



RedHill Biopharma **("RDHL")**

Platow Small Cap Conference

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Corporate Highlights

An emerging U.S. specialty biopharmaceutical company (Nasdaq: RDHL), primarily focused on U.S. commercialization and development of drugs for gastrointestinal (GI) diseases and infectious diseases

Strong U.S. Commercial Footprint and Robust Development Pipeline with Multiple Near-Term Milestones

Promoting Three
FDA-Approved Drugs

Multiple Phase 3 and
Phase 2 Programs



Emerging U.S. Specialty Pharma: Select Programs*

Commercial Products**

Talicia.
(omeprazole magnesium,
amoxicillin, and rifabutin)
delayed-release capsules

Talicia® (omeprazole magnesium, amoxicillin and rifabutin) - *H. pylori* infection in adults

movantik®
(naloxegol) 25 mg tablets

Movantik® (naloxegol) - Opioid induced constipation (OIC) in adults with chronic non-cancer pain***

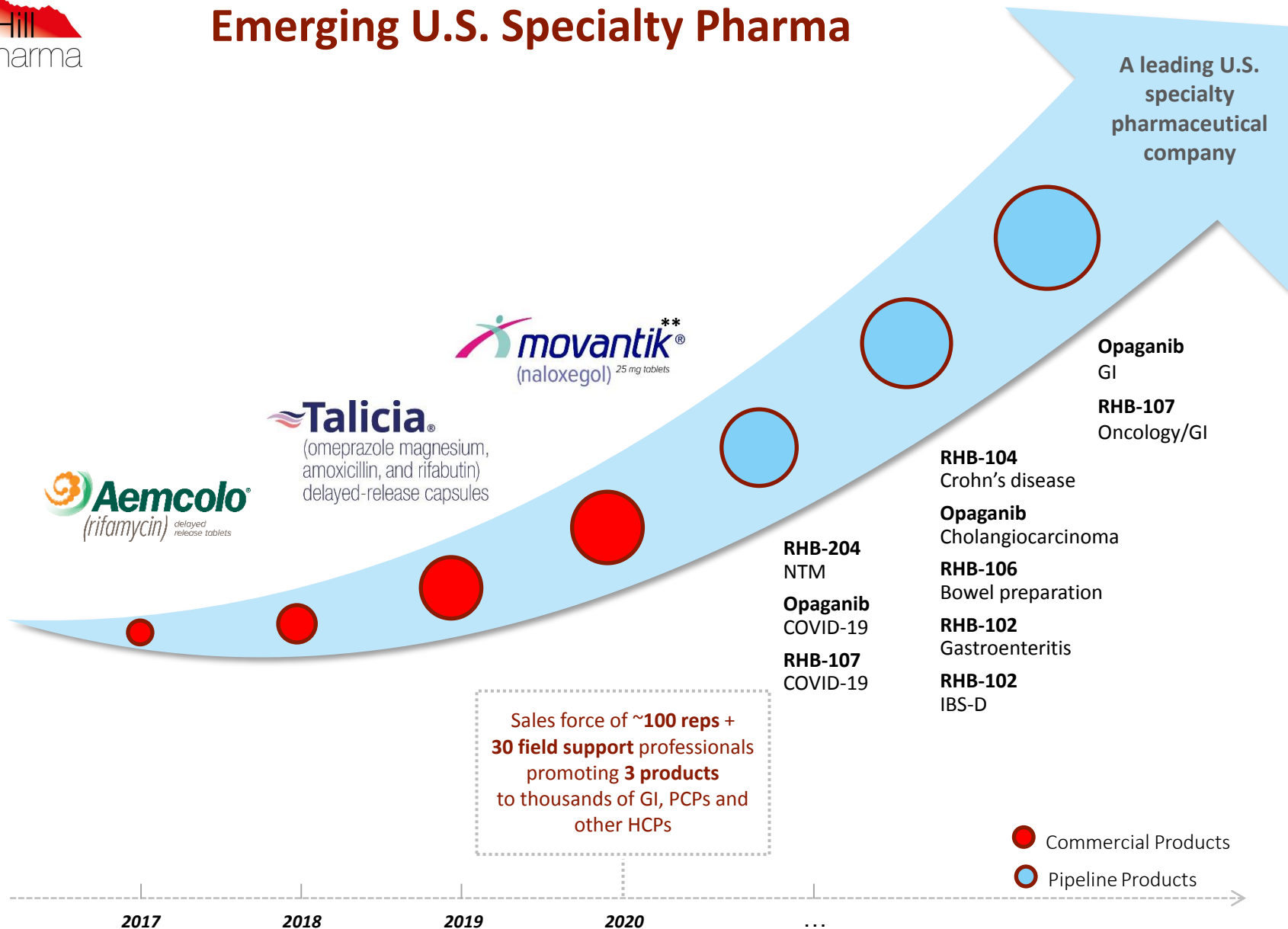
Aemcolo®
(rifamycin) delayed-release tablets

Aemcolo® (rifamycin) - Travelers' diarrhea caused by noninvasive strains of *E. coli* in adults

Development Pipeline****		Pre-Clinical	Phase 1/2	Phase 3	NDA
RHB-204	NTM disease	Phase 3 U.S. study ongoing			
RHB-104	Crohn's disease	Positive results from Phase 3 MAP US study			
RHB-102 (Bekinda®)	Gastroenteritis	Positive results from Phase 3 U.S. study			
	IBS-D	Positive results from Phase 2 U.S. study			
RHB-106	Bowel cleanser	Phase 2/3 studies planned			
Opaganib (Yeliva®)	Oncology Indications + COVID-19	Ongoing Phase 2/3 COVID-19 & Phase 2 oncology program			
RHB-107 (upamostat)	Oncology/GI + COVID-19	Phase 2/3 COVID-19, GI & oncology indications			

* Estimated timeline/indication in the pipeline is subject to changes in development plans and regulatory requirements/clarifications, including complementary/additional studies; ** For full prescribing information see: Aemcolo®: www.Aemcolo.com; Talicia®: www.talicia.com; Movantik®: www.movantik.com; *** Movantik® is a registered trademark of AstraZeneca **** Bekinda® and Yeliva® are proposed tradenames which are subject to FDA review and approval

Emerging U.S. Specialty Pharma



*Presented events are forward looking statements and estimates and are subject to uncertainties including, among others, clinical and regulatory outcomes, marketing approvals, financial resources and commercial viability; This slide and strategic plan is made for illustrative purposes only. Please see "Disclaimer and Forward Looking Statements".

