Press Release

RedHill Biopharma Presents Three New Analyses of Movantik Data at PAINWeek 2021

Two new analyses of Movantik® (naloxegol) data evaluated the safety and efficacy of Movantik in a subgroup of patients aged ≥ 65 years

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Analysis of Movantik effects on rapid and sustained improvement of both spontaneous and complete spontaneous bowel movements in the Movantik group vs. placebo were evaluated across high and low opioid dosages

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Movantik is the U.S. market-leading oral peripherally acting mu-opioid receptor antagonist (PAMORA), approved to treat opioid-induced constipation in adults with chronic non-cancer pain

TEL AVIV, Israel and RALEIGH, NC, September 7, 2021, RedHill Biopharma Ltd. (Nasdaq: RDHL) ("RedHill" or the "Company"), a specialty biopharmaceutical company, today announced presentation at PAINWeek 2021 of three new analyses of Movantik® (naloxegol) Phase 3 study data demonstrating rapid onset of action and sustained and predictable improvement of key symptoms associated with opioid-induced constipation (OIC) in both a subgroup of patients aged ≥ 65 and across both low and high dose opioid therapy.

Two of the posters are dedicated to the subgroup of patients aged ≥ 65, with Movantik achieving significantly better response rates vs. placebo, with rapid onset of action and a higher proportion of subjects achieving spontaneous bowel movement (SBM) and complete spontaneous bowel movement (CSBM) over the first 48 hours of treatment. Additional presented data also shows that naloxegol delivers similar rapid and sustained symptom improvement for patients, irrespective of the opioid dose they are prescribed, including at doses lower than 100 mg of morphine equivalent. The authors conclude that even with lower doses of morphine equivalent, clinicians should be diligent about treating these patients because they still are susceptible to OIC.

The three analyses included pooled data from two large, robust, identically designed Phase 3 studies of Movantik (Kodiak 4 and Kodiak 5; NCT01309841/NCT01323790), involving 891 treated patients across two doses (12.5 mg and 25 mg), compared to a total of 446 patients in the placebo arms.

"With up to 90% of older patients receiving opioids to help cope with chronic pain, and up to 86% of them suffering from symptoms of OIC, these new analyses are particularly important in helping these patients achieve satisfactory control of their pain without the added burden of OIC. Older patients tend to be more susceptible to OIC due to comorbidities, polypharmacy, and reduced physical activity, and it is vital that they have access to therapies such as Movantik, that are shown to be effective in this challenging patient group." **said Dr. Lynn Webster, Pain Researcher and Clinician and Senior Fellow at the Center of U.S. Policy**.

"There has been a shift in clinical practice to try to reduce doses of opioids used to treat chronic pain. However, low dose opioid therapy can prove to be equally troublesome in terms of treatment-related constipation as higher doses and it is important that physicians are diligent in monitoring for signs of OIC," **said Dr. June Almenoff, MD, Ph.D., RedHill's Chief Scientific Officer**. "This new analysis showing Movantik's efficacy irrespective of opioid dose is equally important in supporting the clinical shift to low dose opioid therapy through the management of OIC which can be expected in between 40-80% of patients taking chronic opioid therapy[1]."

New Movantik (Naloxegol) Analyses Presented at PAINWeek 2021:

Poster 1 (poster number 55):
Naloxegol Provided Rapid Onset of Time to First Spontaneous Bowel Movement (SBM), Complete SBM and Predictable Efficacy in Older Adults (Age ≥ 65 Yrs): A Pooled Analysis of Two Phase 3 Studies
Authors: Lynn Webster, Charles Argoff, Charles H. McLeskey, Carol B. Rockett, Enoch Bortey, Theresa Mallick-Searle, Martin Hale

Poster 2 (poster number 59):
Naloxegol Provided Rapid and Sustained Improvement of Opioid-Induced Constipation (OIC) Symptoms in Older Adults Age ≥ 65 Yrs: A Pooled Analysis of Two Phase 3 Studies
Authors: Martin Hale, Charles Argoff, Charles H. McLeskey, Carol B. Rockett, Enoch Bortey, Theresa Mallick-Searle, Lynn Webster

