# Jaguar Health, Inc. (NASDAQ: JAGX)



Overview – June 2021

# **Forward-Looking Statements**

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding the Company's plan to develop and commercialize crofelemer in Europe (excluding Russia) for HIV-related diarrhea and intestinal failure-short bowel syndrome (IF-SBS) indications, the Company's expectation that its Italian subsidiary will be the target company for a SPAC, the Company's expectation that its Italian subsidiary will merge with a SPAC, the anticipated terms of the proposed merger of the Company's Italian subsidiary with the SPAC and the potential range of ownership by the SPAC in the Company's Italian subsidiary post-merger, the endpoints the Company intends to explore in studies, the Company's plans to pursue a possible indication of symptomatic relief of diarrhea from cholera, the Company's plans to pursue additional business development deals, plans to expand the geography for commercialization of crofelemer, and the timing of data results from planned proof of concept studies, field studies, investigator-initiated trials, sponsored studies, and other studies are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the 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 presentation are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation 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 our control. Please see the risk factors identified in our Annual Report on Form 10-K and our other filings with the SEC. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Readers are also advised that our projected sales do not take into account the royalties and other payments we will need to make to our licensors and strategic partners. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we 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.

# What We Do: Develop New Ways and Novel Plant-based Medicines to Treat Gastrointestinal and Mental Health Disorders

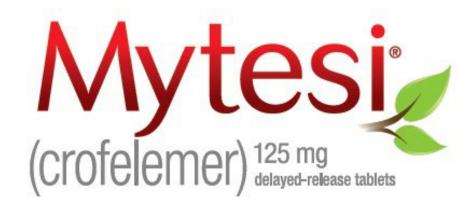
# From Tree to Bottle

Crofelemer was discovered through the science of ethnobotany



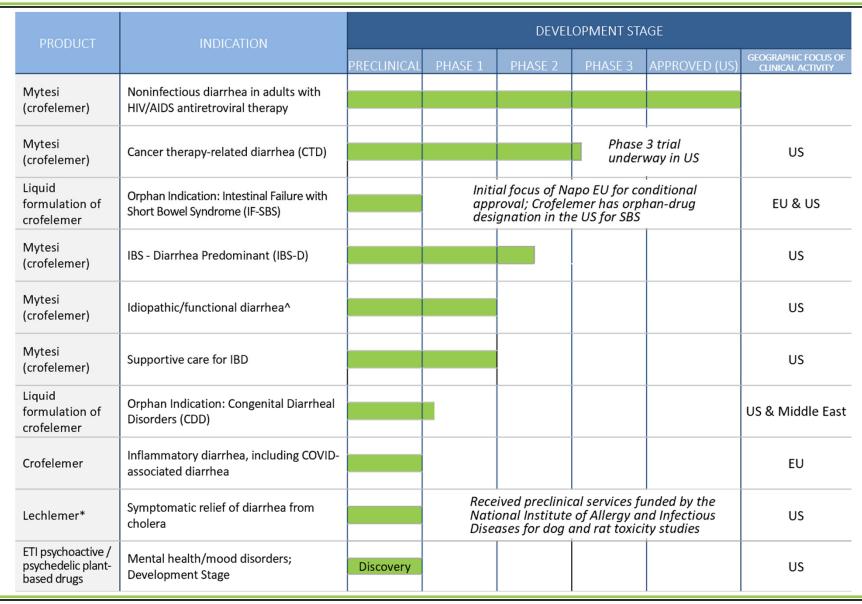


## **Mytesi Current Indication**



Mytesi (crofelemer 125mg delayed-release tablets) is FDA-approved for symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy

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



## **Global Growth Potential—Strategy**

# Hold global rights to FDA-approved product with:

- Chronic safety profile
- Commercial manufacturing in place
- Multiple potential follow-on indications addressing large patient populations in need
- Phase 2 and/or proof-of-concept data for most target indications

# Build value recognition in Jaguar by all stakeholders:

- "Live within our means": Mytesi HIV sales
- Business development partnerships to progress pipeline development globally
  - Knight Therapeutics license for Canada and Israel with milestones of approximately \$18M + royalties





## **How Mytesi Works**

Mytesi is a non-opioid that works differently from other treatments for diarrhea



#### With Mytesi, it's about waterflow

Mytesi normalizes waterflow in the GI tract



Less water flowing into your GI tract = less watery diarrhea





### Mytesi acts locally in the GI tract



Most other diarrhea medicines work by slowing down your GI tract, i.e. opioids cause constipation



Mytesi is a non-opioid, non-antibiotic, non-addictive drug approved for chronic use

