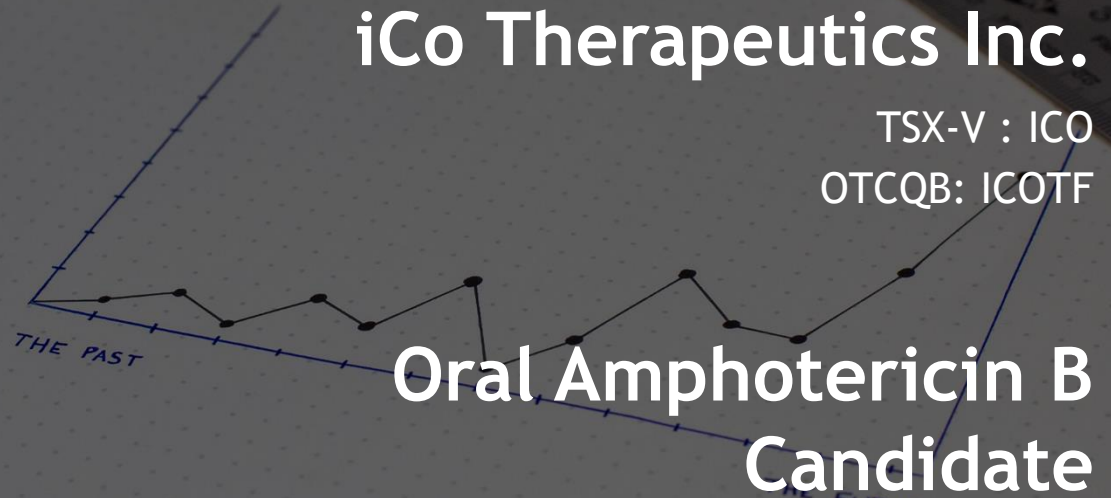




**iCo Therapeutics Inc.**

TSX-V : ICO  
OTCQB: ICOTF



**Oral Amphotericin B  
Candidate**

**Q1 2020 Non-Confidential Presentation**

# 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 Amphotericin 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](http://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 publications<sup>1</sup>.
- FDA granted Orphan Drug Designation to iCo for the Oral Amphotericin B project.

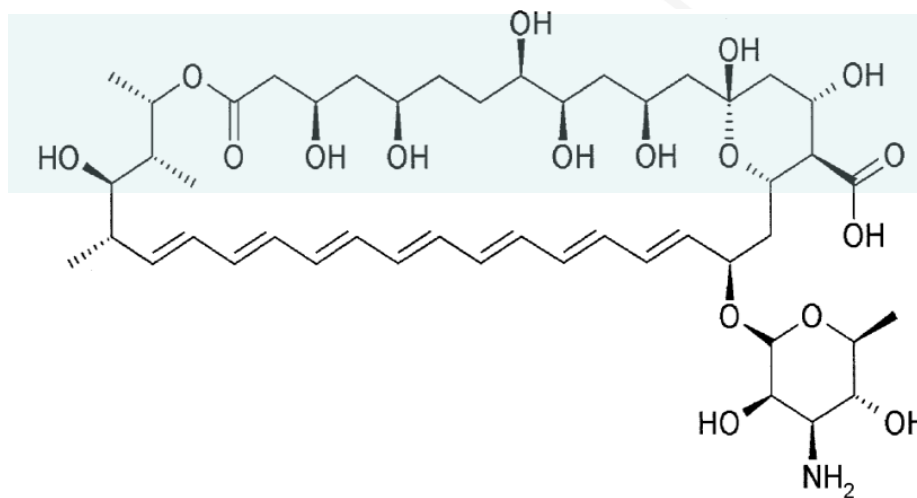
1. Including demonstration of an oral Amphotericin B treatment effect in visceral Leishmaniasis (VL). Wasan, EK, et al "Highly effective oral Amphotericin B formulation against murine visceral Leishmaniasis", Journal of Infectious Disease. 2009 Aug1. 200(3):357-60



# Product Overview

[WWW.ICOTHERAPEUTICS.COM](http://WWW.ICOTHERAPEUTICS.COM)

# 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

# iCo-019: Oral Amphotericin B Product Profile

- **Product** iCo-019
- **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  
Phase 1b multiple dose-escalating study completed, results announced in April 2020; Phase study 2 on hold
- **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/Exclusivity** Oral delivery platform and formulation patents through 2038-2039, numerous countries  
Orphan status for VL.

