Forward Looking Statements

This presentation contains “forward-looking information” within the meaning of applicable securities laws in Canada, including statements about iCo Therapeutic Inc.’s (the “Company” or “iCo”) business and corporate strategy; the initiation, timing, cost, progress and success of the Company’s research and development programs; the Company’s ability to re-dose, formulate and develop drug candidates; the Company’s ability and its partner’s ability to advance product candidates into, and successfully complete, clinical trials; the Company’s expectations regarding the advancement of the Oral Amp B Delivery System and iCo-008 through further studies; the Company’s expectations regarding enrolment and the timing of enrolment in the studies conducted by the Company’s licensees for the Company’s product candidates; the expected therapeutic benefits, effectiveness and safety of the Company’s product candidates, including the Company’s belief that its approach may reduce the risk, time and cost of developing therapeutics by avoiding some of the uncertainty associated with certain research and pre-clinical stages of drug development; the Company’s ability to obtain funding for its operations, including funding for research and commercial activities; the Company’s ability to achieve profitability; and the Company’s expectations regarding milestone payments and royalties with respect to License Agreements. Particularly, information regarding the Company’s expectations of future results, performance, achievements, prospects or opportunities is forward-looking information. In some cases, forward-looking information can be identified by the use of forward-looking terminology such as “may”, “will”, “expect”, “intend”, “estimate”, “anticipate”, “believe”, “continue”, “plans” or variations of such words. In addition, any statements that refer to expectations, intentions, projections or other characterizations of future events or circumstances contain forward-looking information. For this purpose, any statement that is not a statement of historical fact should be considered forward-looking information.

In providing the forward-looking information included in this presentation, the Company has made various material assumptions, including, but not limited to obtaining positive results from the Company’s current clinical trials; obtaining regulatory approvals; assumptions regarding general business and economic conditions; assumptions regarding the cost and timing of each study; the Company’s ability to successfully develop iCo-008 and the Oral Amphoteracin Delivery System; that the Company’s current positive relationships with third parties will be maintained; the availability of future financing on reasonable terms; the Company’s ability to attract and retain skilled staff; assumptions regarding market competition; the products and technology offered by the Company’s competitors and the Company’s ability to protect patents and proprietary rights.

Forward-looking information is also subject to numerous risks and uncertainties, including: the Company’s limited operating history; the possibility that iCo may never achieve profitability; risks involved in completing the clinical development of, and receiving regulatory approval for, iCo’s product candidates; uncertainties related to whether the commercialization of the Company’s product candidates; as well as those risks and uncertainties discussed under “Risks Factors” in the iCo’s Annual Information Form, dated April 30, 2019 and available on the Company’s SEDAR profile at www.sedar.com. Although we have attempted to identify important risk factors that could cause actual results to differ materially from those contained in the forward-looking information in this presentation, there may be other risk factors not presently known to us, or that we presently believe are not material, that could also cause actual results or future events to differ materially from those expressed in the forward-looking information in this presentation.

There can be no assurance that the forward-looking information in this presentation will prove to be accurate, as actual results and future events could differ materially from those anticipated in such information. The forward-looking information contained in this presentation represents our expectations as of the date of this presentation or the date indicated, regardless of the time of delivery of the presentation. iCo undertakes no obligation to update the forward-looking information in this presentation except as required by applicable law. All of the forward-looking information contained in this presentation is expressly qualified by the foregoing cautionary statements.
Oral Amphotericin B Program

• Technology originally licensed from UBC, is a lipid-based formulation applicable to a number of drug classes. Initial work conducted on an oral formulation of Amphotericin B.

• Compelling Risk/Reward profile: Amphotericin B works but drug has toxicity issues and formulation is impractical due to the IV route of administration.

• Accelerated development timelines: de-risked and rapid impact potential given Amphotericin B is a known drug & iCo development is reformulation/repositioning.

• Convincing data generated in multiple species, multiple labs and multiple peer-reviewed publications¹.

• FDA granted Orphan Drug Designation to iCo for the Oral Amphotericin B project.

