

# Jaguar Health, Inc.

(NASDAQ: JAGX)

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Overview – April 2024



# Forward-Looking Statements

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This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding plans by Jaguar Health, Inc. (“Jaguar” or the “Company”) and Napo Therapeutics (formerly known as “Napo EU”) to develop and commercialize crofelemer in Europe for HIV-related diarrhea, short bowel syndrome, congenital diarrheal disorders, and other indications, expectations related to the timing of the commercial launch of products in any market, the expectation that Magdalena Biosciences will leverage Jaguar’s proprietary medicinal plant library and Filament Health’s proprietary drug development technology, the expectation that US\$1,000,000 will be invested in Magdalena Biosciences by One Small Planet, the expectation that Magdalena Biosciences may develop a potential plant-based alternative drug for adult ADHD or other indications that is both safe and efficacious, Jaguar’s plans to pursue additional business development deals, plans to expand the geography for commercialization of crofelemer, statements related to the powder formulation of crofelemer, related to NP-300, the timing of the initiation, completion, results, and publication of Phase 2 studies, Phase 3 studies, proof-of-concept studies, field studies, investigator-initiated trials, sponsored studies, and other studies, statements about possible eligibility for, and possible participation in, revenue generating early access programs, statements about the planned submission of Investigational New Drug (IND) applications to FDA, statements about plans to pursue a Priority Review Voucher (PRV), statements about the possible future market size/potential of indications, and expected milestones appearing on the list of “Upcoming Milestones”, 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 Disorders

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## From Tree to Bottle

Crofelemer was discovered through the science of ethnobotany



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

PRODUCT	INDICATIONS EVALUATED	DEVELOPMENT STAGE					GEOGRAPHIC FOCUS OF CLINICAL STUDIES
		PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	APPROVED (US)	
Mytesi (crofelemer)	Noninfectious diarrhea in adults with HIV/AIDS antiretroviral therapy						US
Crofelemer	Cancer therapy-related diarrhea (CTD)					<i>Phase 3 OnTarget trial</i>	Global
Powder formulation of crofelemer for oral solution	Adult short bowel syndrome (SBS) with intestinal failure		<i>Clinical protocol under development; Crofelemer has orphan drug designation in the EU &amp; US</i>				US & EU
Crofelemer	IBS - Diarrhea Predominant (IBS-D)						US
Crofelemer	Chronic idiopathic diarrhea in non-HIV patients (investigator-initiated POC trial)						US
Powder formulation of crofelemer for oral solution	Pediatric microvillus inclusion disease (MVID), a congenital diarrheal disorder (CDD)		<i>US IND submitted. Clinical protocol under development; Crofelemer has orphan drug designation in the EU &amp; US</i>				US & EU
NP-300*	Symptomatic relief of diarrhea from cholera		<i>See footnotes below</i>			<i>US IND in effect with FDA</i>	US

\*NP-300 and crofelemer have a similar physiological anti-secretory mechanism of action to reduce chloride ion secretion into the gut lumen and improve stool consistency. The Company has previously presented Phase 2 data on crofelemer for the treatment of devastating dehydration in cholera patients from the renowned International Centre for Diarrhoeal Disease Research (icddr,b) in Bangladesh.

\*Potential opportunity for Priority Review Voucher (PRV)

# Expected Near-Term Transformative Activities for Value Enhancement

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- **Expected forthcoming:** Comprehensive results of **pivotal phase 3 OnTarget trial** of crofelemer for prophylaxis of cancer therapy-related diarrhea (CTD) - **Chemotherapy-induced overactive bowel (CIOB)**
  - **A majority of subjects in this placebo-controlled two-stage trial chose to continue on to Stage II**
  - **Abstract outlining the trial design and the neglected medical need accepted by the December 2023 San Antonio Breast Cancer Symposium (SABCS)**
- Investigator-initiated proof-of-concept (POC) crofelemer studies for short bowel syndrome (SBS) with intestinal failure and microvillus inclusion disease (MVID), a rare CDD condition.
  - **POC data targeted in 2024 in support of potential early patient access in specific EU countries**
  - **Investigational New Drug (IND) application for crofelemer activated by FDA in August 2023 for MVID, ultra rare disease**
- **Ongoing:** Business development partnership(s) related to pipeline & global commercialization



\* Key milestones are based on management estimates. Adverse events could negatively affect their business and the timeliness of achieving key milestones.

# Increasing Market Value: Progression from Supportive Care to Impact on Outcome/Cost of Care to Treatment Modifying

**Global market for gastrointestinal agents (Rx & OTC) projected to reach \$21 billion by 2025<sup>1</sup>**

Indication	# of Competitors	Market Size/Potential
HIV-related diarrhea	0	Jaguar estimates the U.S. market revenue potential for Mytesi® to be ~\$50 million in gross annual sales
Cancer therapy-related diarrhea (CTD)	0	Projected to be 1.9 million new cancer cases in US in 2023 <sup>2</sup> >1 million cancer patients receive chemo or radiation in a US outpatient clinic annually <sup>3</sup> Comparable supportive care (CINV) global market projected to reach <b>\$3.9 billion by 2029</b> <sup>4</sup>
Short bowel syndrome (SBS) with intestinal failure / Microvillus inclusion disease (MVID), a congenital diarrheal disorder (CDD)	0	~10,000 to 20,000 people in US have SBS and approximately the same number in Europe. Orphan-drug designation supports potential accelerated approval. Estimated annual US revenue for Takeda's SBS drug Gattex: ~\$555 million. Global SBS market projected to reach <b>\$4.6 billion by 2027</b> with a CAGR of 26% from 2020 to 2027 <sup>5</sup> (doesn't include potential contribution from crofelemer's novel mechanism of action)
IBS - diarrhea predominant (IBS-D)	3	~15% of adult population Most IBS products have estimated revenue potential >\$1.0 billion <sup>6</sup>
Symptomatic relief and treatment of diarrhea from cholera and other pathogens	0	*Potential opportunity for Priority Review Voucher (PRV) PRVs are transferable, and in past transactions by other companies have sold for values ranging from \$67 million to \$350 million <sup>7</sup>

<sup>1</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"

<sup>2</sup> American Cancer Society. Cancer Facts & Figures 2023. Atlanta: American Cancer Society; 2023

<sup>3</sup> <https://www.cdc.gov/cancer/preventinfections/providers.htm#print>

<sup>4</sup> <https://www.ihealthcareanalyst.com/global-chemotherapy-induced-nausea-vomiting-drugs-market/>

<sup>5</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>6</sup> <http://247wallst.com/healthcare-business/2015/04/27/key-analyst-sees-nearly-30-upside-in-ironwood> & <https://www.benzinga.com/analyst-ratings/analyst-color/17/03/9224181/analyst-synergy-pharma-could-achieve-sustainable-profit>

