iCo Therapeutics Inc.

TSX-V: ICO
OTCQB: ICOTF

Bertilimumab/iCo-008 Candidate
Q1 2020 Non-Confidential Presentation
Certain of the statements contained in this presentation are forward-looking statements which involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of the Company, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements.
Bertilimumab/
iCo-008
- Licensed exclusive world-wide rights from Cambridge Antibody Technology (subsidiary of AstraZeneca MedImmune Limited), to develop and commercialize in all indications
- Alexion acquisition of systemic rights to Bertilimumab (iCo-008)
- Human monoclonal antibody against eotaxin-1
- Good safety & clinical history: Phase 1 & 2 (n=126)
- Original license for systemic diseases granted to Immune Pharmaceuticals, terminated, seeking new partnerships
- Two additional Phase 2 clinical studies completed in systemic indications (Bullous Pemphigoid data available, Ulcerative Colitis data pending)
- Phase 2 clinical trials planned in VKC, recent quote from ORA for ocular allergy study
- Fast track designation in the US for bullous pemphigoid
- Orphan designation granted in the US and EU
Bertilimumab: Scientific Rationale
• Bertilimumab is a human monoclonal antibody highly specific to human eotaxin-1
• Eotaxin-1 is also a chemo-attractant for eosinophils, basophils, mast cells and Th2 lymphocytes
• Eotaxin-1 binds with high affinity to Cys-Cys chemokine receptor 3 (CCR3), which is expressed on cells such as eosinophils, basophils, mast cells, dendritic cells and T-helper type 2 cells, these cells constitute the effector cells for eotaxin-1
• The release of eotaxin-1 from certain cells (e.g. epithelial cells, fibroblasts, endothelial cells, T-lymphocytes, monocytes and macrophages), is thought to contribute to the local accumulation of eosinophils in inflammatory conditions (eosinophilia)
Bertilimumab Antibody
Blocks eotaxin-1 from recruiting eosinophils, thereby reducing inflammation.
Bertilimumab
for the treatment of systemic diseases
Bullous Pemphigoid
and Ulcerative Colitis

WWW.ICOTHERAPEUTICS.COM
Bullous pemphigoid (BP):

- Primary objective of the Phase 2 study was to evaluate the safety of bertilimumab.

- Secondary objective was to evaluate the preliminary evidence of clinical efficacy as measured by the BPDAI score (Disease Area Index, a severity outcome measure).

- Study completed in 2018.
Screened 14 subjects, enrolled 11, treated 9

- 2 withdrew consent prior to dosing
- 9 received bertilimumab
- 8 received 3 IV doses of 10 g/kg at biweekly intervals and were followed for 84 days
- 1 received 2 IV doses of 10 g/kg with a biweekly interval and was followed for 60 (following the initial protocol)
- 1 early discontinuation (at day 56)

Safety

- Bertilimumab has been very well tolerated in this study; 8 AEs in 5 subjects
- The SAE was a hospitalization for lower extremity angiography in a subject with peripheral vascular disease and was unrelated to bertilimumab
Efficacy

81% reduction in BPDAI Activity Subscore at day 84 (p=0.015)
- 6 of 7 evaluable subjects achieved a >50% improvement
- 5 of 7 with >70% improvement
- 4 of 7 with >90% improvement

70% reduction in BPDAI Activity Subscore at day 42 (p=0.002)
- 8 of 9 evaluable subjects achieved >50% improvement
- 4 of 9 with >70% improvement
- 1 of 9 with >90% improvement

All six subjects for whom “healing of old lesions” was recorded achieved this by day 28
- Pruritis VAS total score improved 66% by day 42 (p=0.010) and 51% by day 84 (p=0.068)
- ABQOL score improved 37% by day 42 (p=0.051) and 26% by day 84 (p=0.678)
- 4 subjects experienced flares
- 2 of the 3 taper-resistant subjects flared
- One from day 28 to day 56 and had azathioprine 200 mg added (discontinued study at day 56), and the other on d84
- The other two flares were from d42 to d70, and from d56 to d70
- **Ulcerative colitis (UC):** randomized, double blind, placebo-controlled, parallel group, multi-center Phase 2 study, seeking to enroll 42 adult patients with active moderate to severe UC, randomization 2:1

- 3 doses of bertilimumab q2 weeks, 90-day follow-up

- Primary objective of the study is safety and clinical response (UC Mayo Clinic Index) at Day 56

- Secondary objective include mucosal injury, fecal calprotectin (validated inflammation marker), mucosal eotaxin-1 and eosinophil levels, and clinical remission

- Patients are selected based on Mayo score and high levels of tissue eotaxin-1 as well as other standardized clinical criteria

- Developmental path of UC will be determined by the results of the current study

- Study completed, data pending
Systemic competitors:
- Teva Pharmaceutical Industries Ltd., Eli Lily, GlaxoSmithKline plc, and Sanofi S.A./Regeneron Pharmaceuticals Inc. who have drugs targeting conditions involving eosinophils

Ophthalmic (topical) competitors:
- Alcon, Inc., Novartis Ophthalmics (a branch of Novartis Pharmaceuticals Corporation), Santen (acquired Novagali Pharma SA.), Senju
Bertilimumab: Clinical Rationale
Bertilimumab has been administered to 126 patients in phase 1 & 2 studies as well as patients in two additional/current Phase 2 systemic studies.

