

# Napo EU S.p.A.

A wholly owned subsidiary of Napo Pharmaceuticals, Inc.

---

Overview – June 2021



# Important Notifications

---

Dragon SPAC is selling its Units and underlying ordinary shares and warrants (collectively, the “Securities”) only to “accredited investors” in reliance on the exemption from registration set forth in Rule 506(c) of Regulation D promulgated under the Securities Act of 1933, as amended (the “Securities Act”). The Securities have not been and will not be registered under the Securities Act or the securities laws of any state or other jurisdiction, and may not be offered or sold without registration or an applicable exemption from the registration requirements of the Securities Act and applicable state securities or blue sky laws and foreign securities laws.

This document shall not constitute an offer to sell, or the solicitation of an offer to buy, any securities, nor shall there be any sales of the Securities in any jurisdiction in which such offer, solicitation or sales would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction.

No representations and warranties are granted by the entities mentioned in this document regarding the accuracy, completeness, reliability, or correctness of any information contained in this document, and said entities are under no obligation to update the information provided in this document.

## Forward-Looking Statements

Certain statements in this document constitute “forward-looking statements.” All statements other than statements of historical facts contained in this document, including statements regarding plans by Jaguar, Napo Pharma, and Napo EU to develop and commercialize crofelemer in Europe (excluding Russia) for HIV-related diarrhea and intestinal failure-short bowel syndrome (IF-SBS) indications, the intention for Jaguar, through Napo Pharma, to grant Napo EU an exclusive, perpetual, royalty-bearing license to develop and commercialize crofelemer and Napo Pharma’s lechlemer drug product candidate in Europe (excluding Russia) for specified potential indications of crofelemer and lechlemer and an option to license certain additional indications of crofelemer and lechlemer, pending obligations, the company’s plans to complete a trial in SBS patients suitable for the conditional approval pathway in the EU, the intention for Napo Pharma to pursue regulatory approval in the U.S. for SBS, the expectation that the global SBS market will reach \$4.6 billion by 2027 with a CAGR of 26% from 2020 to 2027, the Jaguar’s expectation that Napo EU will be the target company for Dragon SPAC, Jaguar’s expectation that Napo EU will merge with Dragon SPAC, the anticipated terms of the proposed merger of Napo EU with Dragon SPAC, plans to seek public listing/liquidity about 24 months following the consummation of the merger of Napo EU and Dragon SPAC, and the timing of data results from planned studies, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “aim,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this document are only predictions. Jaguar, Napo Pharma, and Napo EU have based these forward-looking statements largely on its current expectations and projections about future events. These forward-looking statements speak only as of the date of this document and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond the control of Jaguar, Napo Pharma, and Napo EU. Except as required by applicable law, Jaguar, Napo Pharma, and Napo EU do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Neither this document nor its delivery to any person should constitute or form part of a prospectus or an offer to sell or a solicitation of an offer to buy any security or offer to enter into any other transaction or commercial agreement, or a commitment of any nature on the part of Jaguar, Napo Pharma, or Napo EU.

# Napo EU S.p.A. (“Napo EU”): Italian Subsidiary of Napo Pharmaceuticals, Inc. (“Napo Pharma”)

---

- **Napo EU is the named target of Dragon SPAC S.p.A. (“Dragon SPAC”)**
- **Napo EU’s Mission:** To expand access to Napo Pharma’s plant-based, proprietary first-in-class drug, crofelemer, to the European\* marketplace
  - *Initial indication:* Intestinal Failure with Short Bowel Syndrome (IF-SBS)
  - *Additional objectives:* To develop and obtain regulatory approval for additional indications for crofelemer in Europe\*, including HIV-related diarrhea, cancer therapy-related diarrhea, and other crofelemer pipeline indications
- **Why a European focus for crofelemer?**
  - Single payer health care systems in Europe have great incentive to focus on mitigating the burden of long-term chronic illness



# Napo EU Funding to Date

---

- Jaguar is providing pre-combination funding loan to Napo EU
- **June 1, 2021:** Jaguar and Dragon SPAC announced the first funding of the Dragon SPAC private financing in an amount equal to approximately **\$10.8 million** (~8.83 million euros), with proceeds to be used for Dragon SPAC's merger with Napo EU in pursuit of Napo EU business plan.



# Key Napo EU Asset

---

- Through Napo Pharma, Jaguar intends to grant Napo EU an **exclusive, perpetual, royalty-bearing license** to develop and commercialize crofelemer and Napo Pharma's lechlemer drug product candidate in Europe\* for specified potential indications of crofelemer and lechlemer and an option to license certain additional indications of crofelemer and lechlemer, pending obligations, including:
  - Target orphan indication (Napo EU's initial focus): Intestinal Failure with Short Bowel Syndrome (IF-SBS); Orphan designation received in US.
  - Noninfectious diarrhea in adults with HIV/AIDS receiving antiretroviral therapy (HIV-related diarrhea)<sup>1</sup>
  - Adult solid tumor patients receiving targeted therapy with or without chemotherapy (cancer therapy-related diarrhea (CTD))<sup>2</sup>
  - Inflammatory diarrhea, including COVID-associated diarrhea
  - Diarrhea related to inflammatory bowel disease (IBD)
  - Irritable bowel syndrome (IBS)
  - Target orphan indication: Diarrhea related to congenital diarrheal disorders (CDD)
- Napo Pharma to provide centralized manufacturing and product supply to Napo EU