8



# **Size of Target Markets**

Global market for gastrointestinal agents (Rx & OTC) expected to reach \$21 billion by 2025.1	Number of Competitors for Crofelemer's Approved/Anticipated Indications	Market Size/Potential			
HIV-D	0	Jaguar estimates the U.S. market revenue potential for Mytesi® to be ~\$100mm in gross annual sales			
СТД	0	~650,000 U.S. cancer patients receive chemotherapy in an outpatient oncology clinic. <sup>2</sup> Comparable supportive care (i.e. CINV) product sales ~\$620 mm, 2013 <sup>3</sup> ; global CINV market projected to reach valuation of \$2.7 bn by 2022 <sup>4</sup>			
IF-SBS/CDD-Orphan	0	Crohn's & Colitis Foundation estimates ~10,000 to 20,000 people in U.S. have SBS. North America is largest SBS market. Orphan-drug designation provides potential financial benefits. Estimated annual U.S. revenue for Takeda's SBS drug Gattex is ~\$555 mm. 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			
IBS-D	3	Most IBS products have estimated revenue potential >\$1.0 bn <sup>6</sup>			
IBD	0 (additive to anti-inflammatory therapy)	Estimated 1,171,000 Americans have IBD <sup>7</sup>			
COVID-associated diarrhea	0	Assuming ~25% population in Europe infected with COVID, diarrhea in acutely infected COVID-19 patients and in COVID recovery patients suffering from long-hauler syndrome could be greater than 50 mm people			
Symptomatic relief of diarrhea from cholera	0	Priority review vouchers have sold for \$60mm to \$350mm <sup>8</sup>			

Research and Markets 2017 report: "Global Gastrointestinal agents Market Size, Market Share, Application Analysis, Regional Outlook, Growth Trends, Key Players, Competitive Strategies and Forecasts, 2017 to 2025"

2 Centers for Disease Control and Prevention. Preventing Infections in Cancer Patients: Information for Health Care Providers (cdc.gov/cancer/preventinfections/providers.htm)

3 Heron Therapeutics, Inc. Form 10-K for the fiscal year ended a December 31, 2016

4 Heron Therapeutics, Inc. Form 10-K for the fiscal year ended a December 31, 2016

5 https://www.prevswipre.com/news-releases/chemotherapy-induced-nausea-and-vomiting-cinv-market-expected-to-reach-2659-million-by-2022-611755395.html

5 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

6 Merrill Lynch forecasts peak US sales of roughly \$1.5 to for Ironyood's Linzess (http://247wallst.com/healthcare-business/2015/04/27/key-analyst-sees-nearly-30-upside-in-ironwood); Rodman & Renshaw estimate peak annual sales of Synergy Pharmaceuticals'

7 Trulance at \$2.3 bn in 2021 (Source: https://www.benzinga.com/analyst-ratings/analyst-seyn-pharma-could-achieve-sustainable-profita)

7 Kappelman, M. et al. Recent Trends in the Prevalence of Crohn's Disease and Ucesaes and Uce

### 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 cancerrelated diarrhea
  - Characterizing unplanned resource utilization associated with cancer-related diarrhea

11

<sup>&</sup>lt;sup>1</sup>National Cancer Institute. Cancer Statistics: http://www.cancer.gov/about-cancer/what-is-cancer/statistics
<sup>2</sup>http://www.tRsparencymarketresearch.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

# 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.





12

<sup>&</sup>lt;sup>1</sup>Managing the Adult Patient With Short Bowel Syndrome, Carol Rees Parrish, MS, RD and John K. DiBaise, MD <sup>2</sup>https://www.medicinejournal.co.uk/article/S1357-3039(07)00027-8/abstract

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

#### **Treatment Pathway**

Nutritional support (delivery of nutrients, electrolytes and fluids):

- Intravenous nutrition or home parenteral nutrition
- Enteral tube feeding (used infrequently)

### Drugs to promote nutrient absorption:

- Anti-motility agents (loperamide and codeine)
- Anti-secretory agents (proton pump inhibitors)

**Surgery** to reconstruct or lengthen the remaining parts of the bowel

Intestinal transplant (in case of progression)

If warranted

#### **Teduglutide**

Given concomitantly with nutritional support

Subcutaneous injection into abdomen, thigh, or arm; different injection site each time



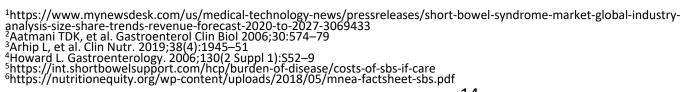
### **SBS Market**

### **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 PN in the US is approximately US\$150,000<sup>6</sup>







# 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 HIVrelated 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





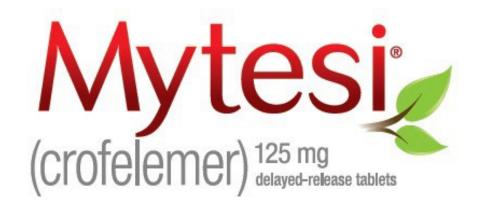
## Napo EU Funding to Date

- 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.