**Movantik® is a registered trademark of AstraZeneca.

Financial Highlights*

RedHill Biopharma Ltd. Nasdaq: RDHL

Market Cap (approx.)	\$338 million
American Depositary Shares (ADSs)	46.67 million (Representing 466.7 million ordinary shares outstanding)
Cash Balance as of March 31, 2021**	Approx. \$92 million



Opaganib (ABC294640, Yeliva®)*

Investigational new drug

*First-in-class, orally-administered sphingosine kinase-2 (SK2) inhibitor
targeting multiple oncology, inflammatory and GI indications*

***Ongoing global Phase 2/3 study and positive top-line data from U.S.
Phase 2 study for COVID-19***

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Phase 2 study for the treatment of cholangiocarcinoma ongoing

Opaganib (Yeliva®) - SK2 Inhibitor for COVID-19 and Oncology, Gastrointestinal and Inflammatory Diseases

The Product	<ul style="list-style-type: none"> - Potential first-in-class, orally-administered sphingosine kinase-2 (SK2) inhibitor - with anti-cancer, anti-inflammatory activities, targeting multiple oncology, inflammatory and GI indications - Potent anti-viral activity, targeting a critical host factor - minimizing potential development of resistance due to viral mutations
Potential Market	<ul style="list-style-type: none"> - Significant market potential - multiple indications with an unmet need
Development Status	<ul style="list-style-type: none"> - Completed numerous successful pre-clinical studies in oncology, GI-Inflammation and radioprotection models, as well as food effect and toxicology studies - Phase 1 study in cancer patients with advanced solid tumors successfully met primary and secondary endpoints - Phase 2a study for treatment of cholangiocarcinoma ongoing <ul style="list-style-type: none"> - Orphan Drug Designation for the treatment of cholangiocarcinoma - Compassionate use for cholangiocarcinoma under Expanded Access Program - Investigator-sponsored Phase 2 study in prostate cancer initiated March 2020 at Medical University of South Carolina (MUSC) - supported by NCI grant to MUSC - Ongoing global Phase 2/3 study - Positive top-line safety and efficacy data from U.S. Phase 2 study in patients hospitalized with COVID-19 pneumonia

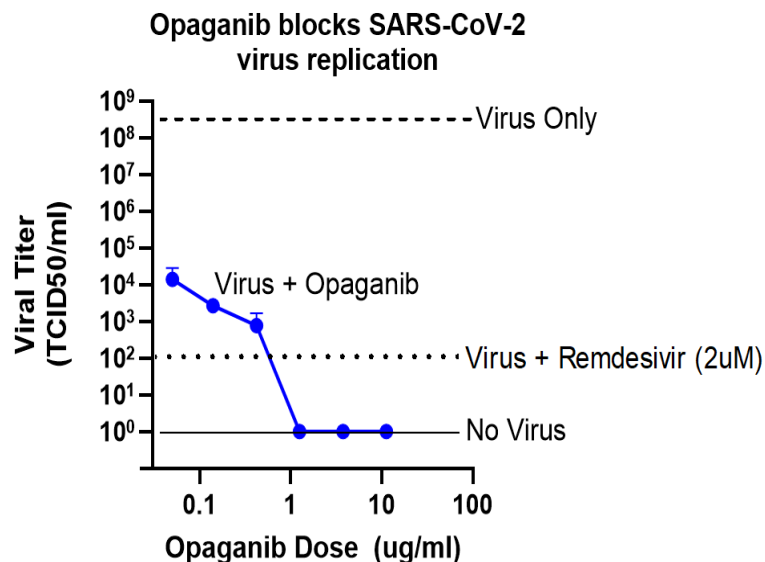
Opaganib (Yeliva®) - Complete Inhibition of SARS-CoV-2

Opaganib's unique MoA combines potent antiviral and anti-inflammatory activities, targeting a host cell component and minimizing likelihood of resistance

Potent Anti-SARS-CoV-2 Activity:

Opaganib evaluated in *in vitro* model of human lung bronchial tissue (EpiAirway™), including positive control of remdesivir:

- Opaganib completely inhibited SARS-CoV-2 viral replication as measured after three days incubation
- Opaganib demonstrated the most potent activity vs. all compounds tested, including remdesivir
- Dose-dependent inhibition of virus production without compromising cell membrane integrity



Opaganib (Yeliva®) - Ongoing Phase 2/3 COVID-19 Study

Global Phase 2/3 Study - Ongoing

Randomized, double-blind, parallel-arm, placebo-controlled global Phase 2/3 study

- Approx. 464 subjects with severe COVID-19 pneumonia in approx. 40 sites
- Primary endpoint: proportion of patients reaching room air by Day 14
- Study approved in 8 countries: Italy, UK, Russia, Israel, Mexico, Colombia, Poland and Brazil; Expansion to U.S.
- Four DSMB recommendations to continue study following independent safety and futility reviews

U.S. Phase 2 Study - Completed

U.S. randomized, double-blind, placebo-controlled Phase 2 study

- Positive top-line safety and efficacy data
- Small sample size of 40 hospitalized patients with COVID-19 pneumonia
- Focused on safety and initial efficacy signals; not powered for statistical significance

- Enrollment for the Phase 2/3 study expected to be completed in the coming weeks
- Collaborations with U.S., European and Canadian suppliers for Manufacturing ramp-up