<sup>1</sup>Currently marketed in the US

<sup>2</sup>Currently in Napo Pharma sponsored Phase 3, NDA-enabling clinical trial in US

# Jaguar/Napo Product Portfolio – Crofelemer Pipeline in a Product

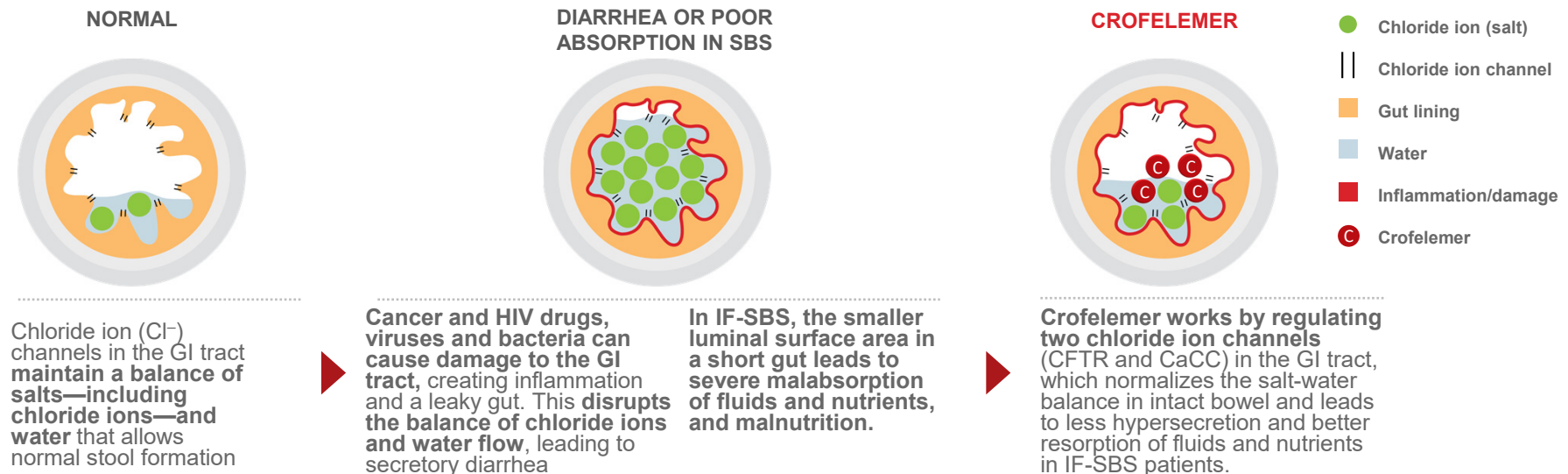
PRODUCT	INDICATION	DEVELOPMENT STAGE					
		PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVED (US)	GEOGRAPHIC FOCUS OF CLINICAL ACTIVITY
Mytesi (crofelemer)	Noninfectious diarrhea in adults with HIV/AIDS antiretroviral therapy						
Mytesi (crofelemer)	Cancer therapy-related diarrhea (CTD)				Phase 3 trial underway in US		US
Liquid formulation of crofelemer	Orphan Indication: Intestinal Failure with Short Bowel Syndrome (IF-SBS)		Initial focus of Napo EU for conditional approval; Crofelemer has orphan-drug designation in the US for SBS				EU & US
Mytesi (crofelemer)	IBS - Diarrhea Predominant (IBS-D)						US
Mytesi (crofelemer)	Idiopathic/functional diarrhea^						US
Mytesi (crofelemer)	Supportive care for IBD						US
Liquid formulation of crofelemer	Orphan Indication: Congenital Diarrheal Disorders (CDD)						US & Middle East
Crofelemer	Inflammatory diarrhea, including COVID-associated diarrhea						EU
Lechlemer*	Symptomatic relief of diarrhea from cholera				Received preclinical services funded by the National Institute of Allergy and Infectious Diseases for dog and rat toxicity studies		US
ETI psychoactive / psychedelic plant-based drugs	Mental health/mood disorders; Development Stage	Discovery					US

^Investigator-initiated trial (IIT)

\*Potential opportunity for Tropical Disease Priority Review Voucher (TDP RV) 6

# Unique Anti-Secretory Mechanism of Action

- Crofelemer is a first-in-class, **gut-restricted**, chloride ion channel modulator that normalizes the increased volume of intestinal fluid and the imbalance of electrolytes in the gut that may result from inflammation and hypersecretion.
- Approved for chronic use
- Modulates **malfunctioning CFTR and CaCC chloride channels to normal levels of activity** to maintain the delicate balance of fluids and electrolytes in intestinal fluid
- Not an opiate or ant motility drug; Crofelemer normalizes stool formation and volume; does not interfere with normal peristaltic activity, that causes constipation
- In patients with IF-SBS who suffer severe malabsorption, crofelemer may help balance the secretion and reabsorption of fluids and facilitate better absorption of major nutrients (proteins, fats, carbohydrates, and vitamins) and micro-nutrients (trace minerals) that support health and survival