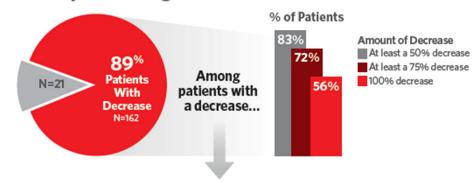
## **Mytesi Current Indication**



Mytesi (crofelemer 125mg delayed-release tablets) is FDA-approved for symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on antiretroviral therapy

# **Adults Living with HIV/AIDS & Take ARTs**

Week 20 on Mytesi 125-mg BID



83% of patients had at least a 50% decrease in watery stools

Over half of patients had no watery stools at all (100% decrease)

### 1 in 5 people living with HIV has diarrhea



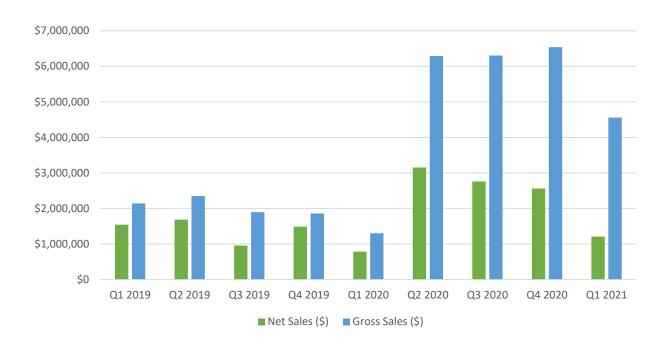
18

MacArthur RD, Clay P, Blick G, et al. Long-Term Crofelemer Provides Clinically Relevant Reductions in HIV-Related Diarrhea. Poster presented at: 9th IAS Conference on HIV Science (IAS 2017); 2017 July 23-26; Paris, France.



### Implemented Comprehensive Patient Access Program April 2020: NapoCares™

- Q1 2021 Mytesi Net & Gross¹ Sales: Approximately \$1.2 Million & \$4.6 Million Respectively
- > 2020 Mytesi Annual Net & Gross Sales: Approximately \$9.3 Million & \$20.4 Million Respectively



A line-by-line reconciliation of gross sales to net sales is included in the appendix on the final slide of this presentation

#### <sup>1</sup>Note Regarding Use of Non-GAAP Measures

Gross sales percentages issued by the Company are based on gross sales figures that represent Mytesi orders placed by wholesalers with Jaguar's third-party logistics warehouse which generate invoiced sales and cashflow for Napo. Gross sales is used internally by management as an indicator of and to monitor operating performance, including sales performance of Mytesi, salesperson performance, and product growth or declines. The Company believes that the presentation of gross sales provides a closer to real-time useful measure of our operating performance. Gross sales is not a measure that is recognized under accounting principles generally accepted in the United States of America ("GAAP") and should not be considered as an alternative to net sales, which is determined in accordance with GAAP, and should not be used alone as an indicator of operating performance in place of net sales. Additionally, gross sales may not be comparable to similarly titled measures used by other companies, as gross sales has been defined by the Company's internal reporting practices. In addition, gross sales may not be realized in the form of cash receipts as promotional payments and allowances may be deducted from payments received from certain customers.

## **Jaguar Health by the Numbers**

# Revenue-Generating Biopharma With an FDA-Approved Drug

64%

2020 Mytesi net sales increased approximately 64% over 2019<sup>1</sup>



148%

2020 Mytesi gross sales increased approximately 148% over 2019<sup>1</sup>

# Summary of NapoCares<sup>™</sup> Programs

At Jaguar and Napo, we remain fully committed to expanding access to Mytesi to all patients in need, with the goal of ensuring that no patient is denied access to Mytesi due to cost

- > April 2020: Expanded NapoCares patient support program by:
  - ➤ Increasing co-pay support for commercially insured patients, which includes allowing the co-pay amount to remain the same whether a patient fills a 30-day or 90-day Mytesi prescription
  - ➤ Increasing the income limit for the Patient Assistance Program (PAP) from 2 times the Federal Poverty Limit to 5 times the Federal Poverty Limit, which will allow more low-income patients to receive Mytesi at no cost
- ➤ Napo's copay program and Patient Assistance Program are components of a comprehensive suite of patient support services that have been rolled out with the support of **AssistRx**, a patient hub services provider