Opaganib Phase 2 COVID-19 Study - Positive Top-Line Data

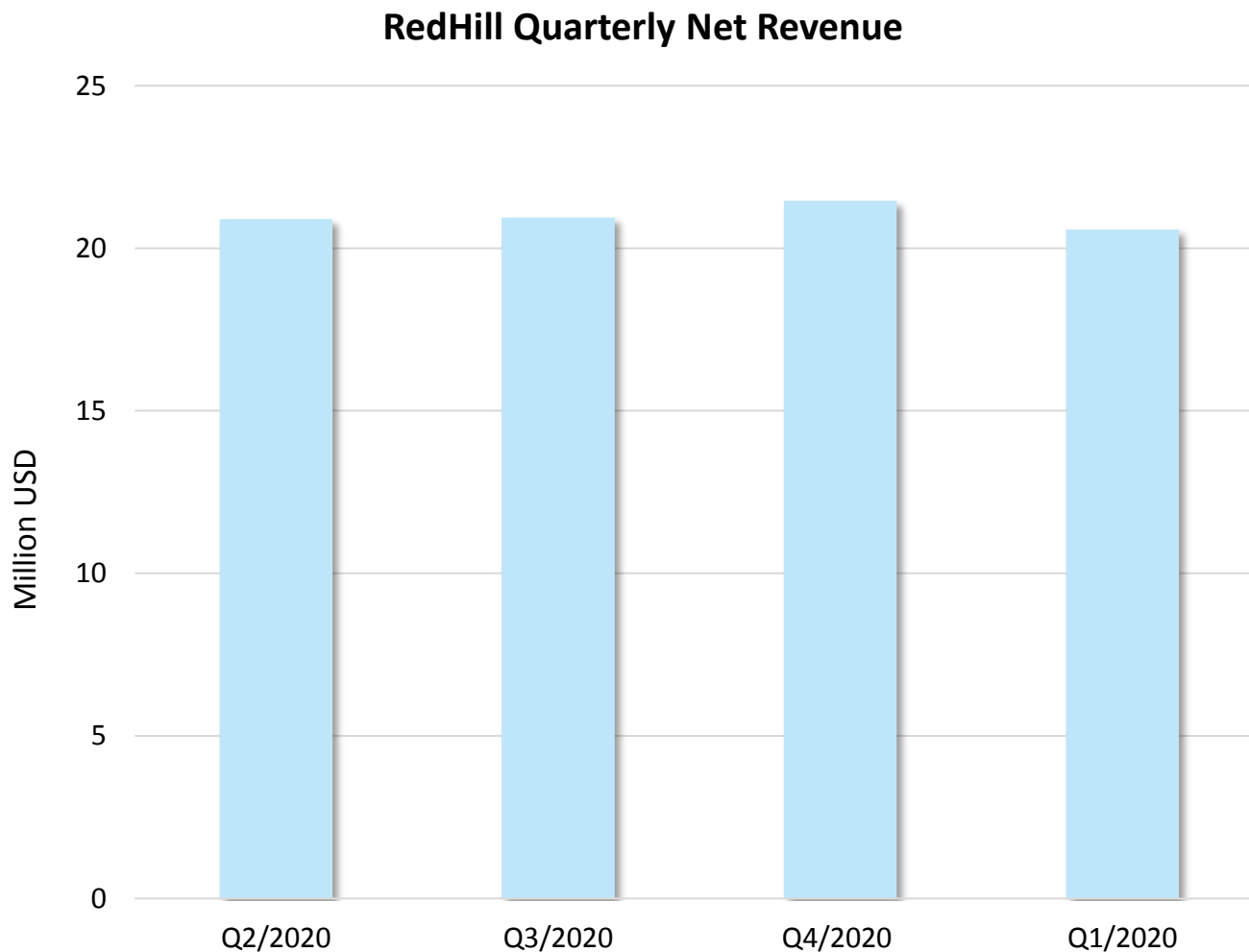
U.S. Phase 2 study of opaganib in patients hospitalized with COVID-19 pneumonia:

Non-powered study of 40 patients, randomized 1:1 to received opaganib or placebo on top of standard-of-care. Follow up for up to 42 days post treatment initiation

Preliminary top-line data demonstrated positive safety and efficacy signals:

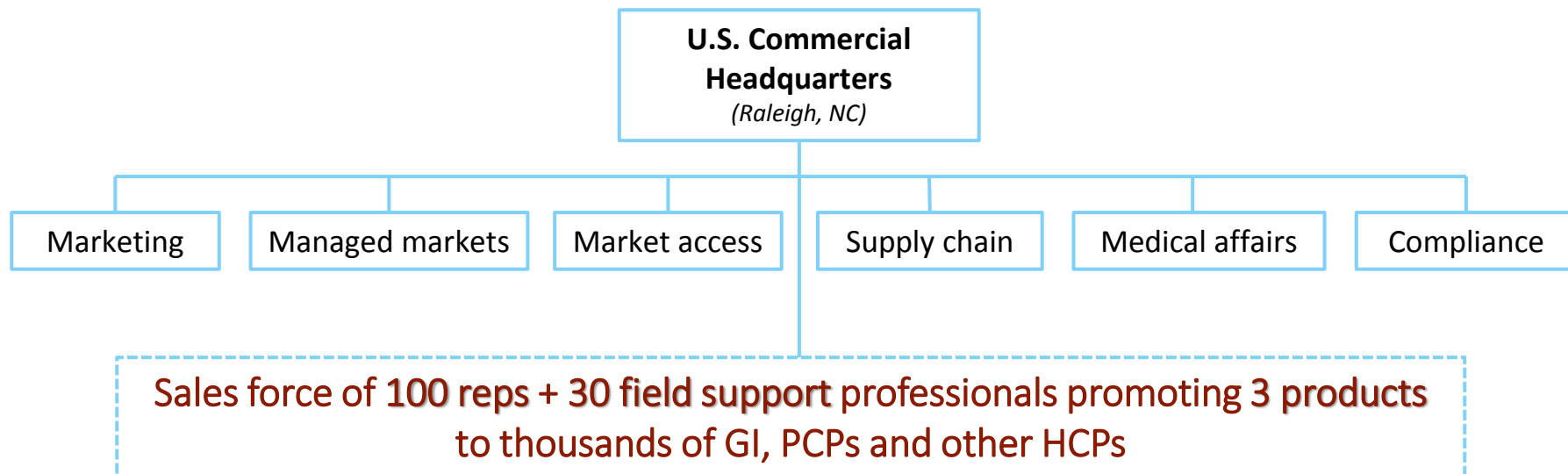
- Opaganib found to be safe, with no material safety differences between the arms. Overall, fewer patients suffered from SAEs in the opaganib arm vs. placebo
- The opaganib arm demonstrated a consistent trend of greater improvement in reducing oxygen requirement by end of treatment on Day 14 across key primary and secondary efficacy outcomes, correlating with clinical improvement as defined by the WHO ordinal scale:
 - ✓ Greater improvement in the proportion of patients reaching room air and no longer requiring oxygen support by Day 14 vs. the control arm (52.6% vs. 22.2%)
 - ✓ Greater improvement in the proportion of patients with 50% reduction in supplemental oxygen by day 14 (89.5% vs. 66.7%)
 - ✓ Higher proportion of patients discharged by Day 14 (73.7% vs. 55.6%)
 - ✓ Greater reduction from baseline of the median total oxygen requirement (AUC) over 14 days (68.0% vs. 46.7%)