# The Importance of What Crofelemer Does

---

- **The gastrointestinal tract is the body's second line of defense of the immune system after the skin. Normal functioning of the small intestine is crucial to optimize a patient's absorption of fluids and nutrients to support life**
- Crofelemer, direct innovation: May benefit patients with conditions such as SBS, HIV and cancer therapy associated diarrhea
- Crofelemer's potential to "enable" innovation: In fields such as targeted cancer therapies (such as TKIs and EGFR)
- Patients with cancer-therapy related diarrhea (CTD) were 40% more likely to discontinue chemotherapy or targeted cancer therapy than patients without CTD<sup>1</sup>
  - Patients with CTD used significantly more healthcare resources, (i.e., emergency department visits and hospitalizations) increasing the overall cost of cancer care.<sup>2</sup>
  - Patients with CTD had nearly 2.9 times higher all-cause total cost than patients without CTD<sup>3</sup>
  - The use of crofelemer to prevent or better control CTD may enable patients to complete their course of therapy with their ideal cancer treatments at recommended doses

---

<sup>1</sup><https://meetinglibrary.asco.org/record/200556/abstract>

<sup>2</sup><https://meetinglibrary.asco.org/record/199750/abstract>

<sup>3</sup><https://meetinglibrary.asco.org/record/199739/abstract>



# Intestinal Failure-Short Bowel Syndrome (IF-SBS) Opportunity: Potential to Impact Patient Mortality and Morbidity

## ➤ IF & SBS Defined:

- ❖ Intestinal failure (IF) is defined as the reduction of intestine function so that fluids and nutrients given by the enteral route are needed to maintain health.
- ❖ SBS is a complex condition characterized by severe **malabsorption of fluids and nutrients** due to surgical resection of bowel segments, congenital anomalies, or disease-associated loss of absorption requiring parenteral nutritional support for survival.
- ❖ SBS patients suffer from **malnutrition, dehydration, imbalances of fluids and salts**, and excessive intestinal fluid output.

## ➤ SBS Patient Population:

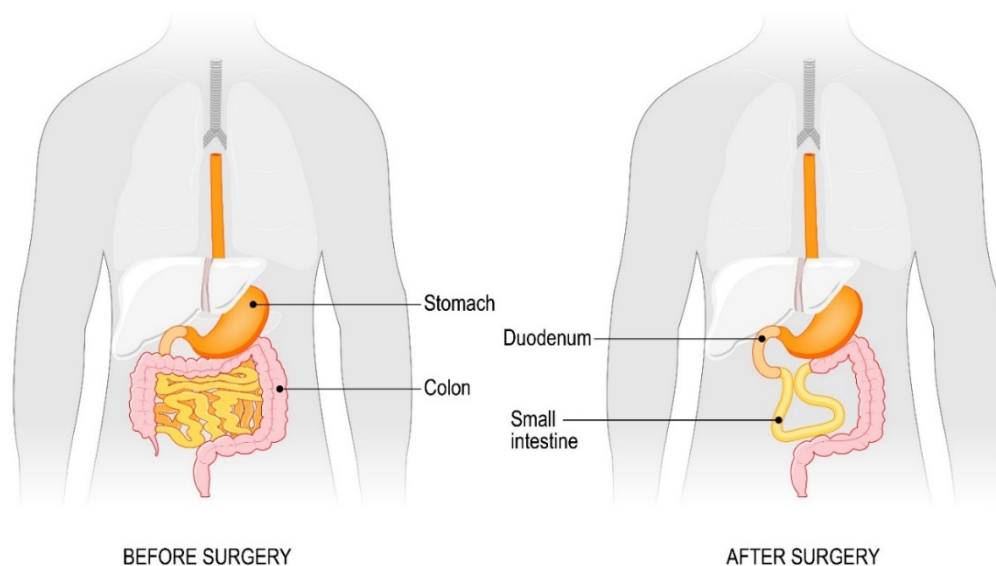
- ❖ Up to **approximately 20,000 SBS in Europe** (and **approximately the same number in US**)
- ❖ In countries such as the United Arab Emirates and Saudi Arabia, much higher incidence.



# The Short Bowel Patient's Life - Catastrophic Loss of Bowel

## The Need for Lifelong Parenteral Nutrition

- Catastrophic loss of bowel due to surgical rejection of diseased or necrotic bowel.
- Resulting Intestinal Failure leads to:
  - Severe malabsorption of fluids and nutrients & malnutrition
  - Excessive intestinal fluid output
  - Lifelong restriction/ adjustment of oral intake of food and liquids
  - Dependence on parenteral nutrition ([PN] intravenous fluids and nutrition for survival).
  - Serious challenges to a patients' ability to carry out activities of daily living, like school or work
  - Significant impact on quality of life
- Lifelong PN leads to potentially life-threatening complications like sepsis and organ failure