Amphotericin B - The Molecule

• A polyene antifungal agent, first isolated from *Streptomyces nodosus* (Gold et al., 1955)
• Amphoteric compound composed of:
  • a hydrophilic polyhydroxyl chain along one side
  • a lipophilic polyene hydrocarbon chain on the other.
• Poorly soluble in water
Oral Amphotericin B: Product Profile

- **Product**: Oral Amphotericin B (Amp B)
- **Class**: Anti-fungal/anti-parasitic
- **Mechanism of Action**: Membrane disruption, Immune stimulant properties. Lymphatic transport may be involved in absorption.
- **Development Stage**: Clinical: IND enabling studies completed, Phase 1 single dose-escalating study completed 2018. Next clinical study using multiple dosing planned in 2019.
- **Indication(s)**: Infectious and Parasitic diseases, including fungal and HIV.
- **Dosage**: Oral: 100 mg capsule format.
- **Formulation**: Lipid-based (not liposomal), includes Peceol, Gelucire and other GRAS approved excipients.
- **IP position**: Oral delivery platform and formulation patents filed in 16 countries in ‘08 and ‘10. Issuance in greater than 10 countries. Orphan status for VL.
Product Profile (2)

- **Positioning**  
  Safer, more practical oral formulation of a well-known broad spectrum antifungal  
  Lower occurrence of resistance  
  Lower impact on drug metabolism than other anti-fungal drugs

- **Superior safety profile**  
  No infusion-related toxicity due to oral dosing  
  No observed kidney nor GI toxicity to date

- **Equal efficacy**  
  Potential to retain potency  
  Tissue distribution indicates drug accumulation over time; PK from Phase 1 demonstrated prolonged plasma half-life and increased AUC compared to closest oral competitor

- **Patient convenience**  
  Simplified method of delivery: No multiple IV infusions or IM injections  
  Reduction in cost and infrastructure to administer

- **Current activities planned**  
  Next clinical study using multiple dosing planned for 2019 in Australia
Other Potential Indications: Immunocompromised complications, HIV and neglected diseases

**Azole-Resistant Candida infections**
Candida species are responsible for a majority of superficial and disseminated fungal infections in humans

**Recurrent Vulvovaginal Candidiasis (RVVC)**, usually defined as four or more episodes of symptomatic VVC within 1 year, affects <5% of women)

- Some genes may be associated with Candida albicans resistance to azoles
- Pir1 gene is described as responsible to induce resistance in C. albicans

**Oropharyngeal Candidiasis (OPC)** - often associated with HIV
- *C. albicans*, depends on previous fluconazole treatment and prior OPC infections;
- Recommended azole treatment: 7-14 days
- Can use Amphotericin B i.v. daily as a salvage therapy if oral Amphotericin B does not show expected efficacy
- Relatively common - numbers may favour Phase II study using oral Amphotericin B
Other Potential Indications: Immunocompromised complications, HIV and neglected diseases

**Histoplasmosis in patients with concurrent tuberculosis**

- Coinfection with tuberculosis in some countries occurs in 8-15% of human immunodeficiency virus (HIV)-infected patients who have histoplasmosis
- Occurs mostly in India, Latin America, etc.
- Difficult treatment due to drug interactions
- Oral Amp B may be beneficial with less drug resistance (prof. Denning)

**Fungal Endophthalmitis**

- Endogenous fungal endophthalmitis represents intraocular dissemination of a systemic fungal infection
- Among the different fungal species, Candida species is the most common cause of infection, followed by Aspergillus species and cryptococcus
- Hospitalized patients with candidemia reveal that 9-37% of patients developed candidal endophthalmitis
- In India, fungi were isolated in 22% of culture-proven endophthalmitis
- Systemic amphotericin has been the treatment of choice because of its broad-spectrum coverage
Other Potential Indications: Immunocompromised complications, HIV and neglected diseases

**Febrile Neutropenia**
- Use fluconazole as a control with a salvage therapy available
- Treatment duration: treat until 2-3 days after patient is asymptomatic (will be specified)

**Chronic Refractory Mucocutaneous Candidiasis (CMC)**
- Persistent or recurrent candidal infection due to inherited T-cell defects
- Typically, only poorly controlled with anti-fungals (azoles)
- Potential for a better improvement with chronic oral Amphotericin B therapy – less resistance, less drug interaction, safe
Opportunities to increase accessibility

Most effective treatment is parenteral amphotericin B resulting in:

1. Loss of income due to hospitalization for IV therapy
2. High cost of administration
3. Risk of infusion-related side effects
4. Risk of systemic toxicity
5. Limited accessibility
6. Not heat stable