Revenue Growth Despite Challenging Pandemic Conditions



Commercial Operations - Strong U.S. Presence

Launched Aemcolo® in Q4/2019, Talicia® in Q1/20 and promoting Movantik® since April 2020



 **Talicia**[®]
(omeprazole magnesium,
amoxicillin, and rifabutin)
delayed-release capsules

 **movantik**^{®*}
(naloxegol) 25 mg tablets

 **Aemcolo**[®]
(rifamycin) delayed
release tablets



Indicated for the treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain

MOVANTIK® (naloxegol)

Important Safety Information

IMPORTANT SAFETY INFORMATION

- **MOVANTIK may cause serious side effects, including:**
 - Opioid withdrawal. You may have symptoms of opioid withdrawal during treatment with MOVANTIK, including sweating, chills, diarrhea, stomach pain, anxiety, irritability, and yawning. Patients taking methadone to treat their pain may be more likely to experience stomach pain and diarrhea. Tell your doctor if you have any of these symptoms
 - Severe Stomach Pain and/or Diarrhea. This can happen within a few days of starting MOVANTIK and can lead to hospitalization. If either of these side effects occurs, stop taking MOVANTIK and call your doctor immediately
 - Tear in your stomach or intestinal wall (perforation). Stomach pain that is severe can be a sign of a serious medical condition. If you get stomach pain that gets worse or does not go away, stop taking MOVANTIK and get emergency medical help right away
- **Do not take MOVANTIK if you:**
 - Have a bowel blockage (intestinal obstruction) or have a history of bowel blockage
 - Are allergic to MOVANTIK or any of the ingredients in MOVANTIK
- MOVANTIK can interact with other medicines and cause side effects, including opioid withdrawal symptoms (see symptoms above). Tell your doctor or pharmacist before you start or stop any medicines during treatment with MOVANTIK
- **Before you take MOVANTIK, tell your doctor about all of your medical conditions, including if you:**
 - Have any stomach, bowel (intestines) problems, including inflammation in parts of the large intestine (diverticulitis), or inflammation and injury of the intestines caused by reduced blood flow (ischemic colitis)
 - Have had recent surgery on the stomach or intestines
 - Have any kidney, or liver problems
 - Are pregnant or plan to become pregnant. Taking MOVANTIK during pregnancy may cause opioid withdrawal symptoms in you or your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with MOVANTIK
 - Are breastfeeding or plan to breastfeed. It is not known if MOVANTIK passes into your breast milk. Taking MOVANTIK while you are breastfeeding may cause opioid withdrawal in your baby. You and your healthcare provider should decide if you will take MOVANTIK or breastfeed. You should not breastfeed if you take MOVANTIK
- **Tell your doctor about all of the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Other medicines may affect the way MOVANTIK works
- **If you stop taking your opioid pain medicine, stop taking MOVANTIK and tell your doctor**
- Avoid eating grapefruit or drinking grapefruit juice during treatment with MOVANTIK
- **The most common side effects of MOVANTIK include:** Stomach (abdomen) pain, diarrhea, nausea, gas, vomiting, headache, and excessive sweating

APPROVED USE FOR MOVANTIK

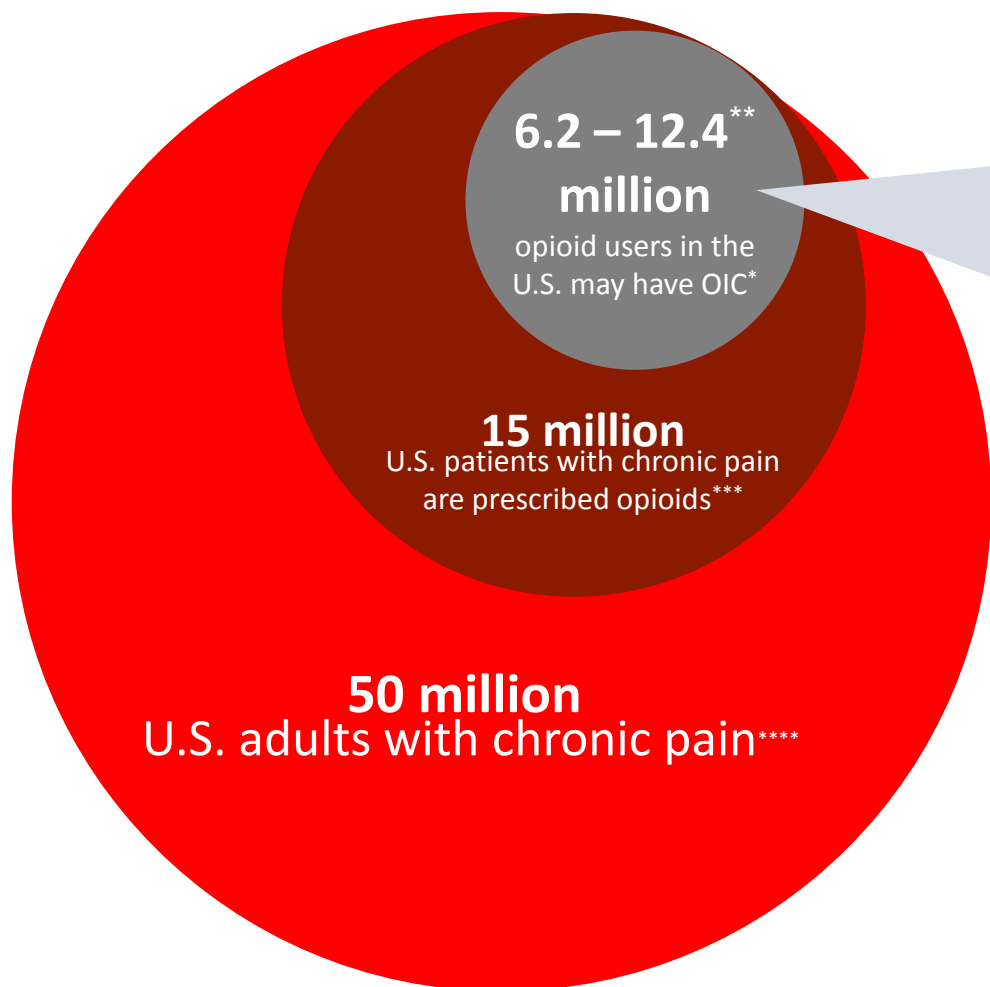
MOVANTIK is a prescription medicine used to treat constipation that is caused by prescription pain medicines called opioids, in adults with long-lasting (chronic) pain that is not caused by active cancer.

