

Filed Pursuant to Rule 433  
Issuer Free-Writing Prospectus  
Dated September 28, 2018 Relating  
to Preliminary Prospectus Dated  
September 28, 2018  
Registration No. 333-227292



# Jaguar Health, Inc.

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## Investor Presentation

September 2018

## 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 the Company's belief that Lechlemer may offer a possible Priority Review Voucher opportunity, the Company's statements regarding planned next steps for clinical trials (including the Company's plan to submit documentation in 1H 2019 to the FDA for the planned formulation of crofelemer for feeding tube administration to support investigation of a pediatric liquid formulation of crofelemer for the possible indication of Congenital Diarrheal Disease (CDD)), and the timing of data results from planned proof of concept, field 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, Form S-1 and the preliminary prospectus to which this relates, 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.

## Free Writing Prospectus Statement

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This presentation highlights basic information about us and the offering to which this communication relates. Because it is a summary, it does not contain all of the information that you should consider before investing in our common stock.

We have filed a registration statement (including a prospectus) on Form S-1 (File No. 333-227292), which has not been declared effective, with the US Securities and Exchange Commission (SEC) for the offering to which this presentation relates. Before you invest, you should read the preliminary prospectus in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about us and the offering.

You may access these documents for free by visiting EDGAR on the SEC website at <http://www.sec.gov>.

The preliminary prospectus, dated September 28, 2018, is available on the website at <http://www.sec.gov>.

Alternatively, H.C. Wainwright & Co., LLC as underwriter in the offering will arrange to send you the prospectus if you request it by calling (646) 975-6996 or by e-mailing [placements@hcwco.com](mailto:placements@hcwco.com).

# Pipeline Within the Brand for Diarrheal Disorders

Portfolio of current and potential diarrheal indications; Lechlemer offers potential Priority Review Voucher



Lechlemer – Potential opportunity for a Tropical Disease Priority Review Voucher. In recent transactions by other companies, Priority Review Vouchers have sold for \$67M-\$350M.  
Cholera

# KnighT Therapeutics: License for Canadian and Israeli Markets

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- On September 24, 2018, Jaguar signed a **Distribution, License and Supply Agreement** with Knight Therapeutics Inc.
- Agreement provides Knight Therapeutics with an exclusive right to commercialize current and future Jaguar human health products in **Canada and Israel**. In accordance with the agreement, the covered territory may be expanded at a later time to include specified countries in **Latin America**.
  - ❖ The Canadian and Israeli markets accounted for an estimated combined total of 2.18% of global pharmaceutical sales in 2014<sup>1</sup>
  - ❖ The markets in the specified countries in Latin America accounted for an estimated combined total of 6.60% of global pharmaceutical sales in 2014<sup>1</sup>
- Upon achievement of certain **regulatory and sales milestones**, Jaguar may receive payments from Knight Therapeutics in an aggregate amount of up to USD \$18,019,743 (based on September 23, 2018 USD-CAD exchange rates) payable throughout the initial 15-year term of the agreement.
- Knight has given a non-binding indication of interest to purchase up to \$1,000,000 in this offering at the public offering price, provided that we raise at least \$9,000,000. This is not a commitment to purchase; therefore, Knight may not purchase any common stock in this offering.”



Montreal, Canada-based Knight Therapeutics Inc. is a specialty pharmaceutical company focused on acquiring or in-licensing and commercializing innovative pharmaceutical products for the Canadian and select international markets.

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<sup>1</sup>The International Federation of Pharmaceutical Manufacturers & Associations "Pharmaceutical Industry and Global Health - Facts and Figures 2017" report

# Our Story: From Tree to Bottle

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Crofelemer  
was discovered  
through the  
science of  
ethnobotany





**RELIEF, PURE AND SIMPLE**

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

# Mytesi Growth Strategy

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- ❖ Bob Griffing, Chief Commercial Officer, started June 2018
- ❖ Targeting high-potential HIV prescribers and GIs that actively treat HIV patients
- ❖ 17 territory managers, telesales representative, regional sales director, and national sales director
  - Two-thirds bring extensive HIV experience from Bristol-Myers Squibb
- ❖ Co-promotion agreement with RedHill Pharma provides 36 sales reps, 4 telesales representatives, and 4 Medical Science Liaisons
  - Napo will continue to book all top-line sales of Mytesi
  - RedHill compensated on a per-prescription-filled basis
- ❖ Launch of integrated digital campaign to activate and educate patients and healthcare providers via contextual and native display ads:





# Jaguar Health By The Numbers

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## Revenue-Generating Biopharma With an FDA-Approved Drug

**312%**

*1H'18 YoY Mytesi Net  
Sales Growth<sup>1</sup>*

*Note: The merger of Napo and  
Jaguar became effective July  
31, 2017. The Napo January  
through June 2017 sales  
figures used in the above  
percentage are from the pre-  
merger period.*



**45%**

*1H'18 YoY  
Growth in Total  
Mytesi  
Prescriptions<sup>2</sup>*

**74%**

*1H'18 YoY Growth in  
Mytesi Wholesaler-to-  
Retailer Shipments<sup>3</sup>*

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<sup>1</sup>Data on file in Jaguar Health General Ledger