Oral amphotericin B overcoming barriers to treatment:

1. Easy to administer/at home administration
2. Decreased cost of administration
3. Lack of infusion-related side effects (i.e. fever, chills etc.)
4. Lack of kidney, liver and GI toxicity
5. Increased accessibility
6. Thermal stability at tropical temperatures
Formulation and Manufacturing

• Formulation has been optimized
• Several derivatives were tested
  - Lead selection based on stability & solubility data,
  - 12+month data available
• Lead chosen for superior attributes
  - Known GRAS excipients
  - Manufacturing process available
  - Low COGS compared to any injectable
    • Easy scale-up
    • Relatively few steps in formulation
Clinical Phase 1 Study Design

A Phase 1, placebo-controlled, single dose ascending study to assess the safety, tolerability, and bioavailability of Oral Amphotericin B in healthy male and non-pregnant female subjects between 18 – 55 years of age.

Objectives:

Primary objective:

• To evaluate the safety and tolerability of multiple dose levels of a single oral administration of oral Amphotericin B

Secondary objective:

• To assess the pharmacokinetics and bioavailability of oral Amphotericin B after a single dose oral administration

Study Design:

• Subjects were randomized into one of four cohorts, each representing an ascending single dose of treatment: 100 mg, 200 mg, 400 mg and 800 mg

• Each cohort consisted of eight subjects where six subjects were randomized to receive the investigational product and two were randomized to receive the placebo

• All subjects were followed for seven days after dosing
Clinical Phase 1 Study Results

A Phase 1, placebo-controlled, single dose ascending study to assess the safety, tolerability, and bioavailability of Oral Amphotericin B in healthy male and non-pregnant female subjects between 18 – 55 years of age.

**Objectives:**

Primary objective: To evaluate the safety and tolerability of multiple dose levels of a single oral administration of oral Amphotericin B

- Study met its primary endpoint of safety and tolerability
- No serious adverse events nor drug-related adverse events
- No gastro-intestinal (GI) side effects, even at the highest dose of 800 mg
- No indication of kidney or liver toxicity

Secondary objective: To assess the pharmacokinetics and bioavailability of oral Amphotericin B after a single dose oral administration

- Secondary endpoint achieved, demonstrating enhanced plasma AUC measures versus direct competition
Oral Amphotericin B Candidate: Next Study Using Multiple Dosing in 2019

- Multiple Oral Amphotericin B Dosing in Australia
  - Treatment for 10 days
  - Follow-up to up to 20 days
  - Study start in 2019

- PK and Tissue Distribution Studies (completed Q4 2016)

- Fasted/fed study and additional dose ranging study (completed Q1 2017)
  - Non GLP and GLP Toxicology Studies completed in Q2 2017

- Phase I Study completed 2018

- Drug Product for multiple dosing study available

- CRO engaged, Ethics Committee submission – pending revisions
  - Site selection and initiation pending
  - FPFV planned for Q4 2019
Intellectual Property & Designations

- Multiple Formulation patent families (issued or filed)
  - Multiple derivatives, including lead candidate
  - Multiple jurisdictions
- Orphan Status in US for VL
Summary

- Solid preclinical package and Phase I safety and pharmacokinetic results
- Next clinical study using multiple dosing initiation in 2019
- Low risk reformulation of known drug
  - Neither kidney nor gastrointestinal toxicity observed in pre-clinical or clinical studies to-date
  - Serum PK of optimized formulation similar to original lipid formulation, showing good therapeutic potential in pre clinical data
  - Tissue distribution similar in a number of key organs
  - Formulation has excellent attributes for target markets (Zone 4).
- Orphan status in the US (VL)
- Open to various partnership models
Antifungal Market
Global Antifungal Market is Large & Could Expand With an Oral Amphotericin B

- Projected to grow to $13.9 billion by 2018*
- Estimated 500,000 severe fungal infections globally for which oral Amphotericin B may be an appropriate treatment

Oral Amphotericin B could be positioned

- An oral step-down therapy from IV Amp B
- Indications not suitable IV administration
  - Post-Transplantation: hematopoietic stem cell and/or solid organ
  - Febrile neutropenia
  - Non-life threatening fungal indications
- Therapeutic window will determine best positioning


Publications