## iCo-019: Oral Amphotericin B 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 antifungals
- **Superior safety profile**
  - No infusion-related toxicity due to oral dosing
  - No observed kidney nor liver toxicity to date
- **Equal efficacy**
  - Potential to retain potency
  - Tissue distribution indicates drug accumulation over time; PK in Phase 1 and 1b demonstrated prolonged plasma half-life and increased AUC compared to closest oral competitor
- **Patient convenience/compliance**
  - No multiple IV infusions or IM injections.
  - Reduction in cost and infrastructure to administer
- **Current activities**
  - Completed Phase 1b study using multiple dosing (Aus)
- **Next Step**
  - Phase 2 clinical study in VVC

# Other Potential Indications: Immunocompromised complications, HIV and neglected diseases

## Azoles-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

## Visceral Leishaniasis (VL)

- Parasitic infection common in tropical, subtropical regions as well as Southern EU
- If untreated almost always causes death
- Amphotericin B IV is a standard treatment which is expensive, not tropically stable and difficult to administer
- Miltefosine is the first oral treatment, with numerous side-effects

# 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

# Antifungal Studies

# Supporting Non-clinical Studies

- PK work in beagles with several derivatives
- Tissue distribution studies in beagles
- Fed/fasted beagle study
- Non-GLP toxicology in beagles, 7-day dose ranging
- GLP toxicology, in beagles, 14-day dose ranging
- Drug stability work ongoing - 18+ month data points available

# Beagle Toxicology Summary: No observed toxicity



- **Biodistribution study in Beagles: N=15**
  - Original formulation: N=3
  - Two derivative formulations: N=12, (one of which moved into further studies)
  - No observed toxicity, comparable PK data between derivatives
- **PK/Tissue distribution fed-fasted (dose escalation) in Beagles: N=4 (M)**
  - No observed toxicity, 500mg dose (5 X 100 mg capsules)
- **7-day Non-GLP in Beagles: N=16**
  - No observed toxicity, BID dosing, doses up to 1000 mg
- **14-day GLP in Beagles: N=38**
  - No observed toxicity, doses up to 600 mg

# 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



# Clinical Phase 1 Results: Dr. Wasan's Commentary



Dr. Kishor Wasan, R.Ph, Ph.D, FAAPS, FCSPS, FCAHS  
Adjunct Professor and Distinguished University Scholar  
Faculty of Pharmaceutical Sciences  
Nanomedicines and Drug Delivery Research Group  
The University of British Columbia  
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Former Dean, College of Pharmacy and Nutrition  
University of Saskatchewan

- The prolonged plasma half-life and increased AUC as a function of dose suggests that the oral Amphotericin B formulation has a long circulation time resulting in the ability of the formulation to increase Amphotericin B tissue concentrations within infected tissues without the associated GI, liver and kidney toxicity
- The data implies potential Amphotericin B exposure at concentrations that would illicit a pharmacological effect.

# Clinical Phase 1b: Study Design

A Phase 1b, Single-Center, Double-Blind, Randomized Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of 100 mg and 400 mg Oral Amphotericin B (iCo-019) or Placebo Administered for 10 Days in Healthy Subjects

## **Objectives:**

Primary objective:

- To evaluate safety and tolerability after repeated administration of 100 mg and 400 mg doses of oral Amphotericin B (iCo-019) for 10 days in healthy subjects

Secondary objective:

- To evaluate pharmacokinetic profile after repeated administration of oral Amphotericin B (10 days) in healthy individuals

## **Study Design:**

- Approximately 12 healthy subjects, aged 18-55 years of age, were randomized to one of the two doses of oral Amphotericin B (100 mg or 400 mg) or a Placebo (5 subjects received oral Amphotericin B and one subject received Placebo in each cohort). Subjects were dosed for 10 days and followed for additional 5 days post-treatment.

# Clinical Phase 1b: Study Results

A Phase 1b, Single-Center, Double-Blind, Randomized Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of 100 mg and 400 mg Oral Amphotericin B (iCo-019) or Placebo Administered for 10 Days in Healthy Subjects

## **Objectives:**

**Primary objective:** To evaluate safety and tolerability after repeated administration of 100 mg and 400 mg doses of oral Amphotericin B (iCo-019) for 10 days in healthy subjects