Poster 3 (poster number 30):
Naloxegol Provides Rapid and Sustained Improvement of Opioid-Induced Constipation (OIC) Symptoms Irrespective of Opioid Dose: A Pooled Analysis of Two Phase 3 Studies
Authors: Jeffrey Gudin, Jeremy A. Adler, June Almenoff, Carol B. Rockett, Enoch Bortey, Richard Rauck, Lynn Webster

About RedHill Biopharma

RedHill Biopharma Ltd. (Nasdaq: RDHL) is a specialty biopharmaceutical company primarily focused on gastrointestinal and infectious diseases. RedHill promotes the gastrointestinal drugs,

Movantik® for opioid-induced constipation in adults[2], **Talicia®** for the treatment of *Helicobacter pylori (H. pylori)* infection in adults[3], and **Aemcolo®** for the treatment of travelers' diarrhea in adults[4]. RedHill's key clinical late-stage development programs include: (i) **RHB-204**, with an ongoing Phase 3 study for pulmonary nontuberculous mycobacteria (NTM) disease; (ii) **opaganib (ABC294640)**, a first-in-class oral SK2 selective inhibitor targeting multiple indications with a global Phase 2/3 program for COVID-19 and Phase 2 studies for prostate cancer and cholangiocarcinoma ongoing; (iii) **RHB-107** (**upamostat**), an oral serine protease inhibitor in a U.S. Phase 2/3 study as treatment for symptomatic COVID-19, and targeting multiple other cancer and inflammatory gastrointestinal diseases; (iv) **RHB-104**, with positive results from a first Phase 3 study for Crohn's disease; (v) **RHB-102**, with positive results from a Phase 3 study for acute gastroenteritis and gastritis and positive results from a Phase 2 study for IBS-D; and (vi) **RHB-106**, an encapsulated bowel preparation. More information about the Company is available at www.redhillbio.com / https://twitter.com/RedHillBio.

About Movantik® (naloxegol)

Movantik® is an opioid antagonist indicated for the treatment of opioidinduced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

Important Safety Information About Movantik

Movantik® (naloxegol) is contraindicated in:

- Patients with known or suspected gastrointestinal (GI) obstruction and patients at risk of recurrent obstruction, due to the potential for GI perforation.
- Patients receiving strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole) because these medications can significantly increase exposure to naloxegol which may precipitate opioid withdrawal symptoms.
- Patients with a known serious or severe hypersensitivity reaction to Movantik or any of its excipients.

Symptoms consistent with opioid withdrawal, including hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, irritability, and yawning, occurred in patients treated with Movantik. Patients receiving methadone as therapy for their pain condition were observed in the clinical trials to have a higher frequency of GI adverse reactions that may have been related to opioid withdrawal than patients receiving other opioids. Patients with disruptions to the blood-brain barrier may be at increased risk for opioid withdrawal or reduced analgesia. These patients (e.g., multiple sclerosis, recent brain injury, Alzheimer's disease, and uncontrolled epilepsy) were not enrolled in the clinical studies. Take into account the overall risk-benefit profile when using Movantik in such patients. Monitor for symptoms of opioid withdrawal when using Movantik in such patients.

Severe abdominal pain and/or diarrhea have been reported, generally within a few days of initiation of Movantik. Monitor and discontinue if severe symptoms occur. Consider restarting Movantik at 12.5 mg once daily.

Cases of GI perforation have been reported with the use of peripherally acting opioid antagonists, including Movantik. Postmarketing cases of GI perforation, including fatal cases, were reported when Movantik was used in patients at risk of GI perforation (e.g., infiltrative gastrointestinal tract malignancy, recent gastrointestinal tract surgery, diverticular disease including diverticulitis, ischemic colitis, or concomitantly treated with bevacizumab). Monitor for severe, persistent, or worsening abdominal pain; discontinue if this symptom develops.

