream signaling of T_{h}2-associated inflammation
- Current downstream therapies ineffective in patients with low levels of eosinophils
- No approved therapies

**Therapies**

- **anti-IgE**
  - Genentech XOLAIR®
  - Marketed

- **anti-IL-5**
  - GSK NUCLARA®
  - Marketed

- **anti-IL-4 and IL-13**
  - REGENERON SANOFI GENZYME DUPIONET®
  - Marketed

- **anti-IL-33**
  - REGENERON RG6149

- **DP2 Agonist**
  - TEVA Fevipiprant AstraZeneca
dubalina

- **anti-CD6/ALCAM**
  - Itolizumab Equilium Phase 1b/2

- **anti-TSLP**
  - AstraZeneca Tezepelumab Phase 3
Itolizumab Targets both T\(_h\)2 and Non-T\(_h\)2 Asthma Pathogenesis

**Scientific Rationale**
- Asthma is a heterogeneous disease with CD6+ T\(_h\)1 (IFN-\(\gamma\)), T\(_h\)2 (IL-4,5,13), T\(_h\)17 (IL-17) and ILC cells and cytokines involved in the pathogenesis
- T\(_h\)17 and ILC cells are steroid resistant
- ALCAM expressed on lung tissues facilitates infiltration of CD6+ T\(_{eff}\) cells
- High T\(_h\)17:T\(_{reg}\) ratio associated with asthma exacerbations

**Translational Validation**
- Modulating CD6-ALCAM pathway attenuates activity and trafficking of T\(_h\)1 (IFN-\(\gamma\)), T\(_h\)2 (IL-4,5,13), T\(_h\)17 (IL-17) cells and cytokines in multiple models of autoimmune and allergic inflammation
- Transcriptional and histological analyses support the presence of increased CD6, CD4 T cells, and ALCAM in the lungs of severe asthma patients

**Clinical Development**
- Uncontrolled moderate to severe asthma proof-of-concept trial to initiate Q2 2019
- Data to inform further development in T\(_h\)2 and non-T\(_h\)2 asthma

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Kim et al., 2028. “Activated leukocyte cell adhesion molecule stimulates the t-cell response in allergic asthma.” American Journal of Respiratory and Critical Care Medicine, 197(8); Li et al., 2017. “CD6 as a potential target for treating multiple sclerosis.” PNAS 114(10): 2687-2692; Bughani et al., 2018. “T cell activation and differentiation is modulated by a CD6 domain 1 antibody itolizumab.” PloS One 12(7): e0180088
CD6 Upregulation and ALCAM Expression in Severe Asthma Patients

Examination of gene expression datasets and lung tissue support the presence of increased CD6, CD4 T cells, and ALCAM in the lungs of severe asthma patients

• Analysis of two different gene expression datasets support the presence of increased CD6, CD4 T cells, and ALCAM in the lungs of severe asthma patients

• Fatal asthma patients lung tissue staining suggests increased numbers of CD6+ cells, upregulation of ALCAM in the lamina propria (mucosa), and co-localization of CD6+ cells with ALCAM expressing tissue

Study of the Mechanisms of Asthma (MAST; NCT00595153); Bronchoscopic Exploratory Research Study of Biomarkers in Corticosteroid-refractory Asthma (BOBCAT) study; Data courtesy of Reynold A. Panettieri, Jr., MD, Rutgers Institute for Translational Medicine and Science
EQUIP Study in Uncontrolled Moderate to Severe Asthma

**Primary Objectives**
- Assess the safety and tolerability of subcutaneous dosing of itolizumab
- Determine optimal subcutaneous dose level(s) of itolizumab

**Secondary Objectives**
- Characterize the pharmacokinetics (PK) and pharmacodynamics (PD) of itolizumab
- Assess the clinical activity of itolizumab (FEV1, ACQ, FeNO, Eos)

**Study Population:** Uncontrolled moderate to severe asthma patients

**Study Design**
- Phase 1b N=32
  - Randomized, double-blind, placebo controlled, dose escalation study

**Phase 1b topline expected H2 2020**

Study to initiate Q2 2019
Lupus nephritis

A heterogeneous disease that is the most frequent and serious manifestation of systemic lupus erythematosus (SLE)

Lupus nephritis patients in the U.S.

100,000

50%-75%

40%

0

9

1

Of patients do not respond to frontline treatments

Of severe, proliferative patients will progress to end-stage renal disease

Approved treatments

Products in development

Product in development that modulates both the activity and trafficking of $T_{eff}$ cells - itolizumab

All numbers are approximate and based on published reports
Current T cell approaches have demonstrated promising efficacy (MMF, Cytoxan), but have significant toxicities and a narrow therapeutic index.