<sup>7</sup> <https://www.raps.org/regulatory-focus/news-articles/2017/12/regulatory-explainer-everything-you-need-to-know-about-fdas-priority-review-vouchers>

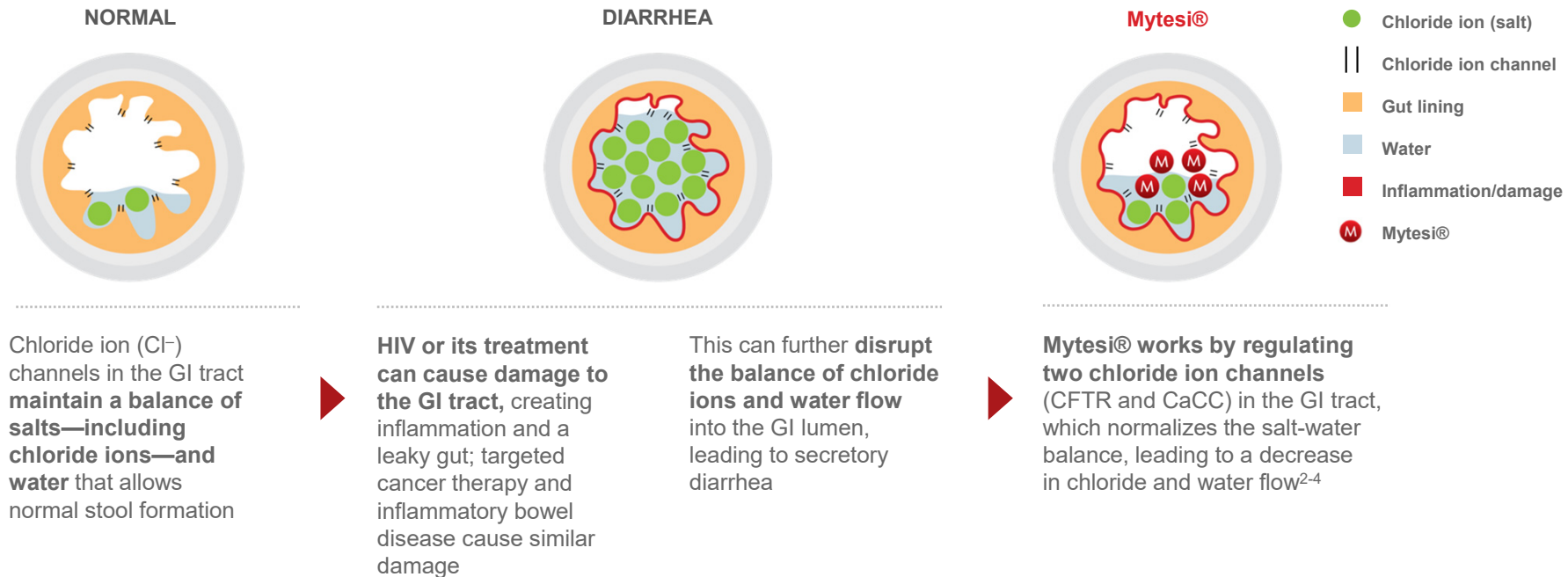
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## **Our crofelemer clinical development programs**

# Crofelemer is a First-in-Class Intestinal Chloride Channel Modulator

*Mytesi® (crofelemer) acts at the **common** last step in a physiological pathway, regardless of cause, thereby **normalizing** defective secretion, **specifically mitigating dehydration***

Crofelemer does not cause constipation or alter motility



**Acts locally** in the gut via allosteric modulation of chloride channels

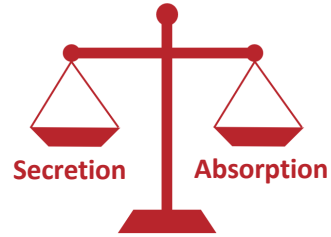
References: 1. Brenchley JM, Douek DC. *Mucosal Immunol.* 2008;1(1):23-30. 2. Mytesi® [package insert]. San Francisco, CA: Napo Pharmaceuticals, Inc; 2020. 3. Tradtrantip L, Namkung W, Verkman AS. *Mol Pharmacol.* 2010;77(1):69-78. 4. Holodniy M, Koch J, Mistal M, et al. *Am J Gastroenterol.* 1999;94(11):3267-3273.



# How Crofelemer Works

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- Crofelemer is a non-opioid that works differently from other treatments for GI dysfunction



## **With crofelemer, it's about waterflow**

Crofelemer normalizes waterflow in the GI tract

Less water flowing into your GI tract = less watery diarrhea = greater nutrient absorption opportunity



**Crofelemer acts locally in the GI tract**



**Opioid medicines (i.e., Imodium, loperamide) work by slowing down your GI tract, i.e., opioid constipation risk**



**Crofelemer is a non-opioid, non-antibiotic, non-addictive drug approved in the US for a chronic use**

# Cancer Therapy-related Diarrhea OnTarget PHASE 3 Trial: *Impact on Outcome*

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- **Impact on outcome**
  - ❖ Roeland, et al<sup>1</sup>: Patients with cancer-related diarrhea (CRD) nearly 2.9 x higher cost than patients without CRD
  - ❖ Okhuysen, et al<sup>1</sup>: **Patients with CTD 40% more likely to discontinue chemotherapy or targeted therapy than those without CTD**
  
- **IIT Phase 2 data presented at December 2021 San Antonio Breast Cancer Symposium and published in *Breast Cancer Research and Treatment* in October 2022**
  - ❖ Statistical significance on collection of secondary endpoints that map to primary endpoint of Phase 3 OnTarget trial
  
- **Features of single Phase 3 pivotal trial, OnTarget:**
  - ❖ **Planned Label:** Prophylaxis and symptomatic relief of diarrhea in adult patients with solid tumors receiving targeted cancer therapies with or without cycle chemotherapy
  - ❖ **Primary endpoint:** Reduction in the average number of weekly loose/watery stools over a 3-month period
  - ❖ **Principal investigator (MD Anderson); US and expanding to international sites**
  - ❖ **256 patients, dbpc (double-blind, placebo-controlled)– Completed, 11% over-enrolled**

<sup>1</sup> Source: Okhuysen PC, et al. Abstract 12111. Presented at: ASCO Annual Meeting (virtual meeting); June 4-8, 2021.

\* Key milestones are based on management estimates. Adverse events could negatively affect their business and the timeliness of achieving key milestones.