The most common adverse reactions with Movantik as compared to placebo in clinical trials were: Abdominal pain (21% vs 7%), diarrhea (9% vs 5%), nausea (8% vs 5%), flatulence (6% vs 3%), vomiting (5% vs 4%), headache (4% vs 3%), and hyperhidrosis (3% vs <1%).

Movantik (naloxegol) is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation.

Click here for the Medication Guide and full Prescribing Information for Movantik.

You are encouraged to report Adverse Reactions to RedHill Biopharma Inc. at 1-833-ADRHILL (1-833-237-4455) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

MOVANTIK is a registered trademark of the AstraZeneca group of companies.

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements may be preceded by the words "intends," "may," "will," "plans," "expects," "anticipates," "projects," "predicts," "estimates," "aims," "believes," "hopes," "potential" or similar words. Forward-looking statements are based on certain assumptions and are subject to various known and unknown risks and uncertainties, many of which are beyond the Company's control and cannot be predicted or quantified, and consequently, actual results may differ materially from those expressed or implied by such forward-looking statements. Such risks and uncertainties include, without limitation; the risk that the Company will not successfully commercialize its products; as well as risks and uncertainties associated with (i) the initiation, timing, progress and results of the Company's research, manufacturing, pre-clinical studies, clinical trials, and other therapeutic candidate development efforts, and the timing of the commercial launch of its commercial products and ones it may acquire or develop in the future; (ii) the Company's ability to advance its therapeutic candidates into clinical trials or to successfully complete its pre-clinical studies or clinical trials or the development of a commercial companion diagnostic for the detection of MAP; (iii) the extent and number and type of additional studies that the Company may be required to conduct and the Company's receipt of regulatory approvals for its therapeutic candidates, and the timing of other regulatory filings, approvals and feedback; (iv) the manufacturing, clinical development, commercialization, and market acceptance of the Company's therapeutic candidates and Talicia®; (v) the Company's ability to successfully commercialize and promote Talicia®, and

Aemcolo® and Movantik®; (vi) the Company's ability to establish and maintain corporate collaborations; (vii) the Company's ability to acquire products approved for marketing in the U.S. that achieve commercial success and build its own marketing and commercialization capabilities; (viii) the interpretation of the properties and characteristics of the Company's therapeutic candidates and the results obtained with its therapeutic candidates in research, pre-clinical studies or clinical trials; (ix) the implementation of the Company's business model, strategic plans for its business and therapeutic candidates; (x) the scope of protection the Company is able to establish and maintain for intellectual property rights covering its therapeutic candidates and its ability to operate its business without infringing the intellectual property rights of others; (xi) parties from whom the Company licenses its intellectual property defaulting in their obligations to the Company; (xii) estimates of the Company's expenses, future revenues, capital requirements and needs for additional financing; (xiii) the effect of patients suffering adverse experiences using investigative drugs under the Company's Expanded Access Program; (xiv) competition from other companies and technologies within the Company's industry; and (xv) the hiring and employment commencement date of executive managers. More detailed information about the Company and the risk factors that may affect the realization of forward-looking statements is set forth in the Company's filings with the Securities and Exchange Commission (SEC), including the Company's Annual Report on Form 20-F filed with the SEC on March 18, 2021. All forward-looking statements included in this press release are made only as of the date of this press release. The Company assumes no obligation to update any written or oral forward-looking statement, whether as a result of new information, future events or otherwise unless required by law.

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[1] Crockett, Seth D., et al. American Gastroenterological Association Institute guideline on the medical management of opioid-induced constipation, Gastroenterology 156.1 (2019): 218-226.
[2] Full prescribing information for Movantik® (naloxegol) is available at: www.Movantik.com.
[3] Full prescribing information for Talicia® (omeprazole magnesium, amoxicillin and rifabutin) is available at: www.Talicia.com.
[4] Full prescribing information for Aemcolo® (rifamycin) is available at: www.Aemcolo.com.