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Rigel Pharmaceuticals Enters Collaboration and License Agreement with Grifols, S.A. to Commercialize Fostamatinib in Europe

- Grifols gains exclusive rights to fostamatinib in all potential indications in Europe and Turkey

- Rigel to receive an upfront payment of $30 million, with the potential for $297.5 million in total regulatory and commercial milestones

- Potential milestones to Rigel include a $20 million payment upon EMA approval of fostamatinib in chronic immune thrombocytopenia (ITP), which is currently under review

- Rigel to receive stepped royalty payments reaching 30% of net sales of fostamatinib

SOUTH SAN FRANCISCO, Calif., Jan. 23, 2019 /PRNewswire/ -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced that it has entered into an exclusive license and supply agreement with Spain-based Grifols, S.A (MCE: GRF, MCE: GRF.P, NASDAQ: GRFS) to commercialize fostamatinib disodium hexahydrate in all potential indications in Europe and Turkey. Grifols is a global healthcare company and a leading producer of plasma-derived medicines for the treatment of rare and chronic diseases, including intravenous immunoglobulin (IVIG) which is used in the treatment of ITP and AIHA. Fostamatinib is commercially available in the U.S. under the brand name TAVALISSE® (fostamatinib disodium hexahydrate) and is the first and only SYK inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment.

"Grifols has a broad presence in Europe and an established position in the hematology commercial landscape, which supports our goal of bringing fostamatinib to patients in these countries," said Raul Rodriguez, President and CEO of Rigel. "Our marketing authorization

application for fostamatinib in chronic ITP is currently under review by the European Medicines Agency, and we anticipate a decision by the end of 2019. This provides a potential opportunity for fostamatinib to begin generating revenue in the European market in 2020."

Under terms of the agreement, Rigel will receive a $30 million upfront cash payment, with the potential for $297.5 million in payments related to regulatory and commercial milestones, which includes a $20 million payment for EMA approval of fostamatinib for the treatment of chronic ITP. Rigel will receive significant stepped double-digit royalty payments based on tiered net sales which may reach 30% of net sales. In return, Grifols receives exclusive rights to fostamatinib in human diseases, including chronic ITP, autoimmune hemolytic anemia (AIHA), and IgA nephropathy (IgAN), in Europe and Turkey. In the event that, in 2021, after the second anniversary of the agreement, fostamatinib has not been approved by the EMA for the treatment of ITP in Europe, Grifols will have the option during a six-month time-frame to terminate the entire agreement which would terminate all their rights to ITP, AIHA, and all other indications. In this limited circumstance, Rigel will pay Grifols $25 million and regain all rights to fostamatinib in Europe and other territories. Rigel retains the remaining global rights to fostamatinib outside the Grifols territories and those rights previously granted to Kissei Pharmaceuticals (in Japan, China, Taiwan and the Republic of Korea).

"Given our global leadership position as a manufacturer of plasma medicines and our in-depth knowledge and expertise in blood disorders, adding fostamatinib to our portfolio is a natural fit for Grifols," said Joel Abelson, President, Bioscience Commercial Division of Grifols. "Its potential in multiple indications, including ITP, may provide significant benefit for patients and is a valuable addition to our portfolio."

On October 4, 2018, the EMA validated the marketing authorization application for fostamatinib in adult chronic ITP, which was submitted by Rigel. The company anticipates a decision from the EMA's Committee on Human Medicinal Products by the fourth quarter of 2019 and potential European approval by the end of 2019.

About ITP

In patients with ITP, the immune system attacks and destroys the body's own blood platelets, which play an active role in blood clotting and healing. Common symptoms of ITP are excessive bruising and bleeding. People suffering with chronic ITP may live with an increased risk of severe bleeding events that can result in serious medical complications or even death. Current therapies for ITP include steroids, blood platelet production boosters (TPOs) and splenectomy. However, not all patients respond to existing therapies. As a result, there remains a significant medical need for additional treatment options for patients with ITP.

About TAVALISSE

Indication

TAVALISSE® (fostamatinib disodium hexahydrate) tablets is indicated in the US for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

Important Safety Information

Warnings and Precautions

- Hypertension can occur with TAVALISSE treatment. Patients with pre-existing hypertension may be more susceptible to the hypertensive effects. Monitor blood pressure every 2 weeks until stable, then monthly, and adjust or initiate antihypertensive therapy for blood pressure control maintenance during therapy. If increased blood pressure persists, TAVALISSE interruption, reduction, or discontinuation may be required.
- Elevated liver function tests (LFTs), mainly ALT and AST, can occur with TAVALISSE. Monitor LFTs monthly during treatment. If ALT or AST increase to >3 x upper limit of normal, manage hepatotoxicity using TAVALISSE interruption, reduction, or discontinuation.
- Diarrhea occurred in 31% of patients and severe diarrhea occurred in 1% of patients treated with TAVALISSE. Monitor patients for the development of diarrhea and manage using supportive care measures early after the onset of symptoms. If diarrhea becomes severe (≥Grade 3), interrupt, reduce dose or discontinue TAVALISSE.
- Neutropenia occurred in 6% of patients treated with TAVALISSE; febrile neutropenia occurred in 1% of patients. Monitor the ANC monthly and for infection during treatment. Manage toxicity with TAVALISSE interruption, reduction, or discontinuation.
- TAVALISSE can cause fetal harm when administered to pregnant women. Advise pregnant women the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose. Verify pregnancy status prior to initiating TAVALISSE. It is unknown if TAVALISSE or its metabolite is present in human milk. Because of the potential for serious adverse reactions in a breastfed child, advise a lactating woman not to breastfeed during TAVALISSE treatment and for at least 1 month after the last dose.