# Importance of the Patient Voice in Managing Cancer Care Effectively

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## *Paradigm shifting treatment with crofelemer*

- Strength of that voice as patients continue targeted therapies for months and years rising, important, and playing a role in what type of cancer treatment fits with the goals and the life of the patient (QoL)
- Patient dignity and comfort paramount
- Cancer patients = everyday people—parents, children, at school, in the workforce



## “Tolerable Toxicities” – Tolerable to Whom?

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But Jaguar strives to make life a little better by taking **one pebble out of the shoe**; one side effect off the table—with preventative treatment of chemotherapy-induced overactive bowel (CIOB)





# Napo Pharmaceuticals' *Make Cancer Less Shitty* Patient Engagement Program




“ If you ask me what’s your worst side effect,  
I’m going to ask you what day of the week is this?  
Because tomorrow is different, the next day is different,  
tonight is different. This morning is different. ”

— Person Living With Metastatic Breast Cancer

## A NEGLECTED PROBLEM


People with cancer experience numerous challenges – including **treatment-related side effects** – that can impact their quality of life (QoL). Supportive care is critical to addressing these challenges.

In a study of patient-reported chemotherapy side effects,



**6 in 10** participants reported having at least one debilitating side effect.<sup>1</sup>

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**81%** of cancer survivors reported they had unmet supportive care needs and reported dissatisfaction with current supportive care services.<sup>2</sup>

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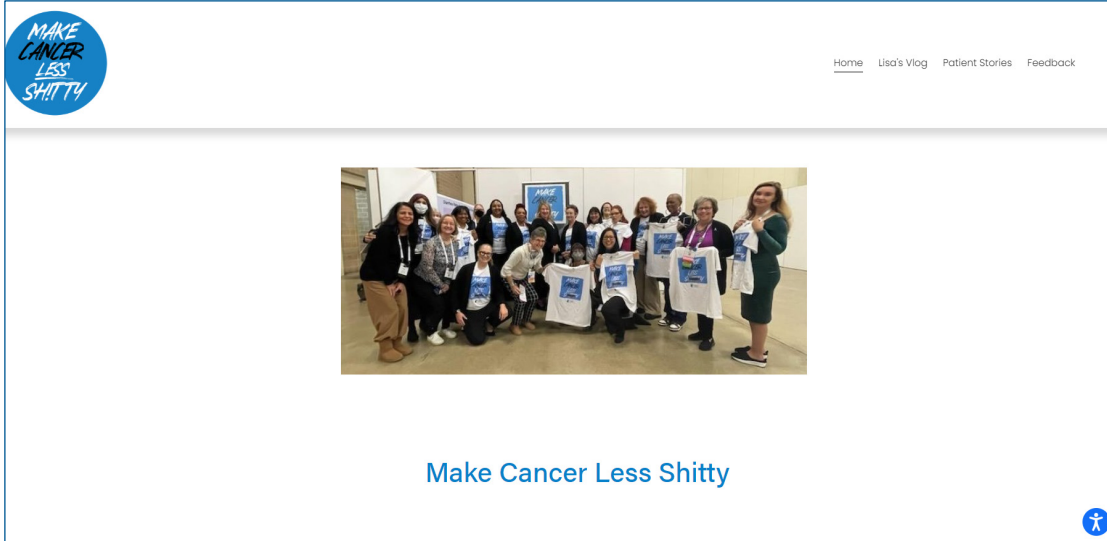
In a survey of oncology community stakeholders (researchers, nurses, medical oncologists, administrators, surgical and radiation oncologists, patient advocates, and nonphysician providers), patient QoL was ranked the most important metric over survival, access to care, and cost.<sup>3</sup>

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There remains an **urgent need** to enhance supportive care as part of overall cancer care to best protect the dignity and QoL of those living with cancer.



# Make Cancer Less Shitty Website & Social Media Pages



## Make Cancer Less Shitty Website

URL: <https://www.makecancerlessshitty.com>

## What Supportive Care Means to Us Group Video (Click image to play video)



Links to MCLS social media pages:

- [Facebook](#)
- [Instagram](#)
- [X](#)



# COMING SOON: A Protective Gel for Oral Mucositis Management



## SOOTHING PAIN RELIEF WITHOUT NUMBING

Gelclair is a prescription gel that is clinically proven to rapidly soothe the pain from oral lesions, including those from oral mucositis. It works by forming a protective layer over the oral mucosa, and by lubricating, hydrating, and coating the damaged tissues.

### BENEFITS:

- Forms a protective layer over oral mucosa
- Rapid pain relief lasting for several hours
- No stinging, drying, or numbing
- Improves ability to eat, drink, swallow, speak, and sleep
- Convenient and easy to use

LEARN MORE



GELCLAIR.COM



### INDICATIONS:

Gelclair has a mechanical action indicated for the management of pain and relief of pain by adhering to the mucosal surface of the mouth, soothing oral lesions of various etiologies, including oral mucositis/stomatitis (may be caused by chemotherapy or radiation therapy), irritation due to oral surgery, traumatic ulcers caused by braces or ill-fitting dentures, or disease. Also, indicated for diffuse aphthous ulcers.

### IMPORTANT SAFETY INFORMATION:

- Do not use Gelclair if there is a known or suspected hypersensitivity to any of its ingredients.
- No adverse effects have been reported in clinical trials, although postmarketing reports have included infrequent complaints of burning sensation in the mouth.
- If Gelclair is swallowed accidentally, no adverse effects are anticipated.
- If no improvement is seen within 7 days, a physician should be consulted.



# Oral Mucositis—A Significant Unmet Medical Need

- Oral mucositis, also called “chemo mouth,” is among the most common and debilitating cancer treatment-related side effects.
- Inflammation, sores and lesions develop on tongue and gums 5-10 days following initial chemotherapy treatment.
- Who suffers from oral mucositis?
  - 100% of patients receiving head and neck radiotherapy
  - Up to 100% of patients undergoing high dose chemotherapy with hematopoietic stem cell transplantation
  - 30-75% patients receiving chemotherapy
- These sores hurt—“I felt like I had shards of glass in my mouth”, said one sufferer. As a result, patients don’t drink/eat and lose weight at a critical time of cancer treatment.
- In addition to radiation and chemotherapy, next generation cancer treatments can also cause these sores.

## Consequences of Oral Mucositis:

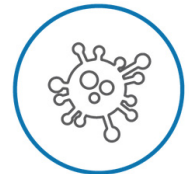
- Mouth pain
- Inability to eat and talk
- Increased risk of infections
- Chemotherapy dose reductions
- Breaks in radiation treatment
- Hospitalization and morbidity
- Cessation of cancer therapy
- Reliance on parenteral nutrition
- Administration of narcotics
- Social isolation and depression
- Incremental cost of OM exceeds \$17,000 for patients with head and neck cancer