# Crofelemer Has a Unique Mechanism of Action that May Benefit IF-SBS Patients

## Approved Drugs Used in SBS:

- ❖ Takeda Pharmaceuticals' **Gattex**<sup>®</sup> (teduglutide) is a GLP-2 analog indicated in the U.S. for the treatment of adults and pediatric patients **1 year of age and older** with SBS who are dependent on parenteral support.
- ❖ **Revestive**<sup>®</sup> is the drug's name in Europe
- ❖ Gattex approval: FDA approval of Gattex was based on an international, 24-week, pivotal Phase 3 trial, known as STEPS.
  - ❖ **Primary endpoint: Defined as a 20% or greater PN/IV volume reduction demonstrated at week 20 and sustained at week 24**
- ❖ Secondary endpoints included reductions in PN/IV volume and additional days off therapy



- ❖ EMD Serono's **Zorbtive**<sup>®</sup> is a recombinant human growth hormone indicated in the U.S. for the treatment of SBS in adult patients receiving specialized nutritional support.
- ❖ The efficacy of Zorbtive was evaluated in a clinical trial in 41 adult SBS patient<sup>1</sup>
  - ❖ Primary endpoint: Change in weekly total intravenous parenteral nutrition (IPN)
  - ❖ After completion of 4 weeks of treatment, patients were re-evaluated as outpatients 12 weeks later



## ➤ Conventional Medications:

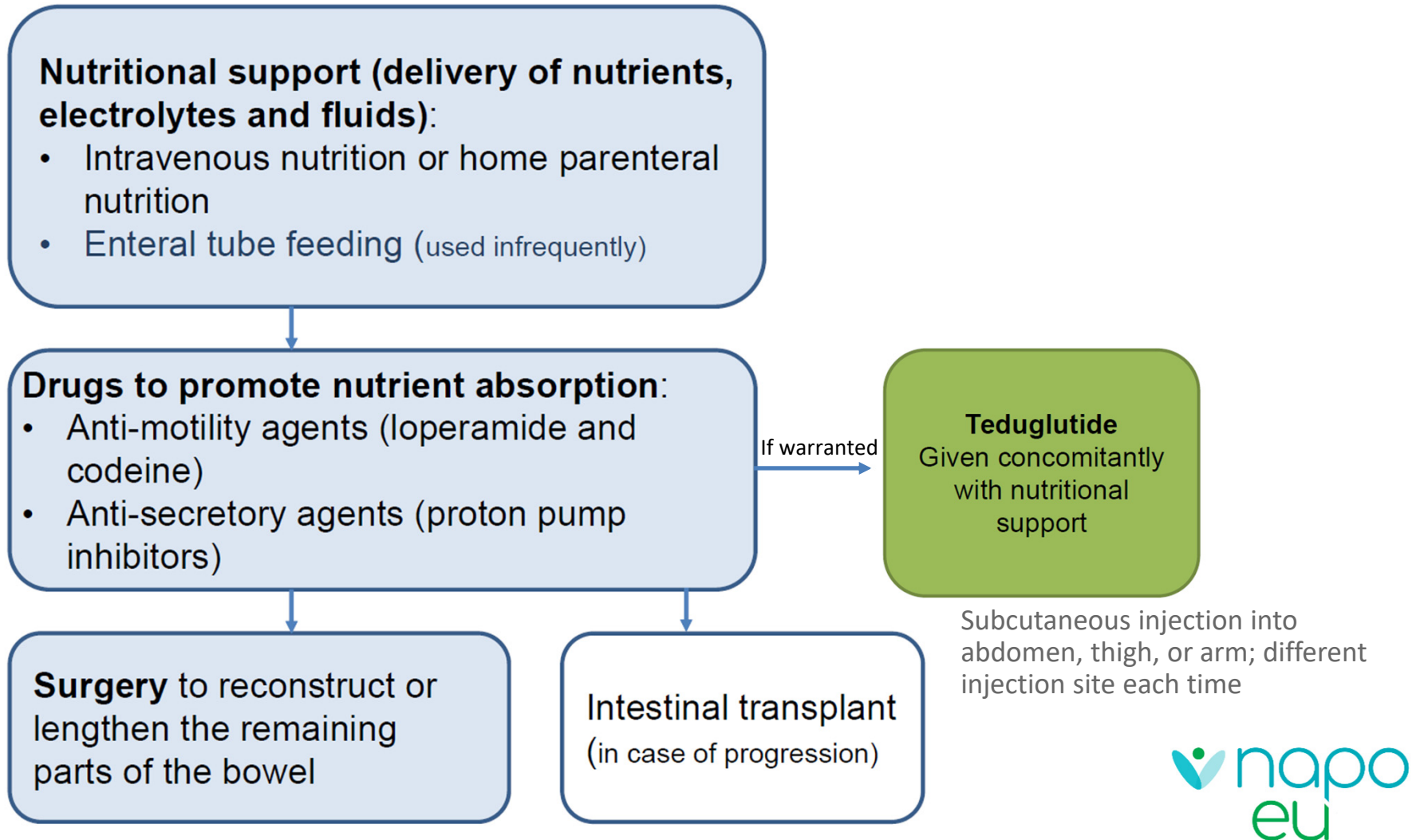
- ❖ SBS symptom relief: The most commonly used medications are antimotility agents to attempt to control high-volume diarrhea.
- ❖ Despite a lack of high-quality evidence supporting the use of these medications, loperamide and diphenoxylate are considered first-line antimotility agents in SBS.