See full prescribing information for Movantik®: www.movantik.com

Movantik® - FDA-Approved for Treatment of Opioid-Induced Constipation

Approved Indication	Treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain
Drug	Oral naloxegol tablets available in 12.5mg and 25mg dosage strengths
Approved	Approved in the U.S. in 2014 - launched in 2015 by AstraZeneca and Daiichi Sankyo
Key Attributes	<ul style="list-style-type: none"> ✓ Specifically designed for opioid-induced constipation ✓ Favorable tolerability and safety profile ✓ Available in two doses ✓ Strong reimbursement coverage
Market Exclusivity	Patent protection extending until at least 2028

OIC is a Large and Underserved Market*



*Bell TJ et al. Pain Med. 2009;10(1):35-42. Dahlhamer J, Lucas J, Zelaya C et al. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults – United States, 2016. MMWR Morb Mortal Wkly Rep. 2018;67:1001-1006. Accessed September 29, 2020. <https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6736a2-H.pdf>. **30.7% of patients with chronic noncancer pain are prescribed opioids. Prevalence of OIC is estimated at between 40% to 81% in patients with chronic noncancer pain. Mathieson S et al. J Int Med. 2020;287:458-474. ***Constipation treatments included OTC laxatives (stool softeners, osmotics, stimulants, salines, and rectal options), prescription laxatives, and behavioral therapies (fiber supplements, increased fluids and exercise, and dietary changes). Coyne KS et al. Clinicoecon Outcomes Res. 2014;6:269-281. ****Vegia AR et al. Pain Res Treat. 2018. doi: 10.1155/2018/5704627 5. Coyne KS et al. Clinicoecon Outcomes Res. 2014;6:269-281.

Movantik - the #1 Prescribed Oral PAMORA*



Over **2,000,000** prescriptions written since 2015**



The **#1 prescribed** oral PAMORA specifically designed to treat OIC**



The American Gastroenterological Association recommends the use of Movantik as one of the prescription options for management of OIC***



Movantik is covered or preferred without prior authorization for the majority of commercial and Medicare Part D patients in the U.S.****

Movantik Acquisition - A Transformative Event for RedHill

RedHill acquired the global rights to Movantik* (excluding Europe and Canada) from AstraZeneca in April 2020

- RedHill benefits from the large investment made by AstraZeneca to make Movantik a brand leader
 - First oral PAMORA approved in the U.S. for the treatment of OIC
- **RedHill is enhancing focus to grow this product**
 - Three consecutive quarters of Movantik prescription (TRx) growth led by RedHill promotion, reversing the trend of prescription decline prior to RedHill acquisition
 - RedHill's sales force is enlarging promotional footprint
 - Targeting gastroenterologists, primary care physicians and additional specialists

Talicia®

(omeprazole magnesium,
amoxicillin, and rifabutin)
delayed-release capsules

Indicated for the treatment of *Helicobacter pylori* infection in adults

***Approved for Marketing by U.S. FDA Following Two Positive Phase 3 Studies
Launched in the U.S.***



Talicia® (omeprazole magnesium, amoxicillin and rifabutin)

Important Safety Information

Talicia contains omeprazole, a proton pump inhibitor (PPI), amoxicillin, a penicillin-class antibacterial, and rifabutin, a rifamycin antibacterial. It is contraindicated in patients with known hypersensitivity to any of these medications, any other components of the formulation, any other beta-lactams or any other rifamycins.

Talicia is contraindicated in patients receiving delavirdine, voriconazole or rilpivirine-containing products.

Serious and occasionally fatal hypersensitivity reactions have been reported with omeprazole, amoxicillin and rifabutin.

Acute Tubulointerstitial Nephritis has been observed in patients taking PPIs and penicillins.

Clostridioides difficile-associated diarrhea has been reported with use of nearly all antibacterial agents and may range from mild diarrhea to fatal colitis.

Talicia may cause fetal harm and is not recommended for use in pregnancy. It may also reduce the efficacy of hormonal contraceptives. An additional non-hormonal method of contraception is recommended when taking Talicia.

Talicia should not be used in patients with hepatic impairment or severe renal impairment.

Cutaneous lupus erythematosus and systemic lupus erythematosus have been reported in patients taking PPIs. These events have occurred as both new onset and exacerbation of existing autoimmune disease.

The most common adverse reactions ($\geq 1\%$) were diarrhea, headache, nausea, abdominal pain, chromaturia, rash, dyspepsia, oropharyngeal pain, vomiting, and vulvovaginal candidiasis.

Talicia® - Approved by U.S. FDA for Treatment of *H. pylori* Infection in Adults

Approved Indication	Treatment of <i>H. pylori</i> infection in adults
Drug	Omeprazole magnesium, amoxicillin and rifabutin 10 mg* / 250 mg / 12.5 mg delayed-release capsules*
Approved	NDA approved by U.S. FDA in November 2019 - launched in March 2020
Key Attributes	<ul style="list-style-type: none"> ✓ Addresses concerns of resistance to clarithromycin and metronidazole ✓ Favorable tolerability and safety profile ✓ Aims to become the new first-line standard-of-care with broader indication ✓ All-in-one capsule: supports ease of adherence and compliance, with a single co-pay
Market Exclusivity	<ul style="list-style-type: none"> – Eligible for extended market exclusivity for total of 8 years under QIDP designation – Patent protection extending until at least 2034
Market Size	<ul style="list-style-type: none"> – Affects over 50% of the world population, with ~2 million U.S. patients treated annually – 2018 U.S. and global markets estimated at up to \$1.4 billion and \$4.8 billion respectively** – Approximately 300% quarter-over-quarter prescription growth and rapid expansion of the prescriber base – National coverage for 167 million lives, with additional coverage expected

* Each delayed-release capsule contains omeprazole 10 mg (equivalent to 10.3 mg omeprazole magnesium), amoxicillin 250 mg, and rifabutin 12.5 mg

** Foster Rosenblatt market analysis, October 2018

Talicia Field Promotion Initiated July 2020

RedHill's U.S. sales force promoting Talicia® to approx. 25,000 gastroenterologists,
primary care physicians and other healthcare providers
Rapid expansion in managed care coverage since launch

Talicia®
(omeprazole magnesium,
amoxicillin, and rifabutin)
delayed-release capsules