21

- Additional components of NapoCares:
  - Support for prior authorizations and appeals
  - Linkage to specialty pharmacies to fill prescriptions
  - Mail order pharmacy support
  - Patient call center to answer questions

### **Entheogen Therapeutics Initiative – First Lead Compound Identified**

Entheogen Therapeutics Initiative to support the discovery and development of novel, *plant-based* medicines derived from psychoactive plants for treatment of mood disorders, neuro-degenerative diseases, addiction, and other mental health disorders.

- Leverage Napo's proprietary library of approximately 2,300 plants and approximately 3,500 plant extracts with ethnomedicinal investigation
- Seeking next generation first-in-class agents, novel mechanisms of action, cures versus symptom relief
- First compound identified for possible psychoses/schizophrenia indications
- ➤ Jaguar's distinct capability based on successful development and commercialization of Mytesi, the first-and-only oral plant-based prescription medicine to receive FDA approval under FDA Botanical Guidance
- Jaguar pursuing collaborations with potential corporate partners with skillsets in clinical development of psychoactive therapies



Picralima nitida plant, a species of West African plant of the genus Picralima in the family Apocynaceae, and the source of the active ingredient alstonine

# **Upcoming Milestones**

- > Q2 2021 Q4 2021: Additional business development activity
- ➤ **1H 2021:** Completion of Phase 4 exploratory study evaluating effect of Mytesi on the microbiome
- Mid-2021: Anticipated timing of merger of Napo EU with Dragon SPAC
- > 2H 2021: Top line results expected for investigator-initiated Phase 2 CTD trial
- Q4 2021: Launch Canalevia for CID & EID in dogs
- ➤ 1H 2022: File clinical trial application (CTA) in EU for initiation of IF-SBS clinical trial
- ➤ 1H 2022: Initiate Phase 1 study of lechlemer for symptomatic relief of diarrhea from cholera
- ➤ 1H 2022: Initiate CDD Phase 1/2 study (orphan indication) US and Middle East



## **Jaguar/Napo Pharma Executive Management Team**

Name / Title	Experience				
<b>Lisa Conte</b> Founder & CEO	<ul> <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>				
Carol Lizak, MBA Chief Financial Officer	<ul> <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> <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> <li>25+ years drug development experience</li> <li>Co-Founded Scion, IndUS and Oceanyx Pharmaceuticals</li> <li>Successfully developed Mytesi® (first pivotal adaptive design) and 7 pharmaceutical products</li> </ul>				
Darlene Horton, M.D. Chief Medical Officer	<ul> <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> <li>Pharmaceutical scientist with experience from drug discovery through manufacturing</li> <li>Developed crofelemer manufacturing process</li> </ul>				
Jonathan Wolin, JD, MBA, CPA Chief of Staff, Chief Compliance Officer & General Counsel	<ul> <li>Extensive experience providing legal advice and guidance to public and private companies in the healthcare and biotechnology industries</li> </ul>				
lan H. Wendt, MBA Chief Commercial Officer	<ul> <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>				
Melissa Yaeger, JD Sr. VP, Regulatory Affairs & Quality Assurance	<ul> <li>Leadership supporting the approval of multiple products</li> <li>International regulatory leadership</li> <li>Gilead, Becton Dickinson, several specialized biotechnology companies</li> </ul>				
Michael K. Guy, DVM, MS, PhD VP, Preclinical & Nonclinical Studies	<ul> <li>20+ years experience in animal and human pharmaceutical development, including clinical development, manufacturing, regulatory and pre-clinical drug discovery</li> </ul>				

24

# **Board of Directors**

Name / Title	Experience
James Bochnowski Chairman	<ul> <li>Founder of Delphi Ventures, one of the first VC firms to focus exclusively on investing in life sciences companies</li> <li>Co-founded Technology Venture Investors</li> </ul>
<b>Lisa Conte</b> Founder, CEO & President	<ul> <li>28+ years of industry experience</li> <li>Obtained first anti-secretory human product FDA approval</li> </ul>
John Micek III Director	<ul> <li>Managing Partner of Verdant Ventures</li> <li>Former Managing Director of Silicon Prairie Partners, LP</li> </ul>
<b>Jonathan B. Siegel</b> Director	<ul> <li>Founded JBS Healthcare Ventures with a focus on public and private healthcare investments</li> <li>18+ years of investment experience</li> </ul>
<b>Greg Divis</b> Director	<ul> <li>CEO of Avadel Pharmaceuticals</li> <li>28+ years of direct operating and global leadership experience in specialty pharmaceuticals</li> </ul>