Hospitalization



Dose reductions



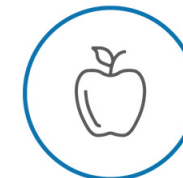
Infections



Talking and eating



Depression



Diet



Increased costs



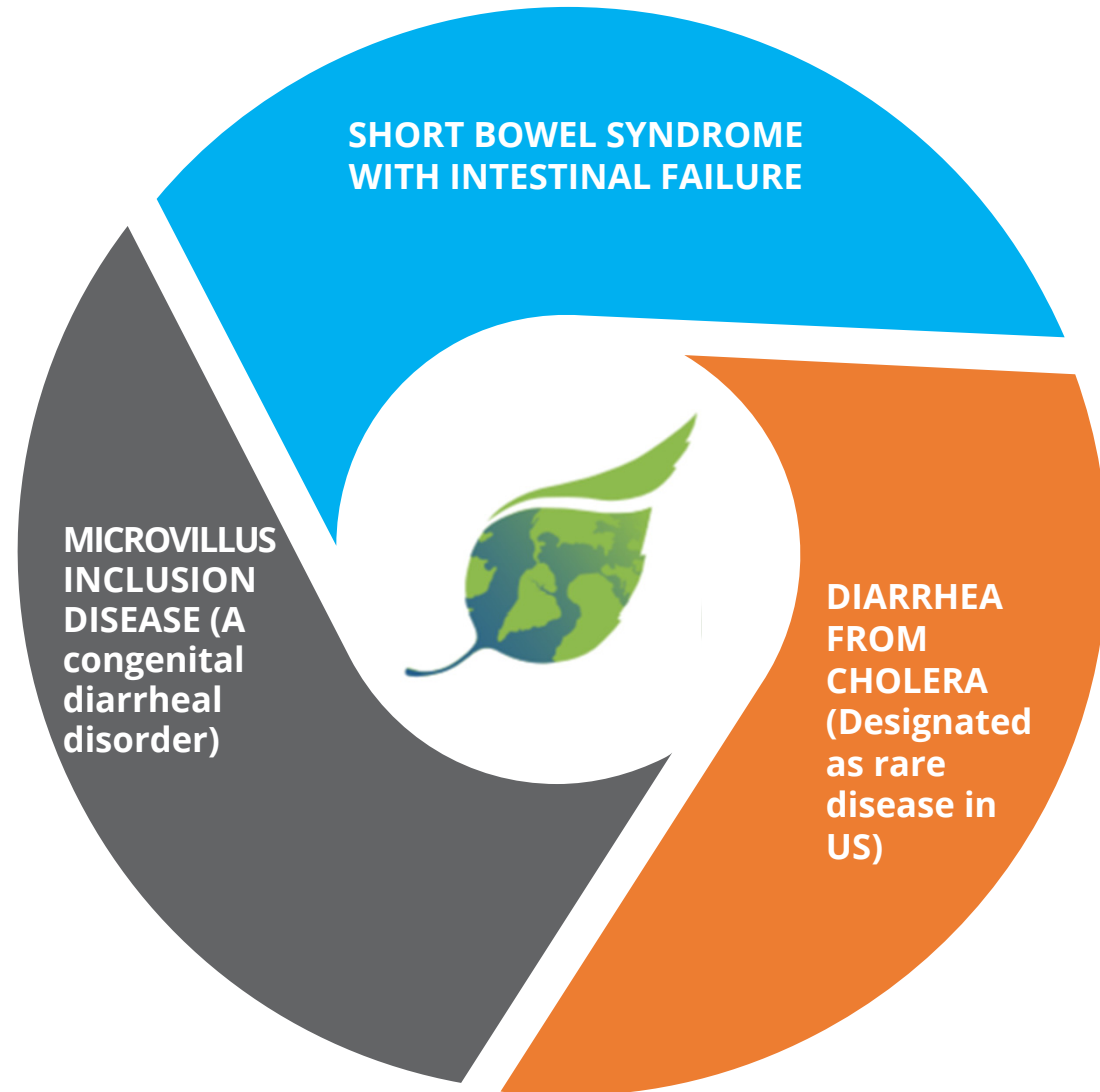
# Cancer Therapy-related Diarrhea OnTarget PHASE 3 Trial: *Impact on Outcome*

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- May 2023: Enrollment completed
- Comprehensive results expected forthcoming

# Jaguar Health's Strategic Focus on Rare Diseases



## Rare diseases, when taken together, are not that rare at all

- **30 million Americans<sup>1</sup>**, or 10 percent of the population, have one of the approximately **7,000 known rare diseases<sup>2</sup>**
- An estimated **30 to 40 million people in the EU<sup>3</sup>** and **400 million worldwide<sup>4</sup>** have a rare disease
- Definition of a rare or orphan disease by region:
  - **US:** When a disease affects **<200,000 people<sup>5</sup>**
  - **EU:** When a disease affects **<1 in 2,000 people<sup>6</sup>**
    - **EU: “Ultra-rare disease”:** When a disease affects **no more than 1 in 50,000 people<sup>7</sup>**
- Reimbursement coverage is often available due the rare disease’s high morbidity and mortality rates, and as a result of support from patient activist groups

<sup>1</sup> & <sup>2</sup> Source: <https://phrma.org/Scientific-Innovation/Progress-in-Fighting-Rare-Diseases>

<sup>3</sup> Source: Harari S. Why We Should Care About Ultra-Rare Disease. Eur Respir Rev. 2016 Jun;25(140):101-3. doi: 10.1183/16000617.0017-2016

<sup>4</sup> Source: <https://rarediseases.org/rare-disease-day-2022-advancing-the-conversation-around-health-equity/>

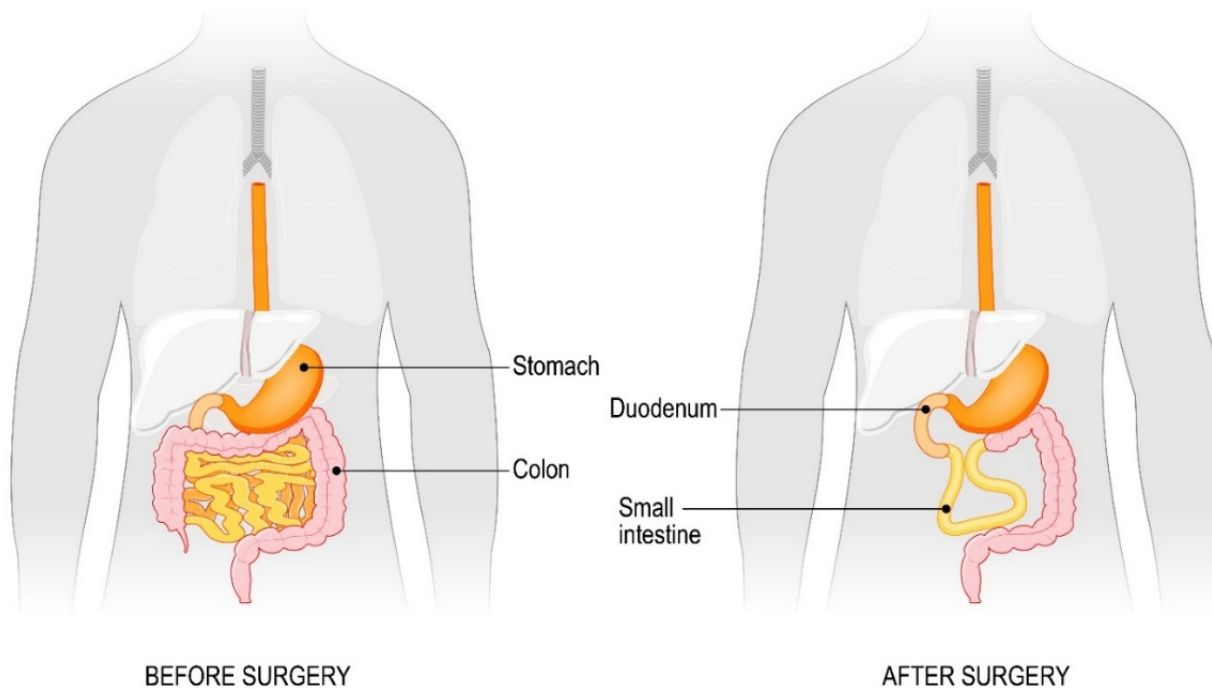
<sup>5</sup> Source: <https://www.fda.gov/patients/rare-diseases-fda#>