<sup>1</sup><https://rarediseases.org/rare-diseases/short-bowel-syndrome/#affected-populations>

# Crofelemer May Reduce Need for Parenteral Support in IF-SBS Patients

## Treatment Pathway



# SBS Regulatory Pathways & Clinical Development Plan

---

- Napo EU will pursue **conditional marketing authorization for crofelemer for IF-SBS** through the European Medicines Agency (EMA), which provides a **fast-track** clinical review process
- **Planned Endpoint:** Reduction of weekly volume of PN
- **Clinical Development:** Complete a global trial (in collaboration with Napo Pharma) in IF-SBS patients suitable for the conditional approval pathway in the EU
  - ❖ Napo EU will pursue orphan drug designation in Europe for crofelemer for IF-SBS
  - ❖ Crofelemer has orphan-drug designation in the US for SBS
  - ❖ Napo Pharma intends to simultaneously pursue regulatory approval in US for IF-SBS
  - ❖ Global clinical trials can be conducted in support of EU and US approval
- **EU Conditional Approval Pathway for Designated Orphan Medicines:**
  - ❖ Designated orphan medicines are eligible for conditional marketing authorization in the EU<sup>1</sup>
  - ❖ Orphan Medicine: A medicine for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition that is rare (affecting not more than five in 10,000 people in the EU)<sup>2</sup>

<sup>1</sup><https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview>

<sup>2</sup><https://www.ema.europa.eu/en/glossary/orphan-medicine>



# SBS Market

## An Expanding Global Opportunity

Despite limited treatment options, the global SBS market exceeded \$568 million in 2019 and is expected to reach **\$4.6 billion by 2027** with a CAGR of 26% from 2020 to 2027, according to a market study report from Vision Research Reports<sup>1</sup>

- Estimated number of US patients on Gattex: **1,475**
- Estimated direct costs of inpatient PS in Europe: Approximately €28,000 to €75,000 per patient (approximately US\$34,000 to US\$91,000 per patient per year<sup>2-4</sup>)
- It is estimated that home parenteral nutrition costs 30%–60% less than the cost of PS in the hospital<sup>5</sup>
- The estimated annual cost for non-hospitalized PS in the US is approximately US\$150,000<sup>6</sup>



NASDAQ:JAGX

<sup>1</sup><https://www.mynewsdesk.com/us/medical-technology-news/pressreleases/short-bowel-syndrome-market-global-industry-analysis-size-share-trends-revenue-forecast-2020-to-2027-3069433>

<sup>2</sup>Aatmani TDK, et al. Gastroenterol Clin Biol 2006;30:574–79

<sup>3</sup>Arhip L, et al. Clin Nutr. 2019;38(4):1945–51

<sup>4</sup>Howard L. Gastroenterology. 2006;130(2 Suppl 1):S52–9

<sup>5</sup><https://int.shortbowelsupport.com/hcp/burden-of-disease/costs-of-sbs-if-care>

<sup>6</sup><https://nutritionequity.org/wp-content/uploads/2018/05/mnea-factsheet-sbs.pdf>

# Napo EU's Partnerships

---

- Napo EU's partnerships will accelerate clinical development, manufacturing of crofelemer, and reimbursement approval

## R&D



## Market Research



## Manufacturing



## Management Recruiting

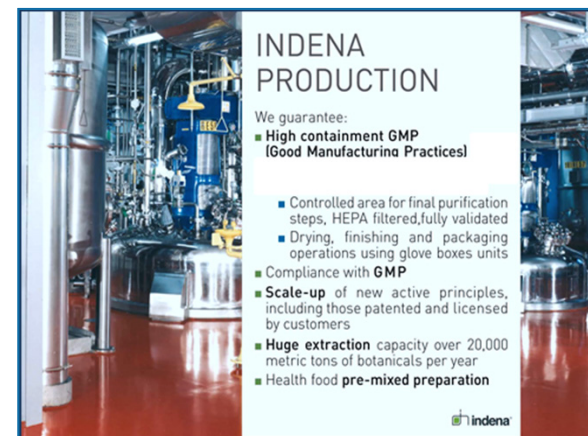


## Regulatory



## Indena - Based in Milan, Italy

- **WORLD LEADER IN PLANT-BASED MANUFACTURING**
  - Indena is a 100-year-old world-class research, development, and commercial manufacturer of pharmaceuticals and botanical extracts. The Indena industrial facility has capacity to produce 50 tons of crofelemer API per year.
  - Indena employs more than 800 staff distributed at 1 R&D Centre, 5 production sites and 5 international branches throughout the world and manages sales in more than 70 countries.
  - Indena produces drug substances under cGMP EMA/FDA guidelines





# Napo EU Funding through Dragon SPAC

---

## Napo EU is the Exclusive Target of Dragon SPAC

- Funding through Dragon SPAC financing and merger with Napo EU
- Dragon SPAC has engaged Equita Group S.p.A., a leading Italian independent investment bank, to advise Dragon SPAC
- Jaguar has engaged New York-based Cantor Fitzgerald & Co., a leading global financial services group, as a capital markets advisor in the U.S. to assist Jaguar in its evaluation of various financing strategies.

