Current Agreements

Dealdoc

Development and licensing agreement for ralinepag and etrasimod

Arena Pharmaceuticals
Everest Medicines

Dec 05 2017

Development and licensing agreement for ralinepag and etrasimod

Companies:	Arena Pharmaceuticals Everest Medicines
Announcement date:	Dec 05 2017
Deal value, US$m:	224 : sum of upfront and milestone payments

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- Filing Data
- Contract

Details

Announcement date:	Dec 05 2017
Industry sectors:	Pharmaceutical
Compound name:	Ralinepag, etrasimod
Exclusivity:	Exclusive
Asset type:	Compound
Therapy areas:	Cardiovascular » Hypertension Immunology » Other autoimmune Respiratory » Pulmonary arterial hypertension
Technology types:	Small molecules
Deal components:	Development Licensing
Stages of development:	Phase II Phase III
Geographic focus:	Asia » China Asia » Hong Kong Asia » Macau Asia » South Korea Asia » Taiwan

Financials

Deal value, US$m:	224 : sum of upfront and milestone payments
Upfront, US$m:	12 : upfront payment
Milestones, US$m:	212 : development and commercial milestone payments
Royalty rates, %:	12 : low double-digit royalties on net annual sales of both ralinepag and etrasimod
Semi-quant royalties:	Low teens

Termsheet

Arena Pharmaceuticals and Everest Medicines have entered into a development and commercialization partnership for ralinepag and etrasimod in mainland China, Taiwan, Hong Kong, Macau, and South Korea.

Arena has granted Everest exclusive rights to develop and commercialize ralinepag and etrasimod in the Territories.

In return, Arena will receive an upfront payment of $12 million, is eligible to receive up to $212 million in development and commercial milestone payments and is entitled to receive up to low double-digit royalties on net annual sales of both ralinepag and etrasimod.

The parties plan to collaborate on development on both products; however, Everest is generally responsible for funding development and commercialization in the Territories.

Press Release

May 2022

Everest Medicines' Licensing Partner Pfizer Presents ELEVATE Pivotal Findings Demonstrating Etrasimod's Potentially Best-in-Class Profile in Ulcerative Colitis

SHANGHAI, May 24, 2022 /PRNewswire/ -- Everest Medicines (HKEX 1952.HK) announced today that its licensing partner, Pfizer Inc. (NYSE: PFE) presented at Digestive Disease Week (DDW) 2022 detailed results from two pivotal studies that make up the ELEVATE UC Phase 3 registrational program evaluating etrasimod, a once-daily, oral, selective sphingosine 1-phosphate (S1P) receptor modulator for the treatment of moderately-to-severely active ulcerative colitis (UC).

Both Phase 3, multi-center, randomized, placebo-controlled trials achieved all primary and key secondary endpoints, with etrasimod demonstrating a safety profile consistent with previous studies. In the 52-week ELEVATE UC 52 study, clinical remission was 27.0% for patients receiving etrasimod compared to 7.4% for patients receiving placebo at week 12 (19.8% differential, P=■.001) and was 32.1% compared to 6.7% at week 52 (25.4% differential, P=■.001). In the 12-week ELEVATE UC 12 study, clinical remission was achieved among 24.8% of patients receiving etrasimod compared to 15.2% of patients receiving placebo (9.7% differential, P=.0264).

The 52-week ELEVATE UC 52 trial utilized a treat-through design which closely mimics real-world clinical practice. Statistically significant improvements were attained in all key secondary endpoints in ELEVATE UC 52. These included endoscopic improvement, symptomatic remission, and mucosal healing at weeks 12 and 52, and corticosteroid-free remission and sustained clinical remission at week 52. All key secondary endpoints were also met at week 12 in ELEVATE UC 12. These included endoscopic improvement, symptomatic remission, and mucosal healing.

Treatment-emergent adverse events (AEs), including serious AEs, were similar between treatment groups in both trials. The most common treatment-emergent AEs in 3% or more of etrasimod-treated patients and greater than placebo up to week 52 in either trial were headache, worsening of UC, COVID-19 infection, dizziness, pyrexia, arthralgia, abdominal pain and nausea. There were no reports of bradycardia or atrioventricular block as serious AEs.