<sup>2</sup>Source: IQVIA Monthly NPA Prescription Data September 12, 2018

<sup>3</sup>Data on file in Jaguar Health General Ledger

# Jaguar Health By The Numbers

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## Strong Prescription and Sales Growth Achievements; All-time High Prescriptions Achieved August 2018

**39%**

*Total Prescriptions (TRx)  
Growth for Mytesi  
3-Month Period Ending  
August 2018 vs Prior 3-  
Month Period; All-time  
TRx high achieved in  
August 2018<sup>1</sup>*



**52%**

*New Prescriptions (NRx)  
Growth for Mytesi for  
3-Month Period Ending  
August 2018 vs Prior  
3-Month Period<sup>1</sup>*

**24%**

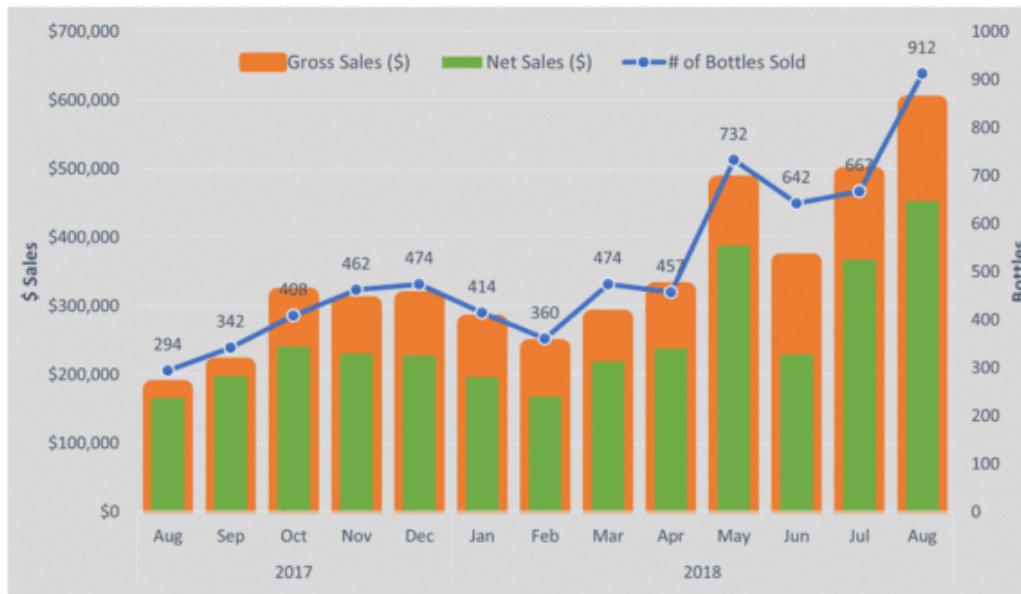
*Growth of Mytesi Net Sales  
3-Month Period Ending August  
2018 vs Prior 3-Month Period<sup>2</sup>*

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<sup>1</sup>Source: IQVIA Monthly NPA Prescription Data September 12, 2018

<sup>2</sup>Data on file in Jaguar Health General Ledger

# Mytesi Gross<sup>1</sup> & Net Sales August 2017 to August 2018



Guidance Estimates for Q3 2018	July	August	Q3 2018 Guidance
Gross Sales	\$489,523	\$594,033	\$1,600,000 to \$1,700,000
Net Sales	\$367,036	\$452,121	\$1,200,000 to \$1,275,000

**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.

Chart data on file in Jaguar Health General Ledger

<sup>1</sup>Non-GAAP measure

In adult HIV patients on ART who have noninfectious diarrhea



## Enough is Enough NORMALIZE with MYTESI

### HIV+ Patients Talk About Diarrhea



*"It's interrupting my daily routine...I'm becoming afraid of it. It seems like I'm changing my life because of my diarrhea."*

**Male, age 62, HIV+ for 3 years**

Photo not of actual patient. Quote is from an actual HIV patient.

### Important Safety Information About Mytesi

Mytesi (crofelemer) is an anti-diarrheal indicated for symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS who are on antiretroviral therapy (ART). Mytesi is not indicated for the treatment of infectious diarrhea. Rule out infectious etiologies of diarrhea before starting Mytesi. If infectious etiologies are not considered, there is a risk that patients with infectious etiologies will not receive the appropriate therapy and their disease may worsen. In clinical studies, the most common adverse reactions occurring at a rate greater than placebo were upper respiratory tract infection (5.7%), bronchitis (3.9%), cough (3.5%), flatulence (3.1%), and increased bilirubin (3.1%).