*Issuer*  
**Dragon SPAC S.P.A.**

*Target:*  
**Napo EU S.P.A.**



*Joint Global Coordinator*



*Joint Global Coordinator*



# Dragon SPAC

---

- **Dragon SPAC** is a recently formed Italy-based initiative with lead sponsorship by **Josh Mailman**, a well-known, New York City-based impact investor. Sponsor return linked to SPAC investor return.
- Dragon SPAC's named target: Napo EU (incorporated in Italy)
- Napo EU meets the Dragon SPAC sponsors' key criteria for proof of concept, addressable market, core due diligence and management team
- **Targeted fund raise:** Up to US\$30 million (first funding of \$10.8 mm completed)
- **Post-merger Combined Company (Napo EU + Dragon SPAC):** Plan to seek public listing/liquidity about 24 months following the consummation of the merger, which public listing/liquidity is subject to market conditions at the time and other factors to be assessed, including SBS clinical results
- **Terms for Investors in Dragon SPAC:**
  - Private financing
  - 100% warrants for investors
  - Investment contingent upon merger with Napo EU



# MOU Between Dragon SPAC and Napo EU

- Napo EU has a non-binding **Memorandum of Understanding** (“MOU”) with Dragon SPAC

## License Fees for Exclusive Rights to Crofelemer and Lechlemer in EU & EEA Payable by Dragon SPAC/Napo EU Combined Company to Napo Pharma

Tier	License to be Granted with Respect to the Following Indications	Aggregate Upfront Payment Due Napo Pharma
Tier A	<ul style="list-style-type: none"><li>• Intestinal failure with Short bowel syndrome (IF-SBS)</li><li>• HIV-related diarrhea</li><li>• Inflammatory diarrhea, including COVID-Related Diarrhea</li></ul>	<ul style="list-style-type: none"><li>• License: US\$10 million</li><li>• License Fee Payment Deadline: Within 60 days of merger</li></ul>
Tier B	<ul style="list-style-type: none"><li>• Cancer therapy-related diarrhea (CTD)</li></ul>	<ul style="list-style-type: none"><li>• License Option Exercise Fee: US\$15 million</li><li>• License Fee Payment Deadline: Option to pay within 24 months of merger</li><li>• First right of negotiation for following 12 months</li></ul>
Tier C	<ul style="list-style-type: none"><li>• Irritable bowel syndrome (IBS)</li><li>• Functional/idiopathic diarrhea</li><li>• Diarrhea in infants and children with congenital diarrhea disorders (CDDs)</li><li>• All other potential indications</li></ul>	<ul style="list-style-type: none"><li>• License Option Exercise Fee: US\$25 million</li><li>• License Fee Payment Deadline: Option to pay within 24 months of merger</li><li>• First right of negotiation for following 12 months</li></ul>

**Other customary milestone and commercial financial terms**

# Napo EU Management, and Board of Directors

---

## ➤ Napo EU Management:

- The search process for qualified candidates has been initiated to fill three key high-level roles (**Managing Director, Chief Medical Officer, and Chief Regulatory Officer**) at Napo EU, each of which will be Milan, Italy-based. Currently Napo EU has management contract with Napo Pharmaceuticals for personnel.
- Currently Napo EU has an Intercompany Services Agreement with Napo Pharma
- Joint Steering Committee for Napo EU to be formed with Jaguar Health/Napo Pharma management

## ➤ Board of Directors:

- A five-member board of directors will be appointed for Napo EU post merger (Lisa Conte is currently the sole member of Napo EU's board of directors. A second member to be named by Jaguar will also serve on combined company board of directors).
- Dragon SPAC has 3 board members:
  - **Joshua Mailman:** NYC-based impact investor; co-founded Social Venture Network (now Social Venture Circle) in 1987; founded Threshold Foundation in 1981; founded Business for Social Responsibility in 1992; founded Serious Change L.P., a \$100M privately held impact fund, in 2006; founding investor in GonoPhone (Grameen Telecom) - only cell phone 40% owned by a social enterprise, current market cap \$4B; founding investor in Global Telesystems with George Soros and Alan Slifka - grew to \$5B market cap; founding investor in Stoneyfield Farms yoghurt company - sold to Danone; early investor in Grove Collaborative – D2C green products, now a \$1B co.; founding investor in Lotus Foods - organic heirloom sustainable rice - now a \$50M co.; founding investor in BKASH - largest mobile payment co. in Bangladesh - \$1B value - Ant Financial partner.
  - **Dr. Niccolò Caderni:** Former European Space Agency Fellow at the University of Cambridge; served as vice president of M&A at Bankers Trust International, managing director at Phillips auction house, chairman of Webiz, the private equity fund of the Italian utility giant, ENEL, and chairman of RAFT, a leading research institute in the field of regenerative medicine
  - **Gianmaria Conti:** Founding partner of CPAssociati, a chartered accountant's professional firm in Italy; extensive experience providing advisory services to national and international companies in the areas of corporate governance, finance transactions, M&A operations, and tax