In these the first studies (n=126) Bertilimumab was well tolerated with no serious adverse events.

No efficacy in ocular allergen challenge - allergen challenge possibly did not provoke a large enough late phase response involving eosinophils, thus the drug could not demonstrate effectiveness; 50% of subjects from two cohorts were withdrawn from the study due to insufficient itch score in both eyes; drug was administered prior to allergen challenge.

We believe clear rationale for other ocular conditions including VKC and AKC.
iCo's Interest is in Ophthalmology: Targeting VKC/AKC

- Clear Technical Rationale
  - Scientific rationale
  - Literature support

- Numbers of patients for clinical trials will be small, even through Phase 3
  - Lower cost
  - Shorter timelines
  - Orphan indication

- No additional toxicology anticipated to move into Phase 2
• VKC is a sight-threatening, deleterious condition
  → Potential for premium pricing
• Chronic, sight-threatening form of ocular allergy
• Potential Orphan Drug status
• May cause severe visual complications
• Predominantly males up to 25 years of age
• Generally reside in warmer, arid, windy climates
• Occurs seasonally but can be perennial
• Prevalence varies by region:
  - approximately 3.2/10000 in Western EU (similar in North America) with 27.8/10000 in Italy
  - main cause of ocular morbidity in Israel
  - high prevalence in Africa (4-5% among children), India, China, Japan, South America - may be a cause of hospital attendance ranging between 3%-6% of patients of all ages and 33%-90% in children and adolescents)
Itchy & Painful

Scratched Cornea
Vision Impairment

Deleterious Condition
• Corneal complications: shield ulcers & keratitis
• Intense itching
• Concomitant with severe photophobia
• Mild to moderate swelling of the conjunctiva
• Foreign-body sensation
• Characteristic ropey, stringy mucous discharge
• Existing therapies primarily aimed at reducing symptoms, preventing serious vision-threatening effects
• Currently, most effective treatment is to eliminate or avoid the allergen

Current Therapies:
• Cold compresses and artificial tears and ointments
• Topical decongestants & antihistamines
• Mast-cell stabilizers can be useful before VKC flares or to keep it under control following acute treatment; often do little to abate symptoms
• NSAIDS may offer relief in moderate cases
• Immunosuppressants may irritate the eye, not very useful for severe forms of VKC, some have a history of safety issues (cyclosporin, tacrolimus)
• Topical (or systemic) steroids
• Omalizumab in severe refractory VKC (anti-IgE antibody)
Patients with corneal ulcers receive additional treatment involving:

- Aggressive cycloplegia (pupil dilation)
- Topical antibiotic drops
- Mucolytic acetylcysteine (disintegrates the mucous)

Corneal scarring with subsequent visual loss may be a result of a severe disease.
<table>
<thead>
<tr>
<th>Compound &amp; Company</th>
<th>Phase</th>
<th>Notes</th>
<th>Delivery</th>
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<tbody>
<tr>
<td><strong>Vekacia</strong> (cyclosporin, DE-076C) &lt;br&gt; Santen</td>
<td>Launched in EU and approved in Canada</td>
<td>Launched in Canada 2019</td>
<td>Eye drops</td>
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<td><strong>Ikervis</strong> (cyclosporin, DE-076B) &lt;br&gt; Santen</td>
<td>Approved in EU for severe keratitis in 2015</td>
<td>Approved in Europe for treatment of severe keratitis in adult patients with <strong>dry eye disease</strong>, that has not improved with <strong>tear substitutes</strong>. But likely to be used off-label for VKC. In addition to a higher concentration, Ikervis employs new delivery methods - new vehicle (excipient) technology that may make cyclosporine more tolerable and more efficacious, applied once a day</td>
<td>Eye Drops/Emulsion</td>
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<td><strong>Talymus</strong> (Tacrolimus, FK506) &lt;br&gt; Senju Pharmaceutical Co., Astellas</td>
<td>Post-launch approval for VKC in Japan</td>
<td>US Food and Drug Administration put a Black-Box warning on the use of FK-506 ointment in the treatment of atopic dermatitis for its potential cause-and-effect of lymphoid malignancy</td>
<td>Eye drops/suspension can be prepared in pharmacy</td>
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• A number of possible formulations for topical, sub-conjunctival, intravitreal delivery

• Potential for reduced systemic toxicity with topical administration (possibility of prophylactic usage)

• Novel mechanism of action for this indication

• Possibly minimizing onset of clinical symptoms by pre-seasonal treatment

• Corticoid-sparing option for treatment of severe VKC cases

• May be used independently or in combination with other agents

• Phase 2 clinical trials planned in VKC/AKC

• Recent quote from Ophthalmic Research Associates (ORA) for ocular allergic study (pre-IND meeting with the FDA, cost of Phase 2 VKC study - expected range US $2.5-3.5M)