CARVYKTI® (ciltacabtagene autoleucel) Granted Conditional Approval by the European Commission for the Treatment of Patients with Relapsed and Refractory Multiple Myeloma

May 26, 2022

- *CARVYKTI® is Legend Biotech's first European Commission-approved product*
- *The approval is based on the pivotal phase 1b/2 CARTITUDE-1 study, which demonstrated an overall response rate (ORR) of 98 percent in patients with relapsed or refractory multiple myeloma following a one-time treatment with ciltacabtagene autoleucel*

SOMERSET, N.J.--(BUSINESS WIRE)--May 26, 2022-- Legend Biotech Corporation (NASDAQ: LEGN) (Legend Biotech), a global biotechnology company developing, manufacturing and commercializing novel therapies to treat life-threatening diseases, today announced that the European Commission (EC) has granted conditional marketing authorization of CARVYKTI® (ciltacabtagene autoleucel; cilta-cel) for the treatment of adults with relapsed and refractory multiple myeloma (RRMM) who have received at least three prior therapies, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy. Legend Biotech entered into an exclusive worldwide license and collaboration agreement with Janssen Biotech, Inc. (Janssen) to develop and commercialize cilta-cel in December 2017.

CARVYKTI® is a chimeric antigen receptor T-cell (CAR-T) therapy featuring two B-cell maturation antigen (BCMA)-targeting single domain antibodies.[1] CAR-T therapy is specifically developed for each individual patient, and it is administered as a single infusion.[1,2]

"The approval of CARVYKTI® by the European Commission marks Legend's first approval in the region and is a significant milestone as we advance our commitment to bring innovative cell therapies to patients with the highest unmet need," said Ying Huang, Ph.D., Chief Executive Officer of Legend Biotech. "The CARTITUDE-1 data showed that CARVYKTI® provides the potential for long, treatment-free intervals for heavily pre-treated patients, and is a valuable treatment option for patients with multiple myeloma. We look forward to working with Janssen to bring this new option to patients across Europe."

This approval was supported by the pivotal CARTITUDE-1 study, including patients who had received a median of six prior treatment regimens (range, 3-18), and had previously received an IMiD, PI and anti-CD38 monoclonal antibody.[3] Findings showed that at a median duration of 18 months follow-up (range, 1.5-30.5), a one-time treatment with cilta-cel resulted in deep and durable responses, with 98 percent (95 percent confidence interval [CI], 92.7-99.7) of patients with RRMM responding to therapy (98 percent overall response rate [ORR] (N=97)).[3,4] Notably, 80 percent of the patients achieved stringent complete response (sCR), a measure in which a physician is unable to observe any signs or symptoms of disease via imaging or other tests after treatment.[3]

The safety of cilta-cel was evaluated in 179 adult patients across two open-label clinical trials (MMY2001 and MMY2003). The most common adverse reactions (≥20 percent) were neutropenia (91 percent), cytokine release syndrome (CRS) (88 percent), pyrexia (88 percent), thrombocytopenia (73 percent), anemia (72 percent), leukopenia (54 percent), lymphopenia (45 percent), musculoskeletal pain (43 percent), hypotension (41 percent), fatigue (40 percent), transaminase elevation (37 percent), upper respiratory tract infection (32 percent), diarrhea (28 percent), hypocalcemia (27 percent), hypophosphatemia (26 percent), nausea (26 percent), headache (25 percent), cough (25 percent), tachycardia (23 percent), chills (23 percent), encephalopathy (22 percent), decreased appetite (22 percent), oedema (22 percent), and hypokalemia (20 percent).[4]

"There continues to be an unmet need for patients with relapsed or refractory multiple myeloma who have exhausted existing treatment options. Data from the CARTITUDE-1 trial have shown that cilta-cel provides deep and durable responses for heavily pre-treated patients. Today's approval by the European Commission reinforces the potential of this new treatment option for multiple myeloma patients in Europe," said Hermann Einsele, Full Professor of Internal Medicine and Director of the Medizinische Klinik und Poliklinik II of the Julius Maximilian University, Würzburg, Germany.*

As a highly personalized medicine, where a patient's own T-cells are reprogrammed to target and kill cancer cells, administration of CAR-T therapy requires extensive training, preparation, and certification to ensure the highest quality product and experience for patients.[2] Through a phased approach, Legend Biotech's strategic partner, Janssen, will work diligently to activate a limited network of certified treatment centers and will aim to increase availability of cilta-cel across Europe, in an effort to provide oncologists and patients with treatment in a reliable manner.