### **Investment Highlights**

### Mytesi (Crofelemer): FDA-Approved Human Drug

- Only FDA-approved diarrhea treatment that's been studied specifically in adults with HIV / AIDS
- Phase 4 microbiome study completed

# Planned Crofelemer Expansion

Progression from supportive care to impact on outcome/cost of care to treatment modifying

- Napo's CTD Phase 3
- Intestinal failure-SBS treatment modifying
- 3 IITs (functional diarrhea, IBS, CTD)

# Non-dilutive Financing for Jaguar

- Royalty deals to fund CTD
- License to Napo EU combination with Dragon SPAC
- Strong cash position

# Potential Priority Review Voucher Opportunity: 2<sup>nd</sup> Generation Product

- Cholera-related diarrhea potential to receive Tropical Disease Priority Review Voucher (PRV)
- Average sale of PRV \$137 million
- Lechlemer preclinical services funded by NIAID
- Reduced COGS

#### **Strategic Partnerships**

- Unencumbered global commercial rights to Mytesi/crofelemer pipeline
- Napo EU wholly owned subsidiary target of Italian Dragon SPAC
- Entheogen Therapeutics Initiative leveraging proprietary 2,300-plant ethnobotanical database

### **Strong Management Team**

- Key management has been with the company for >20 years
- Chairman of board and key investors have invested for >30 years

#### **Proprietary Position**

- ~144 patents (majority do not expire until 2027 2031) and ~42 patents pending
- Sustainable supply of commercial scale of raw material sourcing
- Botanical guidance protection no generic pathway

### **Cancer Therapy-Related Diarrhea (CTD)**

- 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

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

#### **Approved Drugs Used in SBS:**

- ❖ Takeda Pharmaceuticals' Gattex® (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® 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® is a recombinant human growth hormone indicated in the U.S. for the treatment of SBS in adult patients receiving specialized nutritional support.
  - 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 oùtpatients 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.



somatropin) for injection

# 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 <u>fast-track</u> clinical review process

  EUROPEAN MEDICINES AGENCY
- > 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 EU¹
  - ❖ Orphan Medicine: A medicine for the diagnosis, prevention or treatment of a lifethreatening 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</sup>

### **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)¹
  - 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>&</sup>lt;sup>2</sup> Currently in Napo Pharma sponsored Phase 3, NDA-enabling clinical trial in US

## **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



### Study for Pediatric Orphan-Drug Indication: Congenital Diarrheal Disease (CDD)

### Congenital Diarrheal Disease (CDD)

#### Rare Congenital Chronic Intestinal Channel Disease Occurring in Early Infancy

• Severe, lifelong diarrhea; Incidence more prevalent in regions with consanguineous marriage

#### **Treatment Options<sup>1</sup> and Unmet Needs**

• Lifelong need for nutritional intake either parenterally or a feeding tube

#### **NEXT STEPS:**

- > In vitro confirmation of activity required by FDA
- Expect to initiate Phase 1/2 study in 2H 2021
  - US and Middle East sites



"With the early and extreme morbidity and mortality suffered by CDD patients, we welcome the opportunity to participate in the investigation of a novel drug to address the devastating diarrhea and dehydration caused by this lifelong disease for which there is currently no available treatment except parenteral nutrition, and help limit the suffering of patients and their family members."

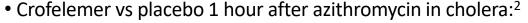
~ Dr. Mohamad Miqdady



### Worldwide per Year

Up to 4 million cases of Cholera<sup>1</sup>

Up to 143K deaths<sup>1</sup>



- ❖ Reduced amount of watery stool, 25-30%
- Indian patient study in adults with severe watery diarrhea:
- Crofelemer statistically significant in all 7 prospectively defined endpoints
- Crofelemer superior for overall clinical success, 79%
   vs. 28%



Lechlemer: Second-Generation Anti-Secretory Agent in Development for Symptomatic Relief of Diarrhea from Cholera

 Jaguar received preclinical services funded by the National Institute of Allergy and Infectious Diseases



¹https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4455997

<sup>3</sup>Bardhan PK EID.'09

<sup>&</sup>lt;sup>2</sup>Bardhan, et.al., '08 US-Japan Cholera Conf.