Etrasimod was developed by Arena Pharmaceuticals, which has recently been acquired by Pfizer. Everest Medicines obtained exclusive rights from Arena to develop, manufacture and commercialize etrasimod in Greater China and South Korea in 2017. Everest Medicines is conducting a phase 3 study for etrasimod in Asia for the treatment of moderately-to-severely active ulcerative colitis, which is expected to complete enrollment in 2023.

"The detailed results from our partner's ELEVATE UC Phase 3 program further demonstrate etrasimod's potential as a best-in-class therapy," said Kerry Blanchard, MD, PhD, CEO of Everest Medicines. "This adds to our confidence in our Asia clinical trial, where we hope to see similar positive results."

The data from ELEVATE UC 52 & UC 12 are expected to form the basis for planned future regulatory filings, which Pfizer expects to initiate later this year. Additional information about the studies can be found at www.clinicaltrials.gov under the identifiers NCT03945188, NCT03996369, and NCT03950232.

About Etrasimod

Etrasimod is an oral, once-a-day, selective sphingosine 1-phosphate (S1P) receptor modulator designed for optimized pharmacology and engagement of S1P receptors 1, 4, and 5. It is being investigated for a range of immuno-inflammatory diseases, including ulcerative colitis, Crohn's disease, atopic dermatitis, eosinophilic esophagitis, and alopecia areata.

About ELEVATE UC 52 and ELEVATE UC 12

ELEVATE UC 52 and ELEVATE UC 12 are pivotal trials that are part of the ELEVATE UC Phase 3 registrational program.

ELEVATE UC 52 is a randomized, double-blind, placebo-controlled trial that utilized a treat-through design. The primary objective of this trial was to assess the safety and efficacy of etrasimod 2 mg once-daily on clinical remission after both 12 and 52 weeks. All patients that dropped out of the study across either treatment arm over the 52-week study were counted as non-responders. The primary endpoint is based on the 3-domain, modified Mayo score (MMS). Key secondary measures included endoscopic improvement, symptomatic remission, and mucosal healing at weeks 12 and 52, and corticosteroid free remission and sustained clinical remission at week 52.

ELEVATE UC 12 is a randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of etrasimod 2 mg once-daily in subjects with moderately-to-severely active UC. The primary objective of this trial was to assess the safety and efficacy of etrasimod on clinical remission at 12 weeks assessed by the FDA-required, 3-domain, modified Mayo score. Key secondary measures included endoscopic improvement, symptomatic remission, and mucosal healing.

62.6% of etrasimod-treated patients in both trials and 61.8% and 62.9% of placebo-treated patients in ELEVATE UC 52 and ELEVATE UC 12, respectively, were naïve to biologic or JAK inhibitor therapy.

About Ulcerative Colitis

UC is a chronic and often debilitating inflammatory bowel disease[i] that affects many people worldwide, including an estimated 3.8 million people in North America and Europe[ii]. Symptoms of UC can include chronic diarrhea with blood and mucus, abdominal pain and urgency[iii]. UC can have a significant effect on work, family and social activities[iv].

About Everest Medicines

Everest Medicines is a biopharmaceutical company focused on developing and commercializing transformative pharmaceutical products that address critical unmet medical needs for patients in Asian markets. The management team of Everest Medicines has deep expertise and an extensive track record of high-quality clinical development, regulatory affairs, CMC, business development and operations both in China and with leading global pharmaceutical companies. Everest Medicines has built a portfolio of eleven potentially global first-in-class or best-in-class molecules, many of which are in late-stage clinical development. The Company's therapeutic areas of interest include oncology, autoimmune disorders, cardio-renal diseases and infectious diseases. For more information, please visit its website at www.everestmedicines.com .