**Please see Full Prescribing Information on pages 4-7.**

**Mytesi**  
(crofelemer) 125 mg  
delayed-release tablets

# Recent Mytesi Media Coverage



## What Your Patients Are Reading...

NEWS ABOUT MYTESI • JANUARY 2017

**a&u**  
dita  
EISE  
RELIEF

**EDGE MEDIA NETWORK**  
Diarrhea Troublesome Side Effect Among HIV+; Mytesi Could Help

**[imstilljosh]**

**POSITIVELY AWARE**  
HIV anti-diarrheal Mytesi  
Previously known as Fospice (generic name cobicistat), only FDA-approved drug for treating HIV-related diarrhea. Has been acquired by Napo Pharmaceuticals and is now marketed under the name Mytesi. The company has launched patient support and patient

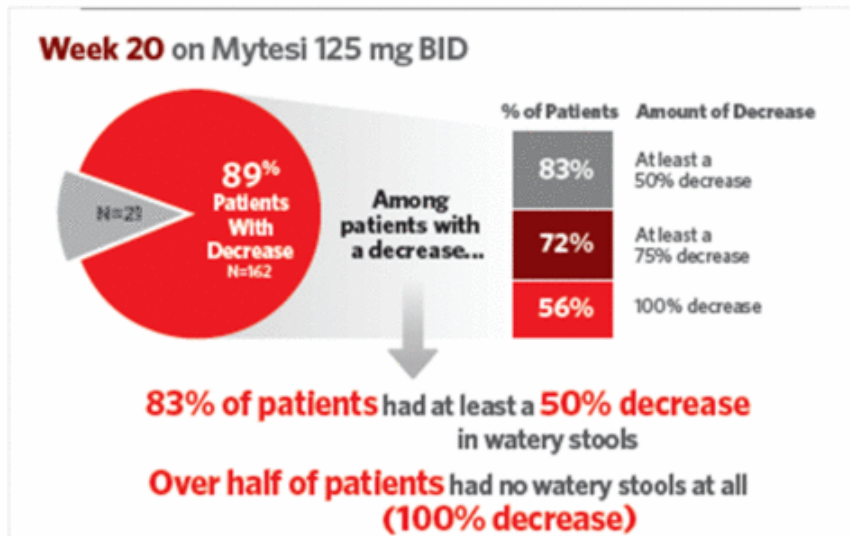
**PA**  
POSITIVELY AWARE  
HIV anti-diarrheal Mytesi  
Need to treat diarrhea in HIV positive people, regardless of drug interactions nor causing constipation.

**POZ**

For more information, please visit [Mytesi.com](http://Mytesi.com)

# Results Over Time With Mytesi

Poster Presentation at  
the 2017 International  
Aids Society Conference  
on HIV Science



<sup>1</sup>Based on a supplemental analysis of data from Napo's ADVENT trial

# Mytesi Coverage and Reimbursement

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- ❖ Signed agreement with the **Aids Drug Assistance Program (ADAP)** in April 2018
  - Provides pricing for Mytesi to each US state's ADAP
  - ADAP's provide Mytesi free of charge to qualified patients and Copay support for patients with insurance coverage
  - **Mytesi available on 29 state ADAPs and actively pursuing remaining states**
- ❖ Covered by all top 10 commercial insurers (>245 million lives)
- ❖ Covered by all top 10 Managed **Medicare** plans (>2.4 million lives)
- ❖ Covered by **Medicaid** in all 50 states
- ❖ **Copay coupon program to remove cost as a barrier to filling their prescription**
- ❖ **Patient Assistance Program** to assist patients with benefit verification, prior authorization, and claims appeals
- ❖ Agreement with direct-to-patient pharmacy Transition Patient Services (TPS) that streamlines patient access to Mytesi and improves adherence



ADAP is state administered for persons living with HIV/AIDS authorized under the Ryan White Act of 2016 and often considered insurance of last resort. These persons are not currently receiving or eligible for Medicaid or other Third-Party insurance. Reserved for lower income patients with annual federal income equal to or below 400% of current federal poverty level (2018 poverty level for single household \$12,140).

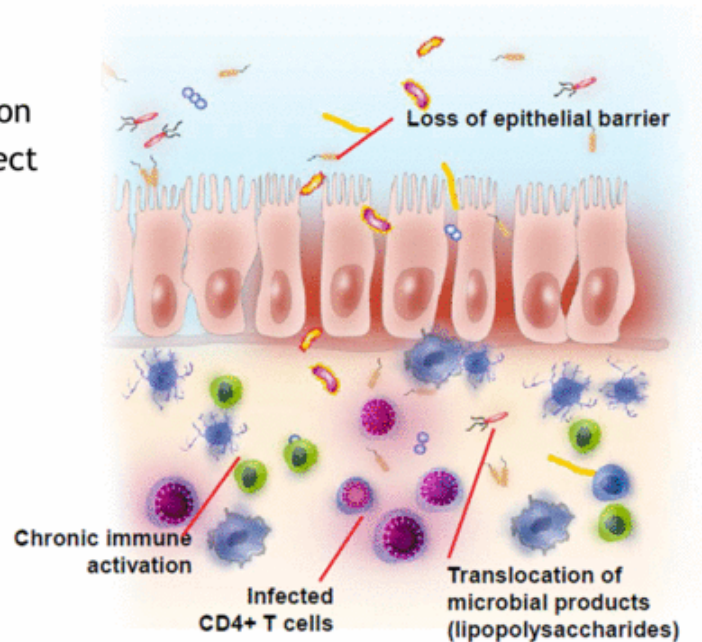
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# Mytesi Additional Opportunities

## HIV Enteropathy

GI tract is profoundly affected by HIV infection

- ❖ HIV enteropathy is due to direct and indirect effects of HIV on the intestinal mucosa
- ❖ Gut inflammation and depletion of T cells continues even after viral load levels are managed
- ❖ Chronic diarrhea remains a significant complaint of people living with HIV/AIDS, particularly those who are older and have lived with the virus for 10+ years