This EC Marketing Authorization follows the approval of CARVYKTI® by the U.S. Food and Drug Administration (FDA) on February 28, 2022.

*Hermann Einsele, M.D., FRCP has not been paid for contributing to this press release.

About CARVYKTI® (ciltacabtagene autoleucel; cilta-cel)

CARVYKTI® is a BCMA-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T-cells with a transgene encoding a chimeric antigen receptor (CAR) that identifies and eliminates cells that express BCMA.[4] BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B-cells and plasma cells.[4] The CARVYKTI® CAR protein features two BCMA-targeting single domain antibodies designed to confer high avidity against human BCMA.[4] Upon binding to BCMA-expressing cells, the CAR promotes T-cell activation, expansion, and elimination of target cells.[4]

In December 2017, Legend Biotech Corporation entered into an exclusive worldwide license and collaboration agreement with Janssen Biotech, Inc. (Janssen) to develop and commercialize cilta-cel.[5]

In April 2021, Legend announced the submission of a Marketing Authorisation Application to the European Medicines Agency seeking approval of cilta-cel for the treatment of patients with relapsed or refractory multiple myeloma. In addition to U.S. Breakthrough Therapy Designation granted in December 2019, cilta-cel also received Breakthrough Therapy Designation in China in August 2020. In February 2019, cilta-cel received Orphan Drug Designation from the U.S. FDA from the European Commission in February 2020, and from the Pharmaceuticals and Medicinal Devices Agency (PMDA) in Japan in June 2020. In May 2022, the Committee for Orphan Medicinal Products recommended by consensus that the orphan designation for cilta-cel be maintained, on the basis of clinical data demonstrating improved and sustained complete response rates following treatment.[6] Cilta-cel was approved the U.S. Food and Drug Administration (FDA) in February 2022.[5]

About CARTITUDE-1

CARTITUDE-1 (NCT03548207)[7] is an ongoing Phase 1b/2, open-label, single arm, multi-center trial evaluating cilta-cel for the treatment of adult patients with relapsed or refractory multiple myeloma, who previously received at least three prior lines of therapy including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 monoclonal antibody. Of the 97 patients enrolled in the trial, 99 percent were refractory to the last line of treatment and 88 percent were triple-class refractory, meaning their cancer did not respond, or no longer responds, to an IMiD, a PI and an anti-CD38 monoclonal antibody.[4]

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that starts in the bone marrow and is characterized by an excessive proliferation of plasma cells.[8] In Europe, it is estimated that more than 50,900 people were diagnosed with multiple myeloma in 2020, and approximately 32,500 patients died.[9] While some patients with multiple myeloma have no symptoms at all, most patients are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[10] Although treatment may result in remission, unfortunately, patients will most likely relapse.[11] Patients who relapse after treatment with standard therapies, including protease inhibitors, immunomodulatory agents, and an anti-CD38 monoclonal antibody, have poor prognoses and few treatment options available.[12,13]

About Legend Biotech

Legend Biotech is a global biotechnology company dedicated to treating, and one day curing, life-threatening diseases. Headquartered in Somerset, New Jersey, we are developing advanced cell therapies across a diverse array of technology platforms, including autologous and allogenic chimeric antigen receptor T-cell, T-cell receptor (TCR-T), and natural killer (NK) cell-based immunotherapy. From our three R&D sites around the world, we apply these innovative technologies to pursue the discovery of safe, efficacious and cutting-edge therapeutics for patients worldwide.

Learn more at www.legendbiotech.com and follow us on Twitter and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

Statements in this press release about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, constitute “forward-looking statements” within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements relating to Legend Biotech’s strategies and objectives; statements relating to CARVYKTI™, including Legend Biotech’s expectations for CARVYKTI™, such as Legend Biotech’s manufacturing and commercialization expectations for CARVYKTI™ and the potential effect of treatment with CARVYKTI™; statements about submissions for cilta-cel to, and the progress of such submissions with, theU.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), the Chinese Center for Drug Evaluation of National Medical Products Administration (CDE) and other regulatory authorities; the anticipated timing of, and ability to progress, clinical trials, including patient enrollment; the submission of Investigational New Drug (IND) applications to, and maintenance of such applications with, regulatory authorities; the ability to generate, analyze and present data from clinical trials; and the potential benefits of Legend Biotech’s product candidates. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. Legend Biotech’s expectations could be affected by, among other things, uncertainties involved in the development of new pharmaceutical products; unexpected clinical trial results, including as a result of additional analysis of existing clinical data or unexpected new clinical data; unexpected regulatory actions or delays, including requests for additional safety and/or efficacy data or analysis of data, or government regulation generally; unexpected delays as a result of actions undertaken, or failures to act, by our third party partners; uncertainties arising from challenges to Legend Biotech’s patent or other proprietary intellectual property protection, including the uncertainties involved in the U.S. litigation process; competition in general; government, industry, and general public pricing and other political pressures; the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation; as well as the other factors discussed in the “Risk Factors” section of the Legend Biotech’s Annual Report filed with the Securities and Exchange Commission on March 31, 2022. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described in this press release as anticipated, believed, estimated or expected. Any forward-looking statements contained in this press release speak only as of the date of this press release.Legend Biotech specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