T cells play a central role in the immunopathogenesis of lupus, with aberrant T cell activation and function leading to defective peripheral tolerance.

T cells also secrete pro-inflammatory cytokines, help B cells generate autoantibodies, and maintain disease through accumulation of autoreactive memory T cells.

B cell directed and single cytokine approaches have previously failed in lupus nephritis.

Current T cell approaches have demonstrated promising efficacy (MMF, Cytoxan), but have significant toxicities and a narrow therapeutic index.
Itolizumab Targets Lupus Nephritis Pathogenesis

**Scientific Rationale**

- T_{eff} cells play a central role in the pathogenesis of lupus
- Multiple T_{eff} cells/cytokines, such as T\textsubscript{h}1/IFN-\gamma, T\textsubscript{h}2/IL-4 and T\textsubscript{h}17/IL-17, have been implicated
- Elevated T\textsubscript{h}17 cells are accompanied by a decrease of T\textsubscript{reg} cells, promoting loss of tolerance

**Translational Validation**

- Supportive preclinical models in lupus and lupus nephritis
- Kidney biopsy analysis reveal upregulation of CD6 and ALCAM expression on infiltrating T cells, innate immune cells, and resident renal cells
- Elevation in urinary ALCAM identifies patients with active lupus nephritis

**Clinical Development**

- Lupus nephritis proof-of-concept trial to initiate H2 2019
- Urinary biomarker strategy to inform patient selection strategy
- Data to inform further lifecycle strategy in lupus (e.g. SLE and cutaneous lupus)
Unbiased screening of >1100 urinary proteins identified urinary ALCAM as a strong predictor of disease activity in lupus nephritis patients.

*Performance of urine protein markers in differentiating active lupus nephritis (N=89) from inactive lupus nephritis (N=60) in African American and Hispanic systemic lupus erythematosus patients - UT Southwestern Medical Center, TX.

### Urinary ALCAM Elevated in Active Lupus Nephritis

**Elevations in urinary ALCAM and/or CD6 (Phase 1b)**

**Identify biomarker and differentiate responders (Phase 2 and 3)**

**Companion diagnostic**

**Commercialization**

A number of therapies have been developed in lupus nephritis and SLE that have failed; reasons include:

1. Heterogeneity of patient population
2. Safety / therapeutic index
3. Trial design

Leveraging urinary biomarkers can optimize drug development in lupus nephritis

1. **Address heterogeneity** – determine patient response by CD6/ALCAM urinary levels
2. **Optimize therapeutic index** – urinary biomarkers to optimize dose selection and maximize therapeutic index
3. **Efficient trial design** – urinary biomarker assessments to guide efficacy analysis and enable optionality for regulatory paths forward

“Lupus nephritis is one of the most common and dangerous complications of lupus. Using urinary biomarkers to guide therapeutic development aligns with our strategy of supporting work that will help accelerate delivery of new treatments.”

Kenneth M. Farber, President and CEO of the Lupus Research Alliance

“Lupus nephritis may de-risk lupus nephritis development.”

“Urinary biomarkers may de-risk lupus nephritis development.”

“Leveraging urinary biomarkers can optimize drug development in lupus nephritis.”
Corporate
Biocon partnership provides **risk-mitigated product supply** on attractive terms

- **CMC completed** and itolizumab currently manufactured at commercial scale in **FDA-regulated facility**
- Drug product supplied at **no cost for 3 concurrent orphan indications** until first U.S. approval; all other clinical supply at cost

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Robust IP portfolio and **12-year Biologics Exclusivity**

Strong balance sheet and lean operating model expected to **fund current development programs into 2021**

Exploring multiple opportunities for **strategic pipeline expansion**

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Biologics Exclusivity is subject to significant uncertainty
Summary

First-in-class: Itolizumab is the first antibody targeting the novel CD6/ALCAM pathway for the treatment of severe immuno-inflammatory disorders

Pipeline-in-a-product: Itolizumab has broad potential disease modifying therapeutic utility

Focused Development: Strong scientific rationale and translational validation supporting initial indications in areas of unmet need; launching multiple clinical studies during 2019

High-value partnership: Biocon partnership provides clinical & commercial product, commercial scale production at FDA regulated facility

Accomplished team: Experienced in drug discovery, development and commercialization

EQ financing: Equillium is capitalized and staffed to deliver on key programs into 2021