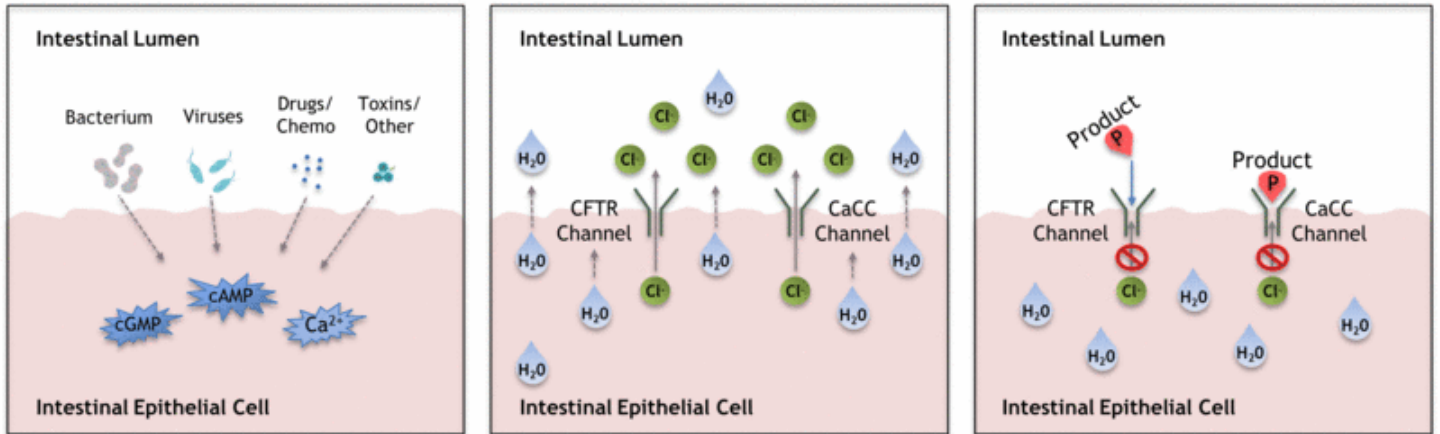
According to data from the U.S. Centers for Disease Control and Prevention, currently more than 50% of people living with HIV are over age 50<sup>1</sup>

<sup>1</sup>HIV Among People Aged 50 and Older, <https://www.cdc.gov/hiv/group/age/olderamericans/index.html>



## Unique Anti-Secretory Mechanism of Action in Mammals

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



**Acts locally** in the gut and is minimally absorbed systemically

# Shortcomings of Other Therapies

Drug	Requires Rx	Other
Imodium	✗	<ul style="list-style-type: none"> <li>▪ Labeled only for acute use</li> <li>▪ Label warning against use with saquinavir</li> </ul>
Tincture of opium	✓	<ul style="list-style-type: none"> <li>▪ Narcotic, use not common</li> </ul>
Lomotil	✓	<ul style="list-style-type: none"> <li>▪ Labeled only for acute use</li> </ul>
Octreotide	✓	<ul style="list-style-type: none"> <li>▪ Injectable, not oral</li> <li>▪ Pain at site of injection</li> </ul>



**Crofelemer**  
Pill burden : 2/day

vs.

**Imodium**  
Pill burden: 8-12/day



	No Constipation	Safety: Locally Acting in the Gut	Safety: No Drug-Drug Interactions	Other Potential Features
Mytesi	✓	✓	✓	Botanical
Imodium	✗	✗	✗	OTC

According to the WHO, there are 1.7 billion cases of diarrheal disease globally annually



# Jaguar Health: A Pipeline in a Product

## Pipeline of High Visibility Follow-On Products Under Development

	Preclinical	Phase 1	Phase 2	Phase 3	NDA	Near-Term Milestones	Market Size/Potential
<b>HIV-D</b> <i>Diarrhea in HIV/AIDS patients on antiretrovirals</i>						Seeking inclusion on World Health Organization (WHO) Essential Medicines List	Jaguar estimates the U.S. market revenue potential for Mytesi® to be ~\$100mm in gross annual sales; Jaguar is seeking partnerships to bring Mytesi to emerging markets and rest of world
<b>CTD</b> <i>Cancer therapy-related diarrhea</i>						Ongoing II Trials; SAB Protocol Design	~650,000 U.S. cancer patients receive chemotherapy in an outpatient oncology clinic <sup>1</sup> Comparable supportive care (i.e. CINV) product sales ~\$620 mm, 2013; projected \$1.0 bn 2020 <sup>2</sup>
<b>IBD</b> <i>Inflammatory bowel disease supportive care</i>						SAB protocol design	Estimated 1,171,000 Americans have IBD <sup>3</sup>
<b>IBS-D</b> <i>Irritable Bowel Syndrome - diarrhea predominant</i>						Partner discussions	Most IBS products have estimated revenue potential >\$1.0 bn <sup>4</sup>
<b>CDD/SBS-Orphan</b> <i>Congenital Diarrheal Disorders and Short Bowel Syndrome</i>						Formulation / POC Abu Dhabi/SAB Protocol Design	Financial benefits of Orphan-Drug Designation
<b>Cholera (hydration maintenance) PRV (lechlemer)</b> * <i>Offer long-term pipeline opportunity for anti-secretory novel mechanism of action</i>						Formulation / POC	We believe lechlemer may support efforts to receive a priority review voucher (PRV) from the U.S. FDA for a cholera indication.*