Drug Interactions

- Concomitant use of TAVALISSE with strong CYP3A4 inhibitors increases exposure to the major active metabolite of TAVALISSE (R406), which may increase the risk of adverse reactions. Monitor for toxicities that may require a reduction in TAVALISSE dose.
- It is not recommended to use TAVALISSE with strong CYP3A4 inducers, as concomitant use reduces exposure to R406.
- Concomitant use of TAVALISSE may increase concentrations of some CYP3A4 substrate drugs and may require a dose reduction of the CYP3A4 substrate drug.
- Concomitant use of TAVALISSE may increase concentrations of BCRP substrate drugs (eg, rosuvastatin) and P-Glycoprotein (P-gp) substrate drugs (eg, digoxin), which may require a dose reduction of the BCRP and P-gp substrate drug.

Adverse Reactions

- Serious adverse drug reactions in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which occurred in 1% of TAVALISSE patients. In addition, severe adverse reactions occurred including dyspnea and hypertension (both 2%), neutropenia, arthralgia, chest pain, diarrhea, dizziness, nephrolithiasis, pain in extremity, toothache, syncope, and hypoxia (all 1%).
- Common adverse reactions (≥5% and more common than placebo) from the FIT-1 and FIT-2 phase 3 clinical trials included: diarrhea, hypertension, nausea, dizziness, ALT and AST increased, respiratory infection, rash, abdominal pain, fatigue, chest pain, and

neutropenia.

Please see www.TAVALISSE.com for full Prescribing Information.

**To report side effects of prescription drugs to the FDA,
visit www.fda.gov/medwatch or call 1-800-FDA-1088 (800-332-1088).**

TAVALISSE is a trademark of Rigel Pharmaceuticals, Inc.

About Rigel (www.rigel.com)
Rigel Pharmaceuticals, Inc., is a biotechnology company dedicated to discovering, developing and providing novel small molecule drugs that significantly improve the lives of patients with immune and hematologic disorders, cancer and rare diseases. Rigel's pioneering research focuses on signaling pathways that are critical to disease mechanisms. The company's first FDA approved product is TAVALISSE™ (fostamatinib disodium hexahydrate), an oral spleen tyrosine kinase (SYK) inhibitor, for the treatment of adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. Rigel's current clinical programs include an upcoming Phase 3 study of fostamatinib in autoimmune hemolytic anemia and an ongoing Phase 1 study of R835, a proprietary molecule from its interleukin receptor associated kinase (IRAK) program. In addition, Rigel has product candidates in clinical development with partners BerGenBio AS, Daiichi Sankyo, and Aclaris Therapeutics.

About Grifols
Grifols is a global healthcare company with more than 75 years of legacy dedicated to improving the health and well-being of people around the world. Grifols produces essential plasma-derived medicines for patients, and provides hospitals and healthcare professionals with the tools, information and services they need to help them deliver expert medical care.

Grifols' three main divisions – Bioscience, Diagnostic and Hospital – develop, produce and market innovative products and services that are available in more than 100 countries.

With a network of 250 plasma donation centers, Grifols is a leading producer of plasma-derived medicines used to treat rare, chronic and, at times, life-threatening conditions. As a recognized leader in transfusion medicine, Grifols offers a comprehensive portfolio of diagnostic products designed to support safety from donation through transfusion. The Hospital Division provides intravenous (IV) therapies, clinical nutrition products and hospital pharmacy systems, including systems that automate drug compounding and control drug inventory.

Grifols is headquartered in Barcelona, Spain, and has 20,000 employees in 30 countries. In 2017, sales exceeded 4,300 million euros. Grifols demonstrates its strong commitment to advancing healthcare by allocating a significant portion of its annual income to research, development and innovation.

The company's class A shares are listed on the Spanish Stock Exchange, where they are part of the Ibex-35 (MCE:GRF). Grifols non-voting class B shares are listed on the Mercado Continuo (MCE:GRF.P) and on the US NASDAQ via ADRs (NASDAQ:GRFS).

For more information, visit www.grifols.com

Forward Looking Statements

This release contains forward-looking statements relating to, among other things, Rigel's partnership with Grifols; Rigel's partnership with Kissei; Rigel's ability to achieve regulatory and commercial milestone payments under its agreement with Grifols; the potential opportunity for fostamatinib to begin generating revenue in the European market in 2020; Rigel's interactions with the EMA; and the timing of the EMA's MAA review process and when Rigel expects a decision. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "planned," "will," "may," "expect," "anticipate," and similar expressions are intended to identify these forward-looking statements. These forward-looking statements are based on Rigel's current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the commercialization and marketing of TAVALISSE; risks that the FDA, EMA or other regulatory authorities may make adverse decisions regarding fostamatinib; risks that TAVALISSE clinical trials may not be predictive of real-world results or of results in subsequent clinical trials; risks that TAVALISSE may have unintended side effects, adverse reactions or incidents of misuses; the availability of resources to develop Rigel's product candidates; market competition; as well as other risks detailed from time to time in Rigel's reports filed with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the period ended September 30, 2018. Rigel does not undertake any obligation to update forward-looking statements and expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein.

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