# Jaguar/Napo Pharma Executive Management Team

Name / Title	Experience
<b>Lisa Conte</b> Founder & CEO	<ul style="list-style-type: none"> <li>30+ years of industry experience</li> <li>Obtained first anti-secretory human product FDA approval</li> <li>Board of directors of Healing Forest Conservancy</li> <li>Raised over \$400 mm</li> </ul>
<b>Carol Lizak, MBA</b> Chief Financial Officer	<ul style="list-style-type: none"> <li>20 years of corporate controllership and financial planning and analysis experience under U.S. GAAP &amp; IFRS</li> <li>10+ years with public companies including foreign subs (5 years in biopharma)</li> </ul>
<b>Steven King, PhD</b> Chief Sustainable Supply, Ethnobotanical Research & IP Officer	<ul style="list-style-type: none"> <li>Served as head of sustainable supply, ethnobotanical research &amp; IP: 1989-2020</li> <li>Board of Directors of Healing Forest Conservancy</li> </ul>
<b>Pravin Chaturvedi, PhD</b> Chief Scientific Officer Chair of Scientific Advisory Board	<ul style="list-style-type: none"> <li>25+ years drug development experience</li> <li>Co-Founded Scion, IndUS and Oceanix Pharmaceuticals</li> <li>Successfully developed Mytesi® (first pivotal adaptive design) and 7 pharmaceutical products</li> </ul>
<b>Darlene Horton, M.D.</b> Chief Medical Officer	<ul style="list-style-type: none"> <li>Biopharmaceutical veteran and leading clinical development expert</li> <li>25 years experience in development of investigational and commercialized biopharmaceutical and drug-device combination products</li> <li>Experienced in design of SBS clinical programs</li> </ul>
<b>David Sesin, PhD</b> Chief Manufacturing Officer	<ul style="list-style-type: none"> <li>Pharmaceutical scientist with experience from drug discovery through manufacturing</li> <li>Developed crofelemer manufacturing process</li> </ul>
<b>Jonathan Wolin, JD, MBA, CPA</b> Chief of Staff, Chief Compliance Officer & General Counsel	<ul style="list-style-type: none"> <li>Extensive experience providing legal advice and guidance to public and private companies in the healthcare and biotechnology industries</li> </ul>
<b>Ian H. Wendt, MBA</b> Chief Commercial Officer	<ul style="list-style-type: none"> <li>Has held commercial leadership roles across sales, marketing and operations at some of the largest brands in the pharmaceutical industry over past 25 years</li> </ul>
<b>Melissa Yaeger, JD</b> Sr. VP, Regulatory Affairs & Quality Assurance	<ul style="list-style-type: none"> <li>Leadership supporting the approval of multiple products</li> <li>International regulatory leadership</li> <li>Gilead, Becton Dickinson, several specialized biotechnology companies</li> </ul>
<b>Michael K. Guy, DVM, MS, PhD</b> VP, Preclinical & Nonclinical Studies	<ul style="list-style-type: none"> <li>20+ years experience in animal and human pharmaceutical development, including clinical development, manufacturing, regulatory and pre-clinical drug discovery</li> </ul>

# Investment Highlights

<b>Crofelemer: FDA-Approved Human Drug</b>	<ul style="list-style-type: none"> <li>▪ Only FDA-approved diarrhea treatment in adults living with HIV/AIDS on ART</li> <li>▪ In development for multiple possible follow-on gastrointestinal indications</li> <li>▪ International supply chain in place with sustainable supply of commercial scale of raw material sourcing</li> </ul>
<b>Short Bowel Syndrome (SBS) Opportunity</b>	<ul style="list-style-type: none"> <li>▪ A treatment that can delay or reduce an SBS patient's reliance on parenteral support will offer significant value to the patient in terms of disease management, dignity, and quality of life and offer significant cost savings to the healthcare system</li> </ul>
<b>Napo EU Formed to Expand Crofelemer Access in Europe*</b>	<ul style="list-style-type: none"> <li>▪ Single payer health care systems in European countries have great incentive to focus on mitigation of burden of long-term chronic illness, particularly in the young</li> <li>▪ Designated orphan medicines are eligible for conditional marketing authorisation through the EMA</li> <li>▪ Financial and regulatory incentives for orphan medicines</li> </ul>
<b>Multiple Crofelemer Indication Expansion Opportunities</b>	<ul style="list-style-type: none"> <li>▪ Napo EU license to study, develop and commercialize crofelemer in Europe* for proposed SBS indication</li> <li>▪ Napo Pharma's CTD-Phase 3 in US</li> <li>▪ File IND for CDD</li> <li>▪ 3 IITs (functional diarrhea, idiopathic diarrhea, CTD)</li> </ul>
<b>Oversight of Napo EU Management by Jaguar &amp; Napo Pharma</b>	<ul style="list-style-type: none"> <li>▪ Napo EU has management contract with Napo Pharmaceuticals personnel</li> <li>▪ The U.S.-based Jaguar and Napo management teams collectively have more than 100 years of experience in the development of gastrointestinal prescription drug, and plant-based products</li> <li>▪ Joint Steering Committee for Napo EU to be formed with Napo Pharmaceuticals</li> <li>▪ Licensor – well funded NASDAQ listed company</li> </ul>
<b>Robust IP Protection</b>	<ul style="list-style-type: none"> <li>▪ Napo Pharma holds ~144 patents (majority do not expire until 2027-2031) and ~42 patents pending</li> <li>▪ Botanical guidance protection – no generic pathway</li> </ul>