\*Priority Review Vouchers are transferable. In recent transactions by other companies, Priority Review Vouchers have sold for \$67M-\$350M. (<https://www.raps.org/regulatory-focus/news-articles/2017/12/regulatory-explainer-everything-you-need-to-know-about-fdas-priority-review-vouchers>)

<sup>1</sup>Centers for Disease Control and Prevention. Preventing Infections in Cancer Patients: Information for Health Care Providers ([cdc.gov/cancer/preventinfections/providers.htm](http://cdc.gov/cancer/preventinfections/providers.htm))

<sup>2</sup>Heron Therapeutics, Inc. Form 10-K for the fiscal year ended December 31, 2016

<sup>3</sup>Kappelman, M. et al. Recent Trends in the Prevalence of Crohn's Disease and Ulcerative Colitis in a Commercially Insured US Population. *Dig Dis Sci.* 2013 Feb; 58(2): 519-525

<sup>4</sup>Merrill Lynch forecasts peak US sales of roughly \$1.5 bn for Ironwood'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' Trulance at \$2.3 bn in 2021 (Source: <https://www.benzinga.com/analyst-ratings/analyst-color/17/03/9224181/analyst-synergy-pharma-couldachieve-sustainable-profit>)

# Napo Scientific Advisory Board (SAB) Members

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**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)

## HIV Physicians SAB

- **Dr. Roscoe Moore Jr., DVM, MPH, Ph.D., DSc.:** Former Assistant United States Surgeon General and a Rear Admiral (Retired) in the U.S. Public Health Service. Dr. Moore was involved in the creation of PEPFAR (the U.S. President's Emergency Plan for AIDS Relief)
- **David Asmuth, MD:** Infectious diseases specialist and Professor of Medicine, UC Davis Health
- **Gary Blick, MD, AAHIVS:** Founder of Health Care Advocates International and BEAT AIDS Project Zimbabwe
- **Christine Wanke, MD:** Director of the Nutrition and Infection Unit; Associate Chair and Professor, Department of Public Health and Community Medicine; Professor, Department of Medicine, Tufts University School of Medicine; Professor, Sackler School of Biomedical Science; Professor, Friedman School of Nutrition Science and Policy

## 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
- **Pravin Chaturvedi, PhD:** Chair of Napo's Scientific Advisory Boards; 25+ years drug development experience in pharmaceutical/biotech field; Successfully developed crofelemer (Mytesi) (first pivotal adaptive design)

## IBD SAB

- **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

## Pediatric Indications (SBS and CDD) SAB

- **Mohammed Miqdady, MD:** Chief of Pediatric Gastroenterology, Hepatology & Nutrition at Sheikh Khalifa Medical City in Abu Dhabi
- **Christopher Duggan, MD:** Senior Physician, Division of Gastroenterology, Hepatology and Nutrition / Director, Center for Nutrition / Medical Director, Center for Advanced Intestinal Rehabilitation, Boston Children's Hospital; Professor of Pediatrics, Harvard Medical School; Professor in the Departments of Nutrition and Global Health and Population, Harvard TH Chan School of Public Health
- **Martin Martin, MD:** Professor, Department of Pediatrics, David Geffen School of Medicine at UCLA
- **Sue Rhee, MD:** Division Chief, Pediatric Gastroenterology, Hepatology and Nutrition Pediatric gastroenterologist and liver specialist, UCSF Benioff Children's Hospital

# Key Opinion Leader (KOL) Advisors to Napo

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## 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, M.D.:** Department of Infectious Diseases, Infection Control, and Employee Health, Division of Internal Medicine, MD Anderson

## Diarrhea Related to IBD

- **Brooks D. Cash, MD, AGAF, FACC, FACP, FASGE:** Division Director, Gastroenterology, Hepatology, and Nutrition Visiting Professor of Medicine, The University of Texas McGovern Medical School
- **David Rubin, MD:** Joseph B. Kirsner Professor of Medicine Section Chief, Gastroenterology, Hepatology and Nutrition Co-Director, Digestive Diseases Center, University of Chicago Medicine
- **Charles Bernstein, MD:** Distinguished Professor of Medicine and Bingham Chair in Gastroenterology Research, University of Manitoba
- **William Sandborn, MD:** Director, Inflammatory Bowel Disease Center Chief, Division of Gastroenterology Professor of Medicine, US San Diego Health
- **Scott Lee, MD:** Associate Professor of Medicine, Digestive Health Center, University of Washington Medical Center
- **Edward Loftus, Jr., MD:** Consultant, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Mayo Clinic
- **Douglas Wolf, MD:** Medical Director of IBD Research at Atlanta Gastroenterology Associates. Clinical Assistant Professor of Medicine, Emory University School of Medicine

## Pediatric Indications (SBS and CDD)

- **Jay Thiagarajah, MD, PhD:** Attending Physician, Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital. Instructor of Pediatrics, Harvard Medical School
- **James Goldenring, M.D., PhD:** Professor of Surgery, Vanderbilt University School of Medicine. Paul W. Sanger Chair in Experimental Surgery. Professor of Cell and Developmental Biology