<sup>6</sup> Source: <https://www.eurordis.org/information-support/what-is-a-rare-disease/>

<sup>7</sup> Source: European Commission Regulation (EU) No.536/2014 of the European Parliament and of the Council of April 16, 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. 2014. Available from: <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536&qid=1421232837997&from=EN>

# Short Bowel Syndrome – Loss of Bowel with Quality-of-Life Changes

- **SBS:** Catastrophic loss of bowel often due to surgical resection of diseased or necrotic bowel (normal 15-25 feet to 5 or less feet) in adults/children (also may be congenital in children).
- **SBS with Intestinal Failure (SBS-IF):** A condition in which your body is unable to absorb enough nutrients from the foods you eat because you do not have enough small intestine. Patients suffer from malnutrition, dehydration, imbalances of fluids and salts, excessive intestinal fluid output, and risk of organ failure.
  - Life-long parenteral nutrition (PN) may be required
  - No “standard of care” drug intervention



Parenteral nutrition backpack for patients with intestinal failure



# A Global Opportunity

- SBS Patient Population:
  - ~10,000 to 20,000 in US
  - ~10,000 to 20,000 in Europe
- Despite limited treatment options, the global SBS market exceeded \$568 million in 2019 and is expected to reach **\$4.6 billion by 2027<sup>1</sup>**
  - Gattex (teduglutide):
    - Estimated share of US market: ~1-2%<sup>3</sup>
    - Annual cost in US: ~\$485,400<sup>4</sup>
    - Multiple biosimilars in development by other companies
    - **“Gattex can make abnormal cells that are already in your body grow faster. There is an increased risk that abnormal cells could become cancer”**
  - Non-hospitalized parenteral nutrition in the US is approximately \$150,000 per year<sup>5</sup>
  - Frequent hospitalizations for infections



<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> Jaguar estimate based on projected Gattex 2020 revenue of 554.9M USD (based on Takeda financial reports) divided by annual per-patient expenditure for Gattex of \$376.2K in 2016 (figure sourced from <https://www.ahip.org/documents/HighPriceDrugsReport.pdf>)

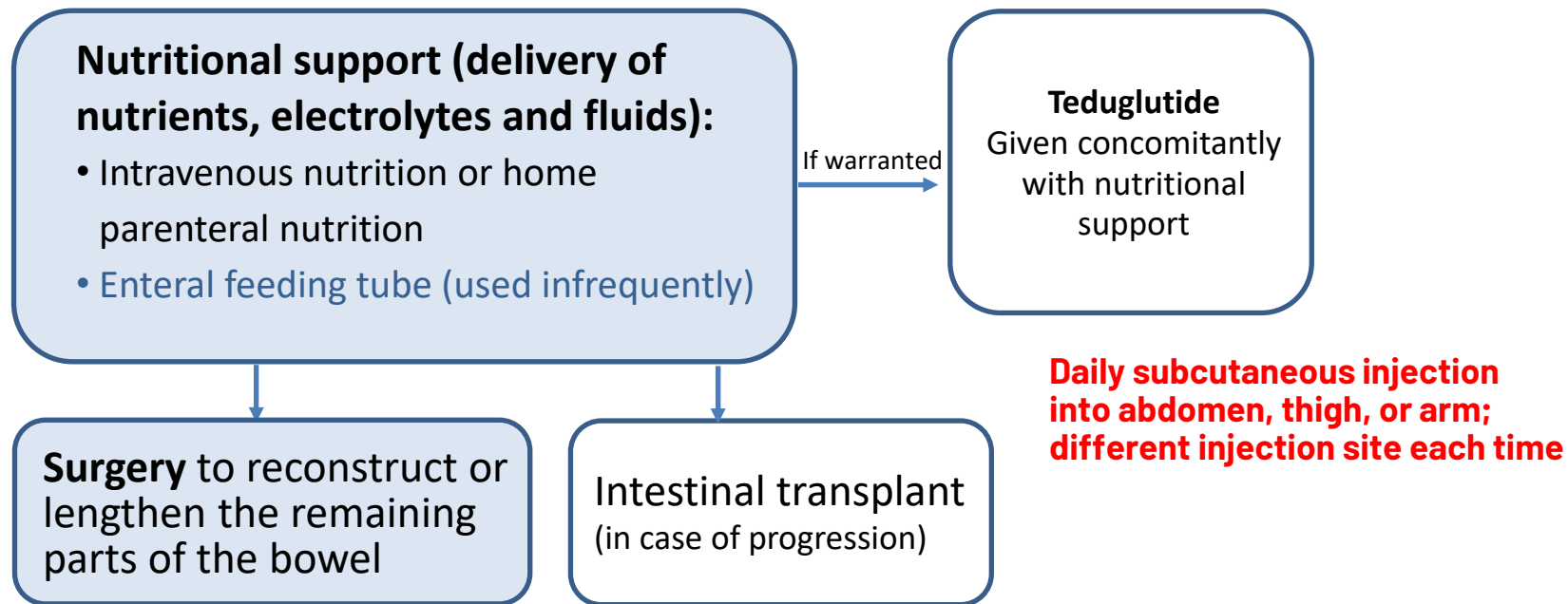
<sup>3</sup> Jaguar estimate based on an estimated US SBS population of 10,000-20,000 people ([www.crohnscolitisfoundation.org/sites/default/files/legacy/assets/pdfs/short-bowel-disease-crohns.pdf](http://www.crohnscolitisfoundation.org/sites/default/files/legacy/assets/pdfs/short-bowel-disease-crohns.pdf))

<sup>4</sup> 10 priciest drugs in America (<https://www.benefitspro.com/2020/08/24/10-priciest-drugs-in-america/?slreturn=20221021163553>)