### **Ongoing Investigator-Initiated and Phase 4 Trials**

### Chronic Idiopathic Diarrhea in Non-HIV Adult Patients

- Yield of Diagnostic Tests and Management of Crofelemer for Chronic Idiopathic Diarrhea in Non-HIV Patients: A Pilot Study
- Single-center clinical research study in adult non-HIV patients at The University of Texas Health Science Center at Houston

#### Functional Diarrhea in Non-HIV Adult Patients

- Randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, and efficacy of crofelemer in subjects with functional diarrhea
- To be conducted at a single center at Beth Israel Deaconess Medical Center, a Harvard Medical School institution in Boston

### Diarrhea in HER2-positive Breast Cancer Patients

- HALT-D: Diarrhea Prevention and Prophylaxis with Crofelemer in HER2 Positive Breast Cancer Patients Receiving Trastuzumab, Pertuzumab, and Docetaxel or Paclitaxel with or without Carboplatin
- Ongoing investigator-initiated study at Georgetown University to obtain preliminary evidence of the effectiveness of crofelemer for the symptomatic relief of diarrhea in HER2-positive breast cancer patients receiving chemotherapy with trastuzumab, pertuzumab, and docetaxel or paclitaxel with or without carboplatin

#### HIV Microbiome Phase 4 Clinical Trial

Analysis of study results underway

### **Patient Case Reports**

- A case report titled Improved Control of
  Tyrosine Kinase Inhibitor-Induced Diarrhea with
  a Novel Chloride Channel Modulator: A Case
  Report was published April 7, 2021 in Oncology
  and Therapy, an international, open access,
  peer-reviewed (single-blind) journal.
- ➤ Patient reference contained in Napo's FDA application for **orphan-drug designation** for crofelemer for SBS

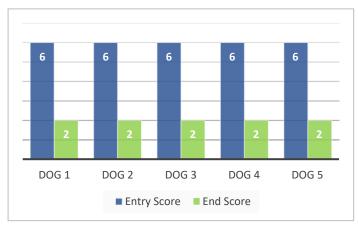


# Chemotherapy-Induced Diarrhea (CID) in Dogs (MU/MS): A Model for Human Development

- ➤ Canalevia<sup>™</sup> is a canine-specific formulation of crofelemer
  - Estimated that >230,000 dogs receive chemotherapy in US each year
    - ❖ Approximately 25% of these dogs suffer from CID
- ➤ Regulatory filing complete for conditional approval of Canalevia for CID under Minor Use/Minor Species (MU/MS), a designation modeled on orphan-drug designation for human drug development
- ➤ CID dog study: Dogs with unformed stools responded, based on a fecal scoring scale of 1 (very hard and dry) to 6 (has texture but no defined shape)

➤ Jaguar is also pursuing conditional approval of Canalevia for exercise-induced diarrhea (EID) under MU/MS

### **CID Dog Study**



Key: End scores of 2 or 3 considered ideal

With receipt of conditional approval, expect to launch for CID in dogs and EID in dogs in Q4 2021

36



### **Capitalization Table & Debt – Fully Diluted**

Capitalization as of May 20, 2021		
Common Shares Outstanding, voting (authorized 150M shares)		137,318,263
Non-Voting Common <sup>1</sup>		2,020
Options Outstanding <sup>2</sup>		
2014 Equity Incentive Plan available for grant includes 5% Evergreen 2021 <sup>3</sup>		6,411,067
Options available for grant (includes 2020 New Employee Inducement Plan) <sup>3</sup>		2,430,636
RSUs <sup>2</sup>		2,038,873
Other – Napo Merger to Jaguar		2,199
Warrants – Jaguar <sup>4</sup>	651,165	
Warrants – Other (weighted average exercise price \$90.00)	1,029	
Warrants – Series 1 (net of conversion)	436,190	
Warrants – Series 2 (July 2019 offering)	401,190	
Warrants – Other	200,780	
Total Warrants		1,690,354
Fully Diluted Shares 5		149,893,412

#### Debt largely from Royalty arrangements as of March 31, 2020: \$25.7 million (current \$1.4M and non-current \$24.3M)

38

<sup>&</sup>lt;sup>1</sup>Represents 2,020 non-voting Common Stock convertible into shares of Common Stock, voting on a 1:1 basis.