## Diarrhea Related to HIV and other Infectious Diseases

- **Patrick Clay, PharmD:** Consultant
- **Herbert DuPont, MD:** Professor and Director, Center for Infectious Diseases, University of Texas Houston School of Public Health
- **Pradip Bardhan, MBBS, MD:** Chief Physician at ICDDR,B, Bangladesh
- **Paulo Pacheco, MD:** Clinical Assistant Professor, Department of Medicine, New York University Langone Health
- **Elie Schochet, MD, FACS:** Colorectal surgeon, Holy Cross Medical Group

## 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
- **Doug Drossman, MD:** Co-Director Emeritus, UNC Center for Functional GI and Motility Disorders Adjunct Professor of Medicine and Psychiatry, University of North Carolina School of Medicine
- **William Chey, MD:** Professor of Internal Medicine and Professor of Nutritional Sciences, University of Michigan School of Public Health

# Jaguar Health: A Pipeline in a Product

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## Cancer Therapy-related Diarrhea (CTD)

- Diarrhea is a common adverse event reported with cancer treatments
- “All-grade” diarrhea rates are often 50-80%
  - ❖ Dose-limiting toxicity for tyrosine kinase inhibitors (e.g., Neratinib) and EGFR mAbs (e.g., Herceptin)

### Puma Biotechnology (NASDAQ: PBYI) Neratinib (Nerlynx™):

- Diarrhea has been reported as the most common side effect of the recently approved CDK 4/6 inhibitor abemaciclib and the pan-HER TKI neratinib, with occurrence ranging from 86% to >95% and grade 3 in over 40% of patients.
- Approved drugs for chemotherapy-induced nausea and vomiting (CINV) include Sustol, Aloxi, Akynzeo and Sancuso. Allied Market Research estimates that sales of CINV drugs may reach \$2.7 billion by 2022 growing ~7.1% per annum.<sup>1</sup>



<sup>1</sup><https://www.prnewswire.com/news-releases/chemotherapy-induced-nausea-and-vomiting-cinv-market-expected-to-reach-2659-million-by-2022-611755395.html>

# Jaguar Health: A Pipeline in a Product

## Two Ongoing Investigator Initiated Studies in CTD



Georgetown  
University

**Primary objective:** Characterize incidence and severity of diarrhea in patients receiving investigational therapy in prophylactic anti-diarrheal management.



JAGX completed CID pilot safety study in dogs: 25% of dogs entering study with unformed feces were resolved.



University of California  
San Francisco

Crofelemer as salvage anti-diarrheal therapy with investigational breast cancer agent, neratinib

**TITLE:** Open label study to characterize the incidence and severity of diarrhea in patients with early stage HER2+ breast cancer treated with adjuvant trastuzumab and neratinib followed by neratinib monotherapy, and intensive anti-diarrhea prophylaxis.

**Primary Objective:** Characterize the incidence and severity of diarrhea in patients with early stage breast cancer receiving adjuvant trastuzumab and neratinib followed by 1 year of neratinib monotherapy in the setting of prophylactic anti-diarrheal management.

### Next Steps:

- Plan to submit protocol to FDA for Special Protocol Assessment discussion Q4 2018
- Pivotal protocol discussion with FDA

# Mytesi Pediatric Orphan-Drug Indications

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## Congenital Diarrheal Disease (CDD)

- Rare, chronic intestinal channel diseases, occurring exclusively in early infancy
- Characterized by severe, lifelong diarrhea and a lifelong need for nutritional intake either parenterally or with a feeding tube
- Incidence much more prevalent in regions where consanguineous marriage is part of the culture, such as in the Gulf Cooperation Council (GCC) and MENA regions
- Related to specific genetic defects inherited as autosomal recessive traits
- Directly associated with serious secondary conditions including dehydration, metabolic acidosis, and failure to thrive, prompting the need for immediate therapy to prevent death and limit lifelong disability

## Short Bowel Syndrome (SBS)

- A complex condition characterized by malabsorption of fluids and nutrients due to congenital deficiencies or surgical resection of small bowel segments
- Patients suffer from symptoms such as debilitating diarrhea, malnutrition, dehydration and imbalances of fluids and salts
- Can stem from genetic disorder or premature birth
- Incidence also much more prevalent in GCC and MENA regions





- Filed for orphan-drug status in US
  - Received orphan status for SBS
- Principal investigator: Dr. Mohamad Miqdady, Chief of Pediatric Gastroenterology, Hepatology & Nutrition at Sheikh Khalifa Medical City in Abu Dhabi
- Jaguar has agreed to fund investigator-initiated trial
- Napo intends to submit documentation in 1H 2019 to the FDA for the planned formulation of crofelemer for feeding tube administration to support this investigation
- **NEXT STEP:**
  - Initiation of IIT



“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

# Mytesi for Diarrhea Caused by Cholera

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- ❖ Study evaluating Mytesi versus placebo 1 hour after Azithromycin in cholera<sup>1</sup>
  - Reducing amount of watery stool, 25-30%, 0-6 hour time periods ( $p=0.025$ )
- ❖ Indian patient study in adults with severe watery diarrhea<sup>2</sup>
  - N=98, randomized 1:1, crofelemer vs. placebo (250 mg Q6H x 2 days)
  - Statistically significant benefits seen in seven prospectively defined clinical endpoints
  - Crofelemer superior for overall clinical success, 79% vs. 28%
- ❖ **NEXT STEPS:**
  - Dispersible tablet formulation of Lechlemer
  - File IND in 2H 2019



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<sup>1</sup>Bardhan, et.al., '08 US-Japan Cholera Conf.