December 2017

Arena Pharma and Everest Medicines Enter Into Development and Commercialization Partnership for Ralinepag and Etrasimod in China

Arena eligible to receive up to $224M, including upfront and milestone payments, in addition to royalties

SAN DIEGO, Dec. 5, 2017 /PRNewswire/ -- Arena Pharmaceuticals (NASDAQ: ARNA), a biopharmaceutical company focused on developing novel, small molecule drugs across multiple therapeutic areas, and Everest Medicines Limited ("Everest"), a C-Bridge Capital-backed biopharmaceutical company focused on developing and commercializing innovative pharmaceutical products in China, announced today that they have entered into a development and commercialization partnership for ralinepag and etrasimod in mainland China, Taiwan, Hong Kong, Macau, and South Korea (the "Territories"). C-Bridge Capital has invested $50 million to fund Everest and has assembled a veteran leadership team with an established track record in both the development of innovative drugs and commercialization in China and globally to rapidly advance select product candidates towards approval and launch. Everest was founded to leverage the evolving regulatory landscape in China aimed at enhancing the drug approval process related to transformative foreign drugs.

"We are very pleased to establish a partnership with Everest and C-Bridge Capital around two of our potential best-in-class product candidates," said Amit D. Munshi, President and Chief Executive Officer of Arena. "With new regulations in place in China to expedite approvals, a significant opportunity for ralinepag and etrasimod exists in early synchronization of development programs. Based on their development and commercialization expertise, as well as strategy for leveraging changes in the regulatory environment, we view Everest as the ideal partner to maximize the value of our drugs in the rapidly growing Chinese market. Arena and Everest are both committed to ensuring that these products are available to patients in China as expeditiously as possible."

Arena is developing ralinepag, a Phase 3-ready next-generation, oral, selective prostacyclin receptor (IP) agonist for the treatment of pulmonary arterial hypertension (PAH), and etrasimod, a Phase 2 oral, next-generation, S1P receptor modulator, being evaluated for multiple autoimmune diseases, including ulcerative colitis, a form of inflammatory bowel disease.

China is the second largest pharmaceutical market in the world, with healthcare expenditures forecasted to grow rapidly in the coming years (>10% annual growth rate from 2017 to 2025).1

"We are very excited to partner with Arena to bring these two highly differentiated investigational drugs to China. We see great promise in the potential for both ralinepag and etrasimod to address significant unmet medical needs in Greater China and we hope to bring them to patients as quickly as possible," said Sean Cao, President of Everest.

"Our strong belief in Everest's capability to be the partner-of-choice for companies with innovative assets with large commercial potential in China is illustrated by our significant investment in Everest's Series A round," said Fu Wei, Chief Executive Officer of C-Bridge Capital. "Arena's potentially best-in-class programs lay a strong foundation for Everest's growing pipeline."

Under the terms of the agreement, Arena has granted Everest exclusive rights to develop and commercialize ralinepag and etrasimod in the Territories. In return, Arena will receive an upfront payment of $12 million, is eligible to receive up to $212 million in development and commercial milestone payments and is entitled to receive up to low double-digit royalties on net annual sales of both ralinepag and etrasimod.

The parties plan to collaborate on development on both products; however, Everest is generally responsible for funding development and commercialization in the Territories.

About Everest Medicines Everest Medicines is a biopharmaceutical company focused on developing and commercializing transformative pharmaceutical products that address critical unmet medical needs for patients in Greater China. The Everest Medicines team has deep expertise and an extensive track record of high quality clinical development, regulatory affairs, CMC, business development and operations both

in China and for leading global pharmaceutical companies. Everest's $50 million Series A financing was led by C-Bridge Capital. For more information, please visit its website at www.everestmedicines.com.

About C-Bridge Capital C-Bridge Capital is a healthcare dedicated private equity firm, focused on growth and late stage investment opportunities. The firm has over US $800 million of assets under management and a notable limited partner base of family foundations and institutional investors around the globe, such as Pavilion Capital, a subsidiary of Singapore state-owned holding company, Temasek. C-Bridge Capital's current portfolio includes China's leading players in pharmaceuticals, medical devices, diagnostics and healthcare services. C-Bridge Capital is committed to supporting commercialization of innovative technologies and companies that fulfill unmet medical needs, thus continuously improving the standard and quality of care for patients. For more information, please visit its website at www.cbridgecap.com/en.