[Home](#) [The Challenge of *H. pylori*](#) [Efficacy](#) [Safety](#) [Dosing & Administration](#) [Information for Patients](#) [Savings Program](#)

Full Prescribing Information

Important Safety Information

Talicia contains omeprazole, a proton pump inhibitor (PPI),
amoxicillin a penicillin-class antibacterial and rifabutin, a

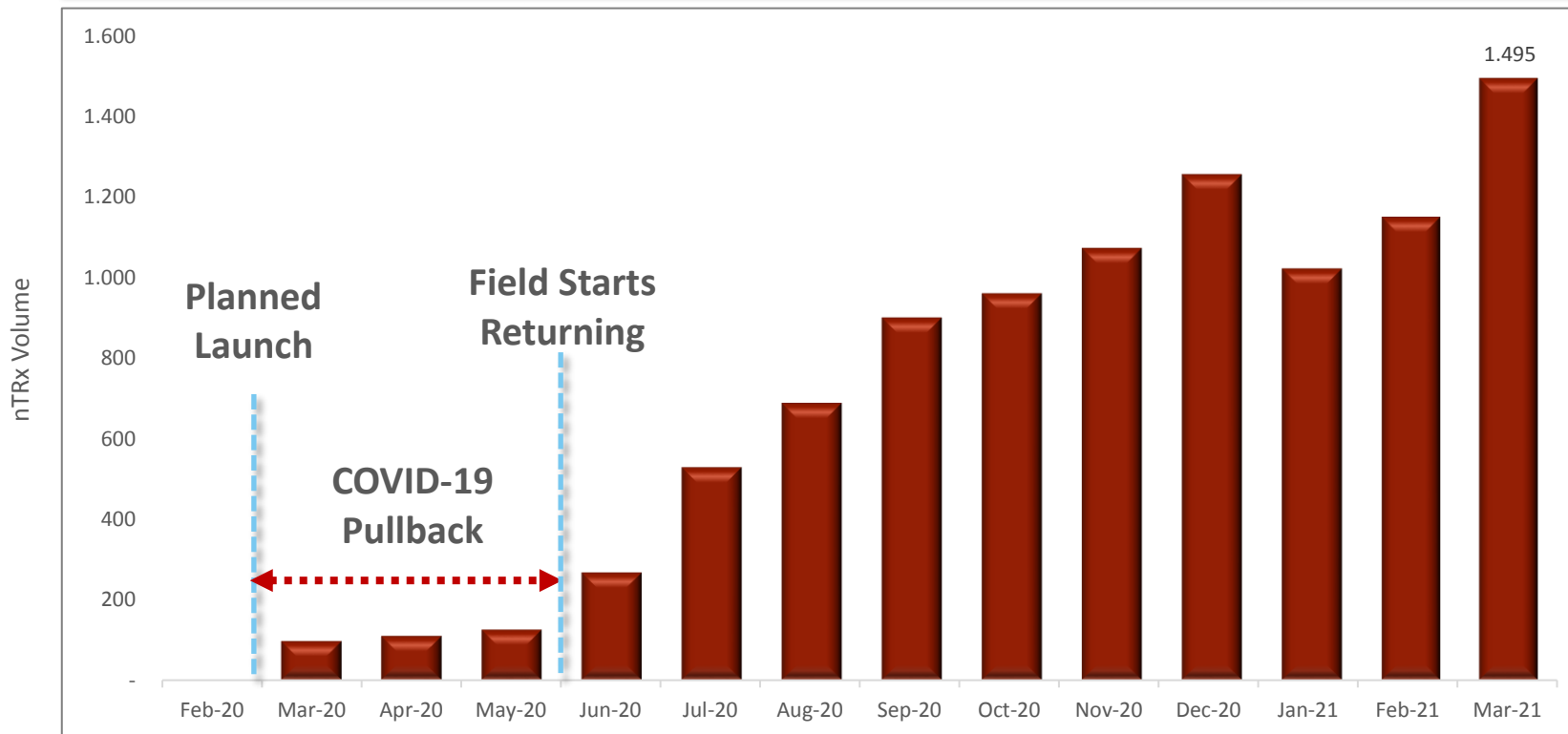
For the treatment of *Helicobacter pylori* infection in adults

**Outsmart Resistance.
Eradicate *H. pylori*.**



Talicia: Strong nTRx Volume Growth With New High for nTRx Volume in March

Talicia nTRx Growth



Continued to achieve new launch year milestones; 11% prescription growth in Q1/21 and anticipating accelerated brand growth in coming months

H. pylori Resistance - An Important Public Health Concern

WHO: *H. pylori* ranked as pathogen with “high priority” need for new treatments

- February 2017 - WHO publishes global priority pathogen list
- Intended to identify the most important resistant bacteria at a global level for which there is an urgent need for new treatments
- H. pylori* (clarithromycin-resistant) categorized as a pathogen for which there is a High Priority need to develop new treatments**

Enterococcus faecium,
vancomycin-resistant
Staphylococcus aureus,
methicillin-resistant,
vancomycin intermediate
and resistant

***Helicobacter pylori*,**
clarithromycin-resistant

Campylobacter,
fluoroquinolone-resistant

Salmonella spp.,
fluoroquinolone-resistant

Neisseria gonorrhoeae,
3rd generation
cephalosporin-resistant,
fluoroquinolone-resistant

FDA: *H. pylori* identified under the GAIN Act as pathogen posing serious threat to public health

- Talicia® received FDA QIDP designation under the GAIN Act for serious or life-threatening infections
- Priority Review
- Extended market exclusivity for a total of 8 years

The three new qualifying pathogens are:

Coccidioides species

Cryptococcus species

Helicobacter pylori

All 18 of the original draft pathogens remain on the list

Resistance Patterns in Pivotal Study Demonstrate Zero to Negligible Resistance For Component Antibiotics in Talicia®

H. pylori Resistance to Standard-of-Care

- H. pylori* culture results from patients across 20 U.S. states supported the high resistance of *H. pylori* to the antibiotics most commonly used for treatment -

Antibiotic	<i>H. pylori</i> Resistance Rate
Metronidazole	44%
Clarithromycin	17%
Amoxicillin	6%
Rifabutin	0%

- Consistent with the literature* describing the diminished efficacy of standard-of-care therapies, open-label part of the study showed 53% eradication of *H. pylori* with standard-of-care**
- Consistent 21-29% treatment benefit of Talicia® vs. the active comparator across all *H. pylori* culture susceptibility and resistance subgroups

*Fallone CA et al. The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults. *Gastroenterology* 2016;151:51–69.