<sup>2</sup>Bardhan PK EID, '09

# Jaguar Health: Lechlemer PRV Potential if Granted

**Priority Review Vouchers (PRVs)** created by US FDA to incentivize development of treatments for neglected or rare pediatric diseases. PRVs may be sold to another developer.

**\$67 Million**  
*July 2014: Sanofi(SNY) purchased PRV from BioMarin (BMRN)*

**\$125 Million**  
*November 2014: Gilead Sciences (GILD) purchased a PRV from Knight Therapeutics*

**\$245 Million**  
*May 2015: Sanofi (SNY) purchased a PRV from Retrophin (RTRX)*

**\$350 Million**  
*August 2015: AbbVie (ABBV) purchased a PRV from United Therapeutics (UTHR)*

**\$125 Million**  
*February 2017: Gilead Sciences (GILD) purchased a PRV from Sarepta Therapeutics (SRPT)*

**\$130 Million**  
*December 2017: Novartis (NVS) purchased a PRV from Ultragenyx (RARE)*

**\$110 Million**  
*April 2018: Jazz Pharmaceuticals (JAZZ) purchased PRV from Spark Therapeutics (ONCE)*

**\$125 Million**  
*November 2017: BioMarin (BMRN) sold PRV to undisclosed party*

**\$81 Million**  
*July 2018: Ultragenyx (RARE) sold to undisclosed party*

**Average Market Value of PRV:  
\$156 Million  
(range: \$67 - \$350 Million)**

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

## Global Partnering Driving Pipeline

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Global partnering for an expanding pipeline provides opportunity for non-dilutive funding and global access to Mytesi and novel anti-secretory agents



- Multiple indications
- Multiple geographies
- Second-generation anti-secretory (lechlemer)
- Strategically sequence indication development priorities, second-generation product pipeline development, and partnering goals on a global basis



# The Management Team

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Name / Title	Experience
<b>Lisa Conte</b> <i>Founder &amp; CEO</i>	<ul style="list-style-type: none"><li>• 28+ years of industry experience</li><li>• Obtained first anti-secretory human product FDA approval</li><li>• Board of directors of Healing Forest Conservancy, Dickey Center for International Understanding (Dartmouth College)</li></ul>
<b>Karen Wright</b> <i>CFO &amp; Treasurer</i>	<ul style="list-style-type: none"><li>• 30+ years of financial experience with biotech companies</li><li>• Former Head of Finance for Clene Nanomedicine</li></ul>
<b>Steven King, PhD</b> <i>EVP, Sustainable Supply, Ethnobotanical Research &amp; IP</i>	<ul style="list-style-type: none"><li>• Served as SVP of Sustainable Supply, Ethnobotanical Research &amp; IP: 1989-2017</li><li>• Board of Directors of Healing Forest Conservancy</li></ul>
<b>Pravin Chaturvedi, PhD</b> <i>Chief Scientific Officer</i> <i>Chair of Scientific Advisory Board</i>	<ul style="list-style-type: none"><li>• 25+ years drug development experience</li><li>• Co-Founded Scion, IndUS and Oceanyx Pharmaceuticals</li><li>• Successfully developed Mytesi® (first pivotal adaptive design)</li></ul>
<b>Robert J. Griffing</b> <i>Chief Commercialization Officer</i>	<ul style="list-style-type: none"><li>• 22+ years at Merck, including Global Brand Leader within Oncology Franchise and, HIV sales and market share strategy</li></ul>
<b>David Sestin, PhD</b> <i>Chief Manufacturing Officer</i>	<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>Pete Riojas</b> <i>National Sales Director</i>	<ul style="list-style-type: none"><li>• 29 years of pharmaceutical industry experience</li><li>• Former Sanofi regional sales director and UCB Pharma national sales director</li></ul>

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# Board of Directors

Name / Title	Experience
<b>James Bochnowski</b> <i>Chairman</i>	<ul style="list-style-type: none"><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> <i>Founder, CEO &amp; President</i>	<ul style="list-style-type: none"><li>• 28+ years of industry experience</li><li>• Obtained first anti-secretory human product FDA approval</li></ul>
<b>Jiahao Qiu</b> <i>Director</i>	<ul style="list-style-type: none"><li>• Principal of BioVeda China Fund, a life science investment firm</li><li>• Extensive experience evaluating, managing &amp; investing in life science firms</li></ul>
<b>John Micek III</b> <i>Director</i>	<ul style="list-style-type: none"><li>• Managing Partner of Verdant Ventures</li><li>• Former Managing Director of Silicon Prairie Partners, LP</li></ul>
<b>Jonathan B. Siegel</b> <i>Director</i>	<ul style="list-style-type: none"><li>• Founded JBS Healthcare Ventures with a focus on public and private healthcare investments</li><li>• 18+ years of investment experience</li></ul>
<b>Jeff Johnson</b> <i>Director</i>	<ul style="list-style-type: none"><li>• Partner at Sagard Holdings</li><li>• Former portfolio manager at Evercore Asset Management and Citigroup Asset Management</li></ul>
<b>Greg Divis</b> <i>Director</i>	<ul style="list-style-type: none"><li>• Chief Operating Officer of Avadel Pharmaceuticals</li><li>• 28+ years of direct operating and global leadership experience in specialty pharmaceuticals</li></ul>
<b>David MacNaughtan</b> <i>Director</i>	<ul style="list-style-type: none"><li>• 25+ years of biopharmaceutical industry experience, with roles spanning financing, venture capital, royalty investing, business development, and process development</li></ul>