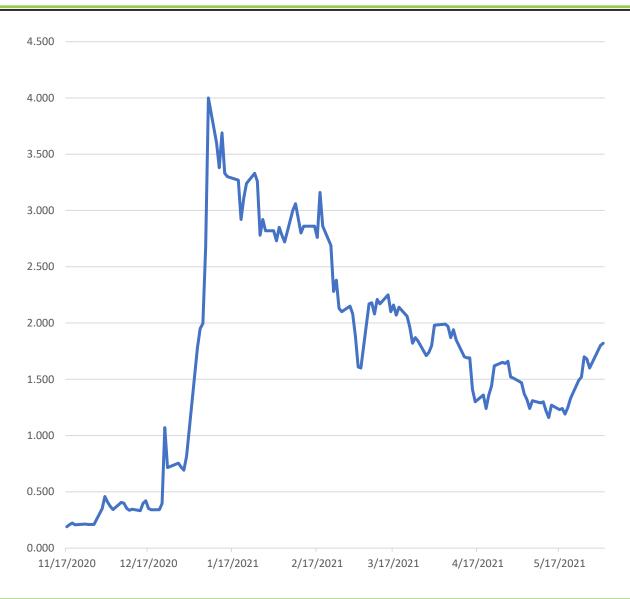
<sup>&</sup>lt;sup>2</sup>Includes 6,411,067 options granted to officers, directors, employees, and 11 consultants (30,249 options are above \$30.80 strike price) and 2,038,873 RSUs.

<sup>&</sup>lt;sup>3</sup>Options available for grant: 2,164,579 under 2014 EIP and 266,057 under 2020 New Employee Inducement Award Plan.

<sup>&</sup>lt;sup>4</sup>Bridge warrants from July 2019 offering 571,875.

<sup>&</sup>lt;sup>5</sup>Less than 1% of the Company's authorized shares of Common Stock available for future issuance.

# **Stock Price Performance Since Announcement of Napo EU**



# Napo Scientific Advisory Board (SAB) Members & Key Opinion Leader (KOL) Advisors to Napo

Pravin Chaturvedi, PhD: Chair of Napo's SABs. Pravin brings 25+ years drug development experience in pharmaceutical/biotech field; Successfully developed crofelemer (Mytesi) (first pivotal adaptive design)

#### Cancer Therapy-Related Diarrhea SAB

- Lee Schwartzberg, MD, FACP: Executive Director of the West Cancer Center, a multispecialty oncology practice affiliated with the University of Tennessee; Chief, Division of Hematology/Oncology, the University of Tennessee Health Science Center
- Eric Roeland, MD: Attending Physician, Center for Palliative Care, Harvard Medical School
- Hope Rugo, MD: Clinical Professor of Medicine, Director Breast Oncology and Clinical Trials Education, Division of Hematology and Oncology, University of California San Francisco

#### Pediatric Indications (CDD/SBS) SAB

- Mohammed Miqdady, MD: Chief of Pediatric Gastroenterology, Hepatology & Nutrition at Sheikh Khalifa Medical City in Abu Dhabi
- Sue Rhee, MD: Division Chief, Pediatric Gastroenterology, Hepatology and Nutrition Pediatric gastroenterologist and liver specialist, UCSF Benioff Children's Hospital

#### **HIV-Related Diarrhea SAB**

- David Asmuth, MD: Infectious diseases specialist and Professor of Medicine, UC Davis Health
- Gary Blick, MD: Chief Medical Officer of Health Care Advocates
   International™, Co-Founder of HIV Advocates and Founder of ZAP (Zimbabwe AIDS Project)

#### KOLs: Cancer Therapy-Related Diarrhea

- Herbert DuPont, MD: Professor and Director, Center for Infectious Diseases, University of Texas Houston School of Public Health
- Pablo C. Okhuysen, MD: Department of Infectious Diseases, Infection Control, and Employee Health, Division of Internal Medicine, MD Anderson

#### KOLs: Diarrhea Related to HIV and Other Infectious Diseases

- Patrick Clay, PharmD: Consultant
- Pradip Bardhan, MBBS, MD: Chief Physician at ICDDR,B, Bangladesh
- Elie Schochet, MD, FACS: Colorectal surgeon, Holy Cross Medical Group

#### **KOLs: Diarrhea Related to IBS**

- Anthony Lembo, MD: Director of the GI Motility and Functional Bowel Disorders Program at Beth Israel Deaconess Medical Center and Associate Professor of Medicine at Harvard Medical School
- Judy W. Nee, MD: Gastroenterologist, Assistant Professor of Medicine, Beth Israel Deaconess Medical Center

#### KOLs: Diarrhea Related to IBD

- Brooks D. Cash, MD, AGAF, FACG, FACP, FASGE: Division Director, Gastroenterology, Hepatology, and Nutrition Visiting Professor of Medicine, The University of Texas McGovern Medical School
- Corey Siegel, MD, MS: Associate Professor of Medicine; Associate Professor of The Dartmouth Institute; Director of the Inflammatory Bowel Disease Center at the Dartmouth-Hitchcock Medical Center