**N=90; therapy in open-label part with patients who failed eradication was determined by the treating physician

Talicia® - Clear Clinical Differentiation Provides Large Potential for Market Opportunity in the U.S. and WW

High Prevalence of *H. pylori*

Over 27M treatments
annually WW*:
U.S.: 2M
5EU: up to 3.2M
Japan: up to 1.4M
China: up to 4.1M

Diminished Efficacy of Standard-of-Care - Approx. 60%

Growing *H. pylori*
resistance has led to
diminished efficacy of
current standard-of-care

Current Brand Medications Lack Clinical Differentiation

Current brands provide
only modest convenience
improvement vs. generics

\$4.8B Global Market

Annual U.S. market for
H. pylori therapies
estimated at \$1.4B*

Talicia® - Potential First-Line Therapy Targeting up to \$1.4B U.S. Market

- **Efficacy** - demonstrated clinical activity with high statistical significance in eradicating *H. pylori* in U.S. pivotal Phase 3 study
- **Addresses concerns of resistance** to clarithromycin and metronidazole
- **Attractive tolerability profile**
- **Potential to become preferred first-line treatment**
- **First all-in-one fixed-dose** - simple regimen potentially improves compliance and efficacy; Additional protection against generic substitution; Single co-pay



Indicated for the treatment of travelers' diarrhea caused by noninvasive strains of *E. coli* in adults

***Approved for Marketing by U.S. FDA
Launched in the U.S. by RedHill - December 2019***



Aemcolo® (rifamycin) - Important Safety Information

INDICATION AND IMPORTANT SAFETY INFORMATION

Aemcolo® is indicated for the treatment of travelers' diarrhea caused by noninvasive strains of *Escherichia coli* (*E. coli*) in adults.

Limitations of Use

Aemcolo® is not indicated in patients with diarrhea complicated by fever or bloody stool or due to pathogens other than noninvasive strains of *E. coli*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Aemcolo® and other antibacterial drugs, Aemcolo® should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

CONTRAINDICATION

Aemcolo® is contraindicated in patients with a known hypersensitivity to rifamycin, any of the other rifamycin class antimicrobial agents, or any of the components in Aemcolo®.

WARNINGS AND PRECAUTIONS

Risk of Persistent or Worsening Diarrhea Complicated by Fever and/or Bloody Stool

Aemcolo® was not shown to be effective in patients with diarrhea complicated by fever and/or bloody stool or diarrhea caused by pathogens other than *E. coli* and is not recommended for use in such patients.

Discontinue Aemcolo® if diarrhea gets worse or persists more than 48 hours and consider alternative antibacterial therapy.

Clostridium difficile-Associated Diarrhea (CDAD)

CDAD has been reported with use of nearly all antibacterial agents and may range in severity from mild diarrhea to fatal colitis.

Consider CDAD in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Development of Drug-Resistant Bacteria

Prescribing Aemcolo® in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

ADVERSE REACTIONS

Discontinuation of Aemcolo® due to adverse reactions occurred in 1% of patients. The most frequent adverse reactions were abdominal pain (0.5%) and pyrexia (0.3%).

Adverse reactions that occurred in at least 2% of Aemcolo®-treated patients and with a higher incidence than in the placebo or ciprofloxacin groups were constipation 3.5% and headache 3.3%, respectively.

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no available data on AEMCOLO use in pregnant women to inform any drug associated risks for major birth defects, miscarriage, or adverse maternal or fetal outcomes.

Lactation

There is no information regarding the presence of AEMCOLO in human milk, the effects on the breastfed infant, or the effects on milk production.

Pediatric Use

The safety and effectiveness of AEMCOLO has not been established in pediatric patients <18 years of age.

See Full prescribing information for Aemcolo® is available at www.aemcolo.com

Launched by RedHill in the U.S. - December 2019

- A rifamycin antibacterial approved by U.S. FDA in Nov. 2018 for the treatment of travelers' diarrhea caused by noninvasive strains of *E. coli* in adults
- In-licensed U.S. rights from Cosmo Pharmaceuticals N.V. in Oct. 2019
- Robust U.S. patent portfolio and FDA QIDP designation, with U.S. marketing exclusivity through 2028

- ✓ Minimally absorbed
- ✓ Targeted delivery system
- ✓ Proven efficacy against *E. coli*
- ✓ Reliable safety and tolerability
- ✓ Simple BID dosing



High Travel Spending Per Person in the U.S. Points to Significant Commercial Opportunity

Travelers' diarrhea is a significant market:

- Approximately **93 million** Americans travel abroad in 2018, of which **60 million** traveled to medium to high risk regions¹
- Travelers' diarrhea may affect up to **70%** of travelers depending on destination and season of travel²
- **> 1/3** of those travelers are seeking health advice prior to leaving³
- **52%** of travelers travel with OTC meds for gastro ailments and **28%** travel with a prescription antibiotic⁴
- The International Society of Travel Medicine (ISTM) recommends **traveling with an antibiotic for self-treatment** when visiting developing regions³



RHB-107 (upamostat)

Investigational new drug

*Potential first-in-class small molecule targeting oncology, inflammatory lung diseases
and GI indications*

U.S. Phase 2/3 COVID-19 ongoing in non-hospitalized patients

RHB-107 - S1 Serine Protease Inhibitor with Ongoing Phase 2/3 COVID-19 Study in Non-Hospitalized Patients

The Drug	Potential first-in-class, orally-administered inhibitor of S1 family of trypsin-like serine proteases with potential for use in the treatment of cancer, inflammatory lung diseases, irritable bowel syndrome, inflammatory bowel disease and pancreatitis
	RHB-107 is a specific and potent inhibitor of human trypsin-3 ($K_i \sim 20\text{nM}$), trypsin-2 ($K_i \sim 75\text{nM}$), trypsin-6 ($\sim 100\text{nM}$), trypsin-1 ($K_i \sim 190\text{nM}$) and matriptase-1 ($\sim 200\text{nM}$)
	Licensed worldwide rights from Heidelberg Pharma (formerly Wilex), excluding China, Taiwan, Macao and Hong Kong
Development Status	Demonstrated clinical safety profile from approx. 200 patients across 10 clinical studies, including Phase 2 studies in locally advanced pancreatic cancer and metastatic breast cancer
	<ul style="list-style-type: none"> – FDA Orphan Drug Designation awarded for treatment of pancreatic cancer – RHB-107 planned to be evaluated in combination with opaganib in an ongoing Phase 2a study in cholangiocarcinoma
	<ul style="list-style-type: none"> – Ongoing U.S. Phase 2/3 study in non-hospitalized patients with symptomatic COVID-19 who do not require supplemental oxygen