\*Excluding Russia

# Appendix

---



### Worldwide per Year

14 Million New Cases  
of Cancer Diagnosed<sup>1</sup>

4 Million  
People  
Receiving  
Chemotherapy<sup>2</sup>

### Diarrhea and Cancer Treatments

- Chemotherapy-induced diarrhea in ~50-80% of treated patients<sup>3</sup>

### Culture of Supportive Care in Cancer Market

- Approved drugs for chemotherapy-induced nausea and vomiting (CINV) include Sustol, Aloxi, Akynzeo and Sancuso
- Allied Market Research estimates that global sales of CINV drugs may reach \$2.7 billion by 2022 growing ~7.1% per annum<sup>4</sup>

### American Society of Clinical Oncology Annual Meeting (ASCO): June 4-8, 2021

- **Abstract associated with CTD by Napo and Napo's collaborators accepted for poster presentation:** *The impact of cancer-related diarrhea on changes in cancer therapy patterns: Real world evidence*
- **Two other CTD-related abstracts from Napo and its collaborators accepted for online publication:**
  - *Healthcare utilization and costs associated with cancer-related diarrhea*
  - *Characterizing unplanned resource utilization associated with cancer-related diarrhea*

<sup>1</sup>National Cancer Institute. Cancer Statistics: <http://www.cancer.gov/about-cancer/what-is-cancer/statistics>

<sup>2</sup><http://www.transparencymarketresearch.com/cinv-market.html>; Transparency Market Research. *CINV Existing and Pipeline Drugs Market: Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2014-2020*

<sup>3</sup><https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3126005/>

<sup>4</sup><https://www.prnewswire.com/news-releases/chemotherapy-induced-nausea-and-vomiting-cinv-market-expected-to-reach-2659-million-by-2022-611755395.html>



- **Crofelemer safety studies acceptable and no new nonclinical toxicity studies required**
  - ❖ Chemistry, manufacturing and controls (CMC) data acceptable
  - ❖ No additional requirements for drug interaction studies for the CTD program
- **Statistically significant results achieved in preclinical study of crofelemer on diarrhea induced in healthy dogs by neratinib, a TKI. Results:**
  - ❖ Study conducted without the prophylaxis or concomitant use of loperamide and demonstrated that crofelemer caused an approximate 30% reduction in the incidence and severity of diarrhea associated with daily oral administration of the pan-HER TKI neratinib (Nerlynx®)
  - ❖ Crofelemer enabled maintenance and tolerability of a higher dose of the selected TKI
  - ❖ Crofelemer-treated groups received ~20% higher doses of the TKI than placebo group
  - ❖ Study funded by Puma Biotechnology, manufacturer of neratinib
- **Features of single Phase 3 pivotal trial:**
  - ❖ **Planned Label:** Symptomatic relief of diarrhea in adult patients with solid tumors receiving targeted cancer therapies with or without cycle chemotherapy
  - ❖ **Principal investigator (MD Anderson) & co-investigators identified**
  - ❖ **Target completion for 256 patients, dbpc (double-blind, placebo-controlled), end of 2022**

# Cholera Tropical Disease Priority Review Voucher (TDPRV) Opportunity: Lechlemer (Second Generation Anti-Secretory Agent)

Priority Review Voucher Transactions			
Date	Market Value (\$M)	Purchaser	Seller
Jul 2014	\$67	Sanofi (SNY)	BioMarin (BMRN)
Nov 2014	\$125	Gilead (GILD)	Knight Therapeutics (KHTRF)
May 2015	\$245	Sanofi (SNY)	Retrophin (RTRX)
Aug 2015	\$350	AbbVie (ABBV)	United Therapeutics (UTHR)
Q2 2016	\$200	Gilead (GILD)	PaxVax
Feb 2017	\$125	Gilead (GILD)	Sarepta Therapeutics (SRPT)
Q3 2017	\$150	Teva Pharma (TEVA)	Undisclosed
Nov 2017	\$125	Undisclosed	BioMarin (BMRN)
Dec 2017	\$130	Novartis (NVS)	Ultragenyx (RARE)
Apr 2018	\$110	Jazz Pharm (JAZZ)	Spark Therapeutics (ONCE)
Jul 2018	\$81	Gilead (GILD)	Ultragenyx (RARE)
Nov 2018	\$80	Eli Lilly (LLY)	Siga Technologies (SIGA)
Mar 2019	\$105	Biohaven Pharma (BHVN)	GW Pharma (GWPRF)
Aug 2019	\$95	AstraZeneca (AZN)	Swedish Orphan Biovitrum AB (SOBI)
Dec 2019	\$95	Undisclosed	Bavarian Nordic
Feb 2020	\$111	Vifor Pharma	Undisclosed
Jul 2020	\$60	Merck	Lumos Pharma, Inc.
<b>Average</b>	<b>\$133</b>		

Sources: <https://www.raps.org/regulatory-focus/news-articles/2017/12/regulatory-explainer-everything-you-need-to-know-about-fdas-priority-review-vouchers>;  
<https://www.globenewswire.com/news-release/2020/07/27/2068182/0/en/Lumos-Pharma-Announces-Sale-of-Priority-Review-Voucher.html>