# Capitalization Table - As of September 15, 2018

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Common shares outstanding:	9,528,103
Non-voting common shares outstanding (as converted to voting common basis):	2,686,749
Preferred stock (as converted to common basis):	<u>3,314,956</u>
Total common and preferred stock:	15,529,808
Warrants:	
119,994 warrants, expiration 5/2022; average exercise price of \$11.25;	1,160,682
731,704 warrants, expiration 1/2019-8/2023; average exercise price of \$4.85;	
308,984 warrants, expiration 12/2018-12/2025; average exercise price of \$1.00	
Options (reserved and issued) and RSU's:	<u>3,709,475</u>
Includes 2,137,943 options priced <\$3.00; and 940,456 > \$3.00/share	
Fully diluted common shares:	20,399,965
Convertible notes:	<u>1,642,852</u>
Proforma fully diluted common shares including potential conversion of notes:	<u>22,042,817</u>

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## Investment Highlights

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### Mytesi: FDA-Approved Human Drug

- Only FDA-approved diarrhea treatment that's been studied specifically in adults with HIV / AIDS
- Global unencumbered rights
- Commercial manufacturing in place
- Approved with chronic safety/locally acting in gut

### Broad Human Product Pipeline

- Potential multiple follow-on human indications of Mytesi with potential blockbuster market and patient opportunity
- Clinical trials include Phase 1 and Phase 2 data

### Priority Review Voucher

- Potential opportunities for non-dilutive funding
- Current market values of PRVs may exceed the current market value of JAGX

### Risk-Mitigated Product Development

- Safety to support approved chronic administration
- Already FDA approved commercial manufacturing facility for crofelemer
- KOL, protocol generation and SPA approach to help mitigate regulatory risk
- Safe and well tolerated with no SAEs reported through present

### Strong Management Team

- Key management has been with the company for >15 years
- Chairman of board and key investors have invested for >25 years
- Original discoverer and developer of successful FDA-approved first-in-class anti-secretory agent, crofelemer - only oral product approved under botanical guidance

### Proprietary Position

- Company patents issued through present: About 140 (majority do not expire until 2027 - 2031)
- Patent applications pending: About 40 (human health)
- Botanical guidance protection. Unique botanical sourcing infrastructure
- Orphan-drug designation



## Appendix A - GAAP and Non-GAAP Basis

	2017	2017	2017	2017	2017	2017	2017	2017	2017	2017	2017	2017
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Gross to Net Sales	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL
Gross Sales-Mytesi	\$ (159,300)	(165,240)	(43,849)	(122,323)	(155,365)	(183,579)	(165,292)	(179,071)	(212,163)	(313,625)	(301,321)	(308,561)
Allowance for sales discounts-Mytesi	3,186	3,305	3,510	8,073	10,254	35,024	10,909	11,633	13,472	17,121	51,309	5,337
Allowance for sales returns-Mytesi	353	1,149	(161,248)	1,743	1,315	1,146	1,151	1,370	630	40,670	0	56,316
Mytesi wholesaler fee										15,012	19,637	19,313
<b>Net Sales-Mytesi</b>	<b>\$ (155,761)</b>	<b>(160,786)</b>	<b>(201,587)</b>	<b>(112,507)</b>	<b>(143,796)</b>	<b>(147,408)</b>	<b>(153,232)</b>	<b>(166,067)</b>	<b>(198,061)</b>	<b>(240,823)</b>	<b>(230,375)</b>	<b>(227,595)</b>

	2018	2018	2018	2018	2018	2018	2018	2018
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug
Gross to Net Sales	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL	ACTUAL
Gross Sales-Mytesi	\$ (274,784)	(238,709)	(281,810)	(321,539)	(477,418)	(363,933)	(489,523)	(594,033)
Allowance for sales discounts-Mytesi	50,245	41,786	14,578	50,392	76,455	84,900	92,186	126,117
Allowance for sales returns-Mytesi	2,129	3,581	24,310	4,395	7,129	4,105	5,921	5,946
Mytesi wholesaler fee	25,984	25,710	23,711	29,344	5,961	46,039	24,380	9,849
<b>Net Sales-Mytesi</b>	<b>\$ (196,426)</b>	<b>(167,632)</b>	<b>(219,211)</b>	<b>(237,408)</b>	<b>(387,873)</b>	<b>(228,889)</b>	<b>(367,036)</b>	<b>(452,121)</b>



## Jaguar Health, Inc.

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### Investor Relations Contact

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