About Etrasimod Etrasimod (APD334), is an oral, next generation, selective sphingosine 1-phosphate (S1P) receptor modulator, discovered by Arena, designed to provide systemic and local cell modulation by selectively targeting S1P receptor subtypes 1, 4 and 5, while avoiding subtypes 2, 3. Etrasimod exhibits potentially best-in-class pharmacokinetics and pharmacodynamics with rapid onset of action and rapid recovery of T lymphocytes. Selective binding with S1P receptor subtype 1 is believed to inhibit a specific subset of activated lymphocytes from migrating to sites of inflammation. The result is a reduction of circulating T and B lymphocytes that leads to anti-inflammatory activity and immune surveillance is maintained. The receptor subtypes 4, 5 exhibit similar activity on additional proliferating immune cell types. Optimized pharmacology and pharmacokinetics may allow superior clinical utility across a broad range of autoimmune conditions.

Etrasimod is an investigational compound not approved for any use in any country.

About Ralinepag Ralinepag (APD811) is an oral, next-generation, selective prostacyclin receptor agonist intended for the treatment of pulmonary arterial hypertension (PAH). Ralinepag was designed by Arena with the goal of achieving therapeutic activity superior to currently available oral prostacyclin receptor agonists and comparable to parenteral treatment options. In non-clinical experiments, ralinepag demonstrated potentially best-in-class activation of the IP receptor resulting in vasodilation, inhibition of smooth muscle cell proliferation and inhibition of platelet aggregation. Additionally, ralinepag pharmacokinetics in humans revealed an approximately 24-hour half-life and a low peak to trough ratio supporting therapeutic blood levels with once daily (QD) dosing.

Ralinepag is an investigational compound not approved for any use in any country.

About Arena Pharmaceuticals Arena Pharmaceuticals is a biopharmaceutical company focused on developing novel, small molecule drugs with optimized receptor pharmacology designed to deliver broad clinical utility across multiple therapeutic areas. Our proprietary pipeline includes potentially first- or best-in-class programs for which we own global commercial rights. Our three most advanced investigational clinical programs are ralinepag (APD811) which has completed a Phase 2 trial for pulmonary arterial hypertension (PAH), etrasimod (APD334) in Phase 2 evaluation for multiple autoimmune indications, and APD371 in Phase 2 evaluation for the treatment of pain associated with Crohn's disease. In addition, Arena has collaborations with the following pharmaceutical companies: Eisai Co., Ltd. and Eisai Inc. (commercial stage), Axovant Sciences (Phase 2 candidate), and Boehringer Ingelheim International GmbH (preclinical candidate).

Filing Data

In December 2017, we entered into a Collaboration and License Agreement, or the Everest Agreement, with Everest regarding the development and commercialization of ralinepag and etrasimod in China, Taiwan, Hong Kong, Macau and South Korea, or the Everest Territories. In January 2019, we and Everest amended the Everest Agreement by entering into two separate agreements, one for each of ralinepag and etrasimod, with the terms for each program that are substantially the same as in the original Everest Agreement. Under the United Therapeutics Agreement, we assigned the separate Everest Agreement related to ralinepag to United Therapeutics.

Under the separate Everest Agreement related to etrasimod, we granted Everest an exclusive, royalty-bearing license to develop, manufacture and commercialize etrasimod (in oral formulations only), in the Everest Territories.

Everest is responsible for all development, manufacture and commercialization of the licensed products in the Everest Territories, and may participate in the portion of our global clinical trials that is conducted in the Everest Territories.

We are eligible to receive development, regulatory and commercial milestone payments from Everest, as well as tiered royalties on net sales ranging from the high single digits to low double digits. Following an initial royalty term, we are eligible to receive a lower trademark royalty if Everest continues to use our licensed product-related trademarks.

Contract

Not available.