#### KOLs: Pediatric Indications (CDD/SBS)

- Jay Thiagarajah, MD, PhD: Attending Physician, Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital. Instructor of Pediatrics, Harvard Medical School
- Alexandra Carey, MD: Director, Home Parenteral Nutrition Program;
   Attending Physician, Division of Gastroenterology, Hepatology and Nutrition,
   Boston Children's Hospital
- Lissette Jimenez, MD: Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital



## Jaguar Health, Inc. (NASDAQ: JAGX)

**Investor Relations Contact** 

Peter Hodge

phodge@jaguar.health

# Appendix A – GAAP and Non-GAAP Basis

#### Mytesi Gross Sales

Mytesi allowance for sales discounts
Mytesi allowance for sales returns
Mytesi wholesaler fee
Adjustment for product donations
Mytesi Net Sales

	Q1 2018	Q2 2018	Q3 2018	Q4 2018	Q1 2019	Q2 2019	Q3 2019	Q4 2019	Q1 2020	Q2 2020	Q3 2020	Q4 2020	Q1 2021
	\$ 795,303	\$ 1,162,890	\$ 1,592,80	1 \$ 2,179,28	9 \$ 2,143,5	13 \$ 2,350,05	8 \$ 1,897,417	\$ 1,858,006	\$ 1,303,954	\$ 6,287,979	\$ 6,303,021	\$ 6,538,564	\$ 4,558,333
nts	\$ (106,609	) \$ (211,747)	\$ (343,11	8) \$ (440,85	2) \$ (463,2	69) \$ (542,70)	8) \$ (417,306	\$ (527,752)	\$ (329,608)	\$ (2,418,488)	\$ (2,806,542)	\$ (3,228,596)	\$ (2,828,991)
	\$ (30,020	) \$ (15,629)	\$ (42,40	3) \$ (79,85	6) \$ (32,1	46) \$ (25,78)	9) \$ (30,999	\$ (31,383)	\$ (18,487)	\$ (77,929)	\$ (106,910)	\$ (69,911)	\$ (20,446)
	\$ (75,405	) \$ (81,344)	\$ (99,84	2) \$ (80,81	0) \$ (104,9	77) \$ (96,82	3) \$ (155,098	\$ (147,649)	\$ (120,850)	\$ (638,296)	\$ (630,288)	\$ (679,001)	\$ (501,380)
	NA	NA	N.	A N	А	NA NA	\$ (336,934	\$ 336,934	N/A	N/A	N/A	N/A	N/A
	\$ 583,269	\$ 854,170	\$ 1,107,43	8 \$ 1,577,77	1 \$ 1,543,1	21 \$ 1,684,73	3 \$ 957,080	\$ 1,488,156	\$ 835,009	\$ 3.153.266	\$ 2,759,280	\$ 2.561.056	\$ 1,207,515

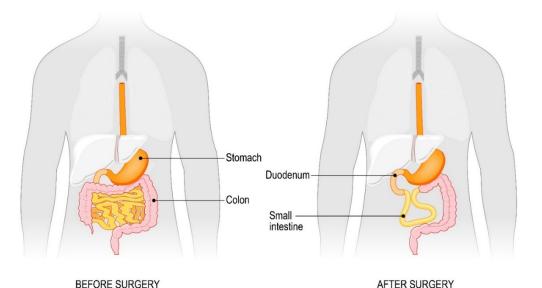
# **Appendix**



### 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 lifethreatening complications like sepsis and organ failure





# Napo EU's Expected Additional Third-party Manufacturer indena

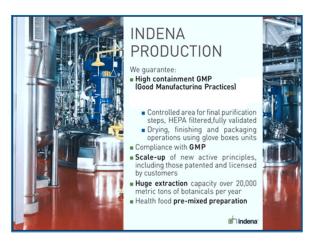


### Indena - Based in Milan, Italy

#### 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 Investment Highlights**

Crofelemer: FDA-Approved Human Drug	<ul> <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>			
Short Bowel Syndrome (SBS) Opportunity	<ul> <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>			
Napo EU Formed to Expand Crofelemer Access in Europe*	<ul> <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>			
Multiple Crofelemer Indication Expansion Opportunities	<ul> <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>			
Oversight of Napo EU Management by Jaguar & Napo Pharma	<ul> <li>Napo EU has management contract with Napo Pharmaceuticals personnel</li> <li>The US-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>			
Robust IP Protection	<ul> <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>			

<sup>\*</sup>Excluding Russia

# **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.					
Average	\$133							

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

47