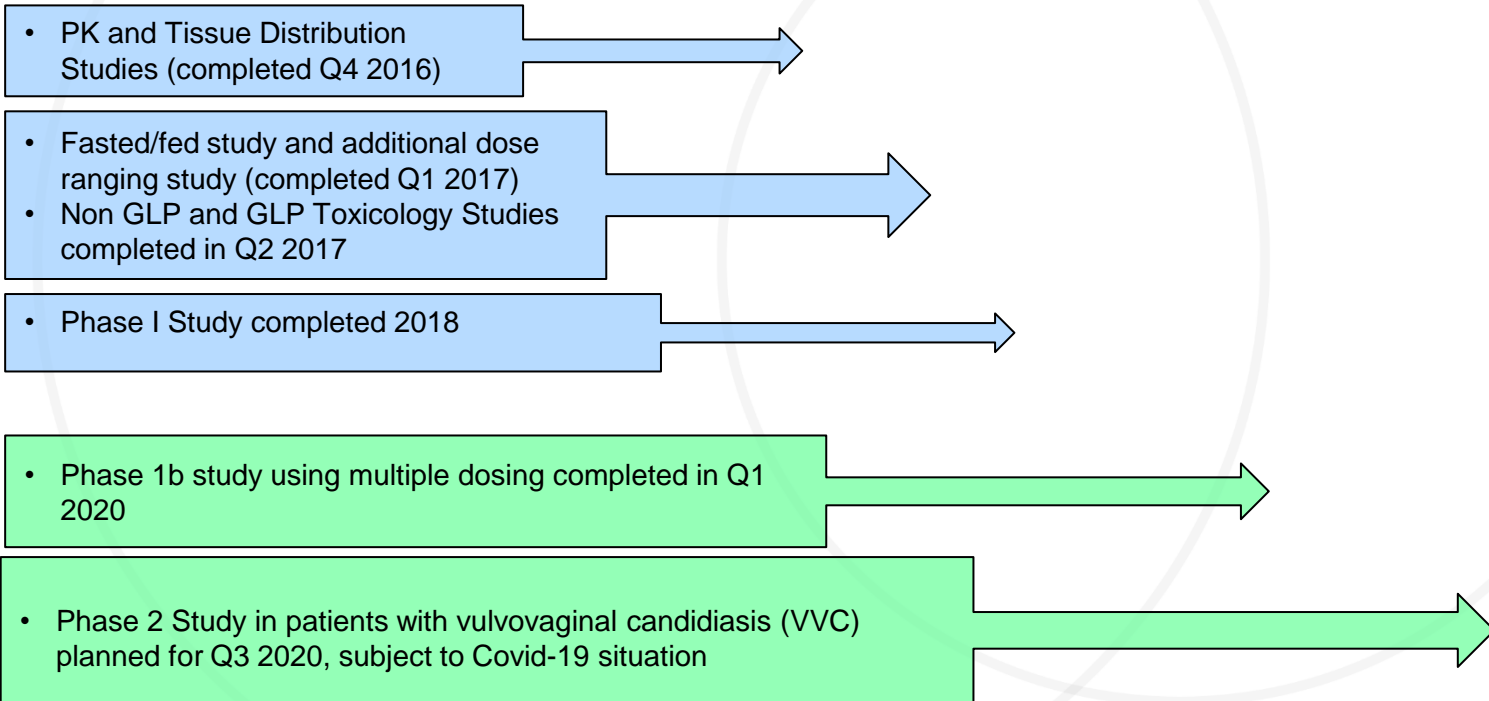
Study met its primary endpoint of safety and tolerability

- No serious adverse events nor drug-related toxicity events
- Both repeated drug doses were well tolerated
- 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

- Data analysis ongoing

# Oral Amphotericin B Candidate: Next Study Phase 2 in VVC Patients



# Formulation and Manufacturing

- Formulation has been optimized
- Several derivatives were tested
  - Lead selection based on stability & solubility data,
  - 18+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

# 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 and Phase Ib safety and pharmacokinetic results
- Phase 1b clinical study using multiple doses completed, full results expected in Q2 2020
- Phase 2 study in patients with VVC planned to start in Q3 2020
- Low risk reformulation of known drug
  - Neither kidney nor liver 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

\* Source <http://www.prnewswire.com/news-releases/antifungal-drugs--technologies-and-global-markets-278429091.html>

# 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

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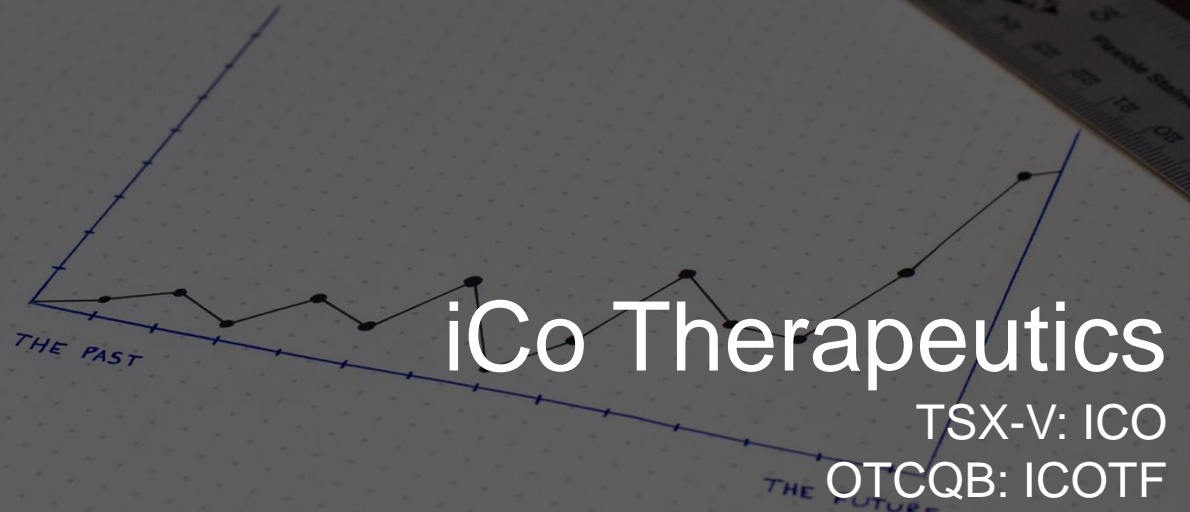
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iCo Therapeutics

TSX-V: ICO

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