RHB-107 - Ongoing Phase 2/3 COVID-19 Study

Ongoing U.S. Phase 2/3 study with RHB-107 in non-hospitalized patients with symptomatic COVID-19 not requiring supplemental oxygen

- ✓ **Study design:** 310 patients to be enrolled in a 2-part, multicenter, randomized, double-blind, placebo-controlled, parallel-group Phase 2/3 study
- ✓ **Innovative use of home-based monitoring technologies** with home nursing support allowing patients participate from home
- ✓ **Primary endpoint:** time to sustained recovery
- ✓ Patients will be tested for specific viral strain

RHB-107 expected to be effective against emerging viral variants with mutations in the spike protein

- ✓ Demonstrated potent inhibition of SARS-CoV-2 viral replication in in vitro model of human bronchial tissue
- ✓ Targets human cell factors involved in viral entry
- ✓ Simple once-daily orally-administered treatment



RHB-204

Investigational new drug

Targeting pulmonary nontuberculous Mycobacteria (NTM) disease - with QIDP designation, including Fast-Track development status

U.S. Phase 3 Study Ongoing

RHB-204 - Targeting First-Line Pulmonary NTM Disease

Planned Indication	<ul style="list-style-type: none"> - Pulmonary nontuberculous mycobacteria disease (NTM) caused by MAC infection
The Product	<ul style="list-style-type: none"> - Patent-protected, oral all-in-one combination of three antibiotic drugs (clarithromycin, clofazimine and rifabutin) each known to be active against NTM disease caused by MAC*
Key Attributes	<ul style="list-style-type: none"> - Targeting first-line treatment - potential new standard-of-care for a disease with no FDA-approved first-line therapy - Convenient stand-alone oral therapy for a chronic disease requiring extended treatment - Unique dosing combination - optimizing exposure for safety and efficacy
Market Size	<ul style="list-style-type: none"> - U.S. market potential estimated at approx. \$530M in 2021**
Development Status	<ul style="list-style-type: none"> - Phase 3 study ongoing - QIDP and Fast-Track Designation granted, providing eligibility for rolling NDA review, Priority Review and accelerated approval - Orphan Drug designation extends potential U.S. market exclusivity to a total of 12 years post-approval

RHB-204 for Pulmonary NTM - Background and Epidemiology

- **Difficult to treat infection with no FDA-approved first-line standard-of-care**
- NTM are a ubiquitous bacteria, mostly non-pathogenic but can cause human disease¹
- Pulmonary manifestations account for 80-90% of NTM associated disease²
- Approximately 80% of pulmonary NTM infections in the U.S. are associated with *Mycobacterium avium* complex (MAC)³
- Pulmonary NTM disease symptoms can include fever, weight loss, chronic or recurring cough, chest pain, blood in sputum and fatigue⁴
- NTM have high levels of drug resistance and require long term dosing with three or more antibiotics²
- NTM is considered an orphan disease with an estimated 110,000 pulmonary NTM patients in the U.S. in 2017⁵



1 Wassilew et al, RESPIRATION 2016 2 Griffith DE, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases Am J Respir Crit Care Med. 2007;175(4):367-416; 3 American Thoracic Society; 3 Prevots DR et al, Am J Respir Crit Care Med 2010; 4 Daley et al CHEST 2017; 5 Foster Rosenblatt/Company estimates

RHB-204 - Phase 3 Study Ongoing

A Phase 3 study to assess the efficacy and safety of RHB-204 as a first-line treatment of pulmonary nontuberculous mycobacteria (NTM) disease caused by *Mycobacterium avium* complex (MAC)

Study Initiated	<ul style="list-style-type: none"> - November 2020
Study Design	<ul style="list-style-type: none"> - Multi-center, randomized, double-blind, two-part, placebo-controlled, parallel-group Phase 3 study; 3:2 randomization - Up to 40 U.S. clinical sites - Two-part study – endpoints evaluated at Month 6; Sustainability of clinical benefit and durability of microbiological response assessed at Month 16 and three-months post treatment completion
Patient Population	<ul style="list-style-type: none"> - 125 subjects with symptomatic MAC lung disease
Endpoints	<ul style="list-style-type: none"> - Sputum culture conversion (SCC) at Month 6 of treatment - Safety and tolerability - Patient-reported outcomes, including improvements in physical functioning, respiratory symptoms and fatigue



Thank You!

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Emerging U.S. Specialty Pharma: Select Programs*

Commercial Products**

Talicia.
(omeprazole magnesium,
amoxicillin, and rifabutin)
delayed-release capsules

Talicia® (omeprazole magnesium, amoxicillin and rifabutin) - *H. pylori* infection in adults

movantik®
(naloxegol) 25 mg tablets

Movantik® (naloxegol) - Opioid induced constipation (OIC) in adults with chronic non-cancer pain***

Aemcolo®
(rifamycin) delayed-release tablets

Aemcolo® (rifamycin) - Travelers' diarrhea caused by noninvasive strains of *E. coli* in adults

Development Pipeline****		Pre-Clinical	Phase 1/2	Phase 3	NDA
RHB-204	NTM disease	Phase 3 U.S. study ongoing			
RHB-104	Crohn's disease	Positive results from Phase 3 MAP US study			
RHB-102 (Bekinda®)	Gastroenteritis	Positive results from Phase 3 U.S. study			
	IBS-D	Positive results from Phase 2 U.S. study			
RHB-106	Bowel cleanser	Phase 2/3 studies planned			
Opaganib (Yeliva®)	Oncology Indications + COVID-19	Ongoing Phase 2/3 COVID-19 & Phase 2 oncology program			
RHB-107 (upamostat)	Oncology/GI + COVID-19	Phase 2/3 COVID-19, GI & oncology indications			

* Estimated timeline/indication in the pipeline is subject to changes in development plans and regulatory requirements/clarifications, including complementary/additional studies; ** For full prescribing information see: Aemcolo®: www.Aemcolo.com; Talicia®: www.talicia.com; Movantik®: www.movantik.com; *** Movantik® is a registered trademark of AstraZeneca **** Bekinda® and Yeliva® are proposed tradenames which are subject to FDA review and approval