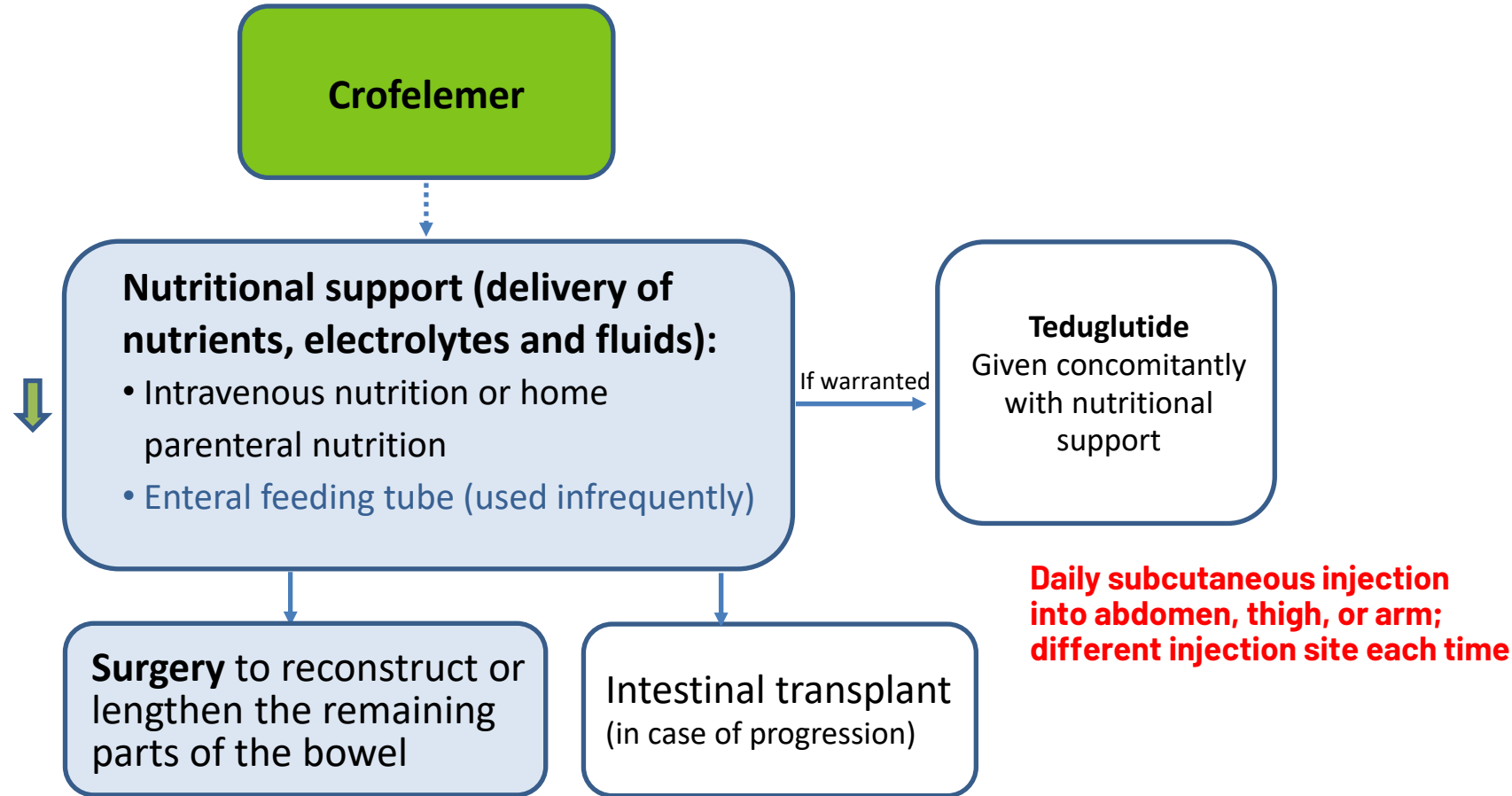
<sup>5</sup> <https://nutritionequity.org/wp-content/uploads/2018/05/mnea-factsheet-sbs.pdf>

# Current Treatment Pathway for SBS-IF Patients

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# Proposed Treatment Pathway: Crofelemer May Reduce Need for Parenteral Nutrition in SBS-IF Patients



**Reduction of parenteral nutrition would lead to improvement of patients' quality of life**

# Microvillus Inclusion Disease (MVID): An Ultra Rare CDD

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MVID is an ultra rare congenital diarrheal disorder (CDD) that affects newborns and children and leads to significant morbidity and mortality from **severe secretory diarrhea, intestinal failure**

## Key Milestones:

- **Investigational New Drug (IND) application for crofelemer for MVID activated by FDA in August 2023**
- Single digit number of patients treated to receive approval?



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\* Adverse events could negatively affect the timeliness of submitting the Investigational New Drug (IND) application. There is a probability that the FDA may not approve Company's IND application.

# Napo Therapeutics: Exclusive Licensee of Jaguar's Crofelemer Drug Product for Europe

> 90% owned by Jaguar

- **Napo Therapeutics' Mission:** Rare disease business model
- **Initial orphan target indications:** Short bowel syndrome (SBS) with intestinal failure, and microvillus inclusion disease (MVID), a congenital diarrheal disorder (CDD)
  - Pursuing accelerated conditional marketing authorization from the European Medicines Agency (EMA) under orphan drug designation
  - In 2023 Jaguar & Napo Therapeutics supporting six investigator-initiated proof-of-concept (POC) studies of crofelemer in patients with SBS and CDD
  - Publication of POC data from these trials could support early patient access to crofelemer for SBS or CDD in specific EU countries
  - Early access programs, which do not exist in the US, are revenue generating, and reimbursable for participating patients



\* There is a probability that accelerated conditional marketing authorization may not be granted, which may negatively impact Company's business operations and projected revenue



# NP-300 Drug Candidate for the Symptomatic Relief of Diarrhea from Cholera and Other Pathogens

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**Cholera is designated as a rare disease in the United States, where nearly all reported cases are acquired during international travel**

## **Our NP-300 Drug Candidate:**

- Second-generation anti-secretory drug
- Same source plant as crofelemer
- Clinical proof-of-concept for the CFTR ion channel MOA of NP-300 demonstrated by crofelemer for the reduction of diarrhea-associated dehydration in cholera patients: International Centre for Diarrhoeal Disease Research (icddr,b) in Bangladesh
- IND activated
- Plan to pursue Priority Review Voucher (PRV) (in past transactions by other companies PRVs have sold for values ranging from \$67M - \$350M)



# Canalevia®-CA1 (Crofelemer): A New Standard of Care For Treatment of Chemotherapy-induced Diarrhea (CID) in Dogs Launched April 2022

Canalevia-CA1 received conditional approval in December 2021—the first and only product indicated for CID in dogs to receive any type of approval from FDA

Approximately 1 in 4 dogs will, at some stage in their life, develop neoplasia. Almost half of dogs over the age of 10 will develop cancer. ~6 million new cancer diagnoses are made in dogs each year in the U.S.