References

---

[1] Martin, T. Updated Results From CARTITUDE-1: Phase 1b/2 Study of Ciltacabtagene Autoleucel, a B-cell Maturation Antigen–Directed Chimeric Antigen Receptor T Cell Therapy, in Patients with Relapsed/Refractory Multiple Myeloma. Abstract #549 [Oral]. Presented at the 2021 American Society of Hematology (ASH) Annual Meeting & Exposition Annual Meeting.

[2] NHS. CAR-T Therapy. https://www.england.nhs.uk/cancer/cdf/car-t-therapy/. Accessed May 2022.

[3] Usmani, S. Ciltacabtagene autoleucel, a B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T-cell (CAR-T) therapy, in relapsed/refractory multiple myeloma (R/R MM): Updated results from CARTITUDE-1. Abstract #8005 [Oral]. Presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting.

[4] European Medicines Agency. CARVYKTI (Ciltacabtagene Autoleucel) Summary of Product Characteristics. May 2022.

[5] CARVYKTI™ (ciltacabtagene autoleucel), BCMA-Directed CAR-T Therapy, Receives U.S. FDA Approval for the Treatment of Adult Patients with Relapsed or Refractory Multiple Myeloma. Available at: https://legendbiotech.com/wp-content/uploads/2022/02/CARVYKTI%E2%84%A2-ciltacabtagene-autoleucel-BCMA-Directed-CAR-T-Therapy-Receives-U.S.-FDA-Approval-2.pdf. Accessed May 2022.

[6] European Commission. Community Register of Orphan Medicinal Products. Available at: https://ec.europa.eu/health/documents/community-register/html/o2252.htm. Accessed May 2022.

[7] ClinicalTrials.gov. A Study of JNJ-68284528, a Chimeric Antigen Receptor T Cell (CAR-T) Therapy Directed Against B-Cell Maturation Antigen (BCMA) in Participants with Relapsed or Refractory Multiple Myeloma (CARTITUDE-1). Available at: https://clinicaltrials.gov/ct2/show/NCT03548207. Accessed May 2022.

[8] American Society of Clinical Oncology. Multiple myeloma: introduction. Available at: https://www.cancer.net/cancer-types/multiple-myeloma/introduction. Accessed May 2022.

[9] GLOBOCAN 2020. Cancer Today Population Factsheets: Europe Region. Available at: https://gco.iarc.fr/today/data/factsheets/populations/908-europe-fact-sheets.pdf. Accessed May 2022.

[10] American Cancer Society. Multiple myeloma: early detection, diagnosis and staging. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8740.00.pdf. Accessed May 2022.

[11] Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. Am J Hematol. 2020;95(5),548-567. doi:10.1002/ajh.25791.

[12] Kumar SK, Dimopoulos MA, Kastritis E, et al. Natural history of relapsed myeloma, refractory to immunomodulatory drugs and proteasome inhibitors: a multicenter IMWG study. Leukemia. 2017;31(11):2443- 2448.

[13] Gandhi UH, Cornell RF, Lakshman A, et al. Outcomes of patients with multiple myeloma refractory to CD38- targeted monoclonal antibody therapy. Leukemia. 2019;33(9):2266-2275.

View source version on businesswire.com: https://www.businesswire.com/news/home/20220525005944/en/

Investor Contacts:
Joanne Choi, Senior Manager of Investor Relations, Legend Biotech
joanne.choi@legendbiotech.com

Crystal Chen, Manager of Investor Relations, Legend Biotech
crystal.chen@legendbiotech.com

Press Contact:
Tina Carter, Corporate Communications Lead, Legend Biotech
tina.carter@legendbiotech.com
(908) 331-5025

Source: Legend Biotech