Pet owners' willingness to pay for life saving treatments and procedures increases with patient comfort.

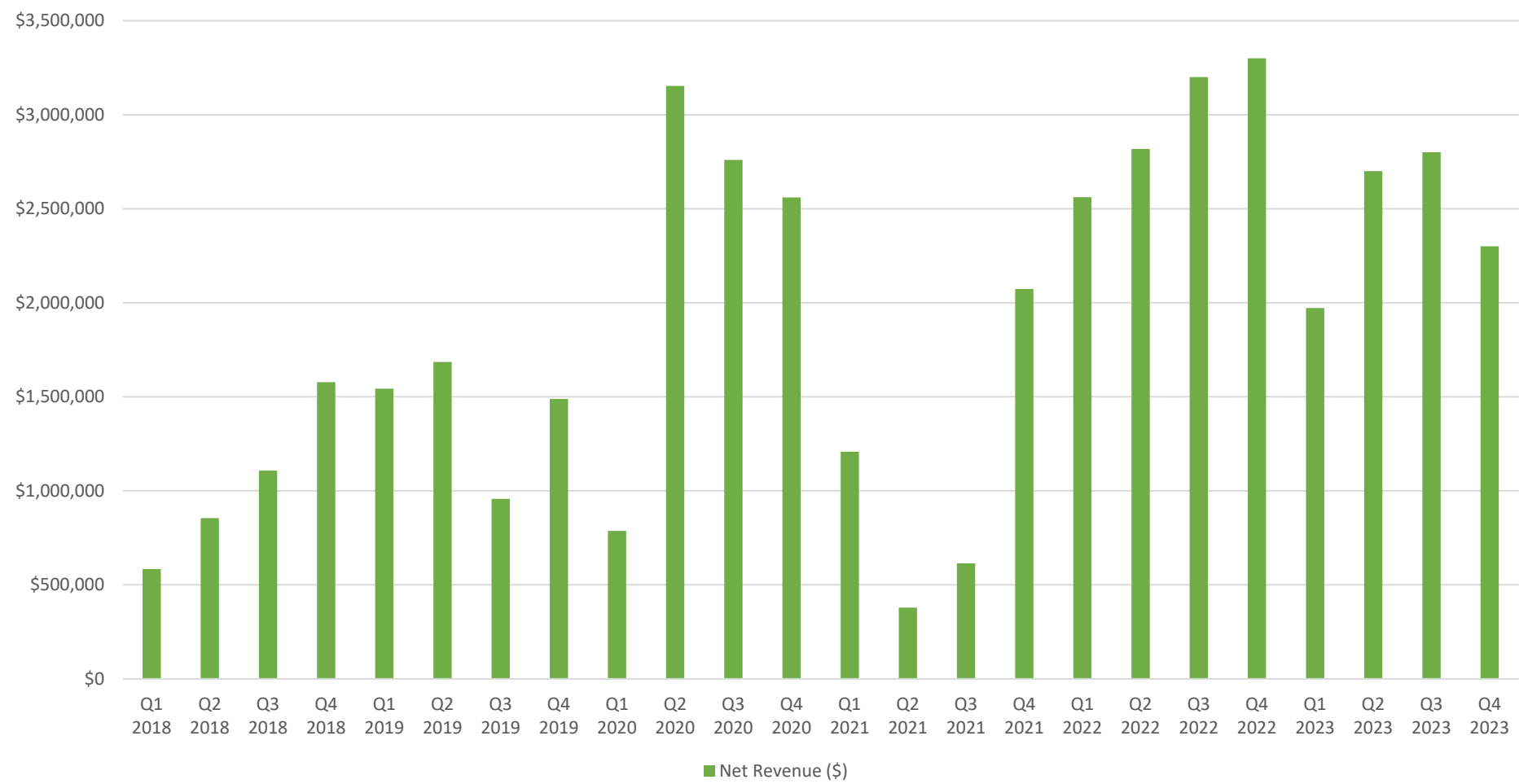
For the most part, dogs receive human chemotherapeutic agents during treatment and suffer the same side effects as humans, which means ~40% of treated dogs may have their chemotherapy reduced, changed, or discontinued due to diarrhea—which can compromise the full benefit of the chemotherapy agent.

Similar dynamics to human specialty market, but with greater correlation between gross and net revenue with pet owner paying out of pocket.

Conditional approval in dogs is similar to orphan drug designation in humans.



# Net Revenue



# Jaguar and Filament Health, with Funding from One Small Planet, Form Joint Venture *Magdalena Biosciences* to Develop Botanical Pharmaceutical Drug Candidates for Mental Health Illnesses

***Magdalena currently valued at US\$5.0 million based on initial funding of US\$1.0 million from One Small Planet***

- Magdalena Biosciences leverages Jaguar's proprietary 2300 medicinal plant library
- Jaguar owns ~40% of Magdalena
- **Goal of Collaboration:** To extend the botanical drug development capabilities of Jaguar to:
  - Develop pharmaceutical-grade, standardized drug candidates for mental health disorders **including attention-deficit/hyperactivity disorder (ADHD) in adults**
  - **Partner with a potential future licensee** to develop and commercialize these novel plant-based drugs



# Magdalena Biosciences

Program to support the discovery and development of **novel psychoactive medicines derived from plants** for mental health and CNS disorders

- Leverage Company's proprietary library of ~2,300 plants and ~3,500 plant extracts with ethnomedicinal investigation
- Seeking next generation first-in-class agents, novel mechanisms of action, disease modifying agents

## Eight key agents being pursued by psychedelic-focused companies:

- LSD and derivatives
- Psilocybin and derivatives (mushrooms in the genus *Psilocybe*)
- Iboga and derivatives
- Toad sections from *Bufo Alvarius* 5-MeO-DMT
- MDMA (referred to as ecstasy or Molly)
- Ketamine
- Mescaline and derivatives (peyote is most well-known source but not only source)
- DMT and derivatives (most well-known source is the *Banisteriopsis* and *Psychotria viridis* mixture known as Ayahuasca)



*Picralima nitida* plant, the source of the active ingredient alstonine

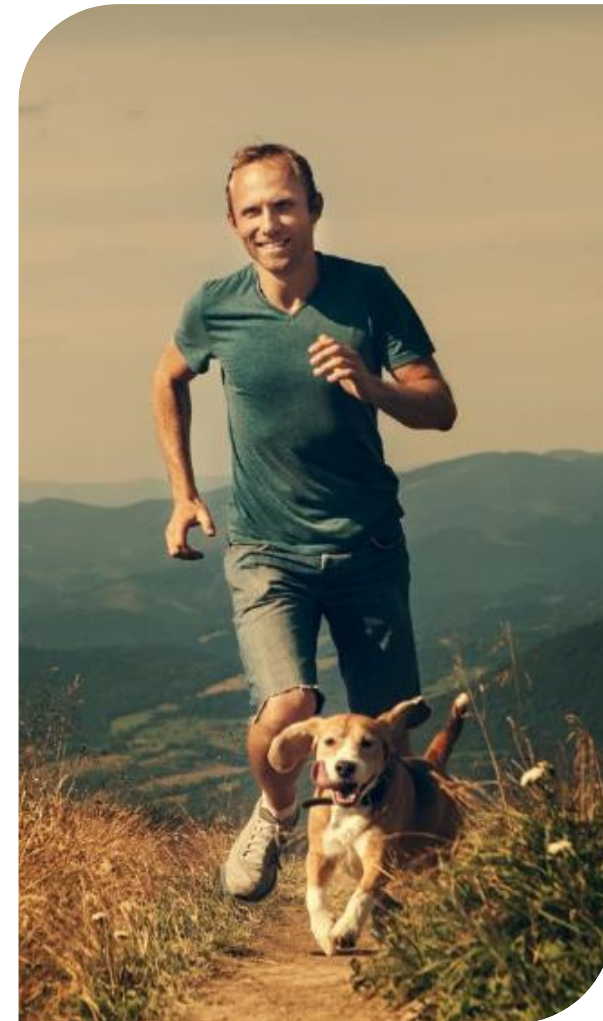


Peyote (*Lophophora williamsii*), a source of mescaline



# Key Milestones

- **Expected forthcoming:** Comprehensive results of pivotal phase 3 OnTarget trial of crofelemer for cancer therapy-related diarrhea (CTD) expected
- **Q2 2024:** Additional rare disease initiatives, real world PRO
- **Q2 2024:** Targeting: ASCO publication/presentation of OnTarget results
- **Q3 2024:** Initiate commercial launch for Gelclair®
- **2024:** Investigator-initiated proof-of-concept (POC) studies of crofelemer for SBS and CDD
- **2024:** Publication of POC data for SBS and CDD, supporting the potential for expanded patient access through early access programs in specific EU countries for these diseases
- **2024-2025:** Participation in revenue generating early access programs in EU for crofelemer for SBS and CDD
- **Ongoing:** Business development partnership(s) related to pipeline & global commercialization



\* Key milestones are based on management estimates. Adverse events could negatively affect Company's business and the timeliness of achieving key milestones.

# Jaguar/Napo Pharmaceuticals 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 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>Karen J. Brunke, PhD</b> Executive VP, Corporate & Business Development	<ul style="list-style-type: none"> <li>30+ years experience in research, operations and BD in pharma/biotech</li> <li>Primary responsibility in deals with MedImmune, Astellas; closed GSK deal</li> <li>Successfully developed GMOs at Sandoz while Research Director</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; 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</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>Allison A. Shrier, M.D.</b> Napo Pharmaceuticals VP, Clinical Research & Medical Affairs	<ul style="list-style-type: none"> <li>Physician-scientist-entrepreneur with expertise in oncology &amp; metabolism</li> <li>Expertise in end-to-end drug discovery &amp; development including population identification, target product profiles development, hit design, selection &amp; optimization, preclinical &amp; clinical study planning</li> </ul>

# Napo Therapeutics Scientific Advisors

Name / Title	Experience
<b>Mohammed Miqdady, MD</b>	<ul style="list-style-type: none"> <li>Division Chief of the Pediatric Gastroenterology, Hepatology &amp; Nutrition Division at Sheikh Khalifa Medical City in the United Arab Emirates. American Board certified in Pediatric Gastroenterology, Hepatology and Nutrition. Also serves as an Adjunct Staff at the Cleveland Clinic in Ohio, U.S.</li> </ul>
<b>Loris Pironi, MD</b>	<ul style="list-style-type: none"> <li>Full Professor of Food and Dietetic Sciences (Clinical Nutrition), School of Medicine, Department of Medical and Surgical Science, University of Bologna. Chairman of the Home Artificial Nutrition &amp; Chronic Intestinal Failure Working Group of the European Society for Clinical Nutrition and Metabolism (ESPEN). Chairman of the Scientific Committee of the Italian Society for Artificial Nutrition and Metabolism (SINPE).</li> </ul>
<b>Antonino Morabito, MD</b>	<ul style="list-style-type: none"> <li>Professor of Pediatric Surgery University of Florence and Chief of Surgery at the Meyer Children's Hospital. Consultant Intestinal Failure Surgeon, Salford Royal Foundation Trust-University of Salford.</li> </ul>
<b>Francisca Joly, MD</b>	<ul style="list-style-type: none"> <li>University Professor – Hospital Practitioner, Department of Gastroenterology, MICI and Nutritional Assistance, Beaujon Hospital, Paris. President of the SFNCM Francophone Clinical Nutrition and Metabolism Society. Associate manager of MaRDi center (Rare Digestive Diseases) for adults (coordination: Necker-Enfants Malade Hospital &amp; Robert Debré Hospital)</li> </ul>
<b>Simon Gabe, MD MSc BSc MBBS FRCP</b>	<ul style="list-style-type: none"> <li>Consultant Gastroenterologist at St Mark's Hospital in Harrow. He co-chairs the supra-regionally funded Intestinal Rehabilitation service, one of two centers in the UK funded to provide this service. He was appointed as Senior Lecturer at St Mark's and Imperial College in 2000.</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
- Supply chain in place

## Planned Crofelemer Expansion

- **Progression from supportive care to impact on outcome/cost of care to treatment modifying**
- Napo's CTD - Phase 3 OnTarget study, comprehensive results expected forthcoming
- SBS with intestinal failure - treatment modifying
- 3 IITs (functional diarrhea, IBS, IBD)

## Strategic Focus on Rare Diseases

- SBS with intestinal failure
- Initial CDD target indication: microvillus inclusion disease (MVID)
- Other rare diseases, real world PRO

## Canalevia-CA1 for chemotherapy-induced diarrhea (CID) in dogs

- Canalevia-CA1 FDA conditionally approved December 2021
- Estimated 6 million new cancer diagnoses in dogs each year in US; 25-40% experience diarrhea
- Management of CID in dogs is a comfort issue for dogs and may also help dogs better tolerate chemo and improve the home/living environment for owners

## Strategic Partnerships

- Unencumbered global commercial rights to Mytesi/crofelemer pipeline
- License deals completed in Europe, Canada, Middle East; ongoing discussions for Asia, LATAM
- Magdalena Biosciences leveraging proprietary 2,300-plant ethnobotanical database

## Strong Management Team

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

## Proprietary Position

- ~148 patents (majority do not expire until 2027 - 2031) and ~50 patents pending
- Sustainable supply of commercial scale of raw material sourcing
- Botanical guidance protection – no practical generic pathway





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

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