REGULATORY NEWS – 26th JANUARY 2022

FDA Accepts for Review Libtayo® (cemiplimab-rwlc) in Combination with Chemotherapy for 1L Treatment of Advanced NSCLC

- FDA accepted for review the supplemental Biologics License Application (sBLA) for PD-1 inhibitor Libtayo® (cemiplimab-rwlc) in combination with chemotherapy as first-line treatment in advanced NSCLC.
- The target action date for the FDA decision is September 19, 2022.
- The sBLA is supported by results from a randomized, multicenter Phase 3 trial that investigated Libtayo in combination with a physician's choice of platinum-doublet chemotherapy (Libtayo combination), compared to platinum-doublet chemotherapy alone.
- Enrolled patients (n=466) had locally advanced or metastatic NSCLC, irrespective of PD-L1 expression level or tumor histology, and with no ALK, EGFR or ROS1 aberrations.
- A regulatory filing has also been recently submitted to the European Medicines Agency.
- The Phase 3 trial supporting the sBLA was stopped early after the Libtayo combination demonstrated a significant overall survival improvement compared to chemotherapy alone.

Voluntarily withdrawal of the use of Zydelig for follicular lymphoma and small lymphocytic leukemia

- In 2014, Zydelig® (idelalisib) received accelerated approval from the U.S. Food and Drug Administration (FDA) to treat relapsed follicular B-cell non-Hodgkin lymphoma (FL) and relapsed small lymphocytic leukemia (SLL). Approval was based on a Phase 2 study in indolent non-Hodgkin lymphoma showing that 54% of those with FL and 58% of those with SLL had an objective response as assessed by an Independent Review Committee.
- Continued approval for these indications was contingent upon providing evidence supporting confirmation of clinical benefit in FL and SLL. With an evolved treatment landscape for FL and SLL, enrollment into the confirmatory study has been an ongoing challenge. As a result, Gilead formally notified the FDA of its decision to voluntarily withdraw these indications from the U.S. market.
- Zydelig was also approved in 2014 to treat relapsed CLL in the U.S. Additionally, Zydelig has marketing authorization to treat CLL and FL in the EU, UK, Canada, Australia, New Zealand and Switzerland. None of these approvals are affected by the proposed withdrawal. Thus, Zydelig will remain on the market in the U.S. for CLL and for CLL and FL in the EU, UK, Canada, Australia, New Zealand, and Switzerland.
- Gilead continues to work collaboratively with the FDA to complete the withdrawal of the FL and SLL indications in the U.S. and with healthcare professionals to support those currently being treated with Zydelig. People receiving Zydelig for relapsed FL or SLL in the U.S. should discuss their treatment options with their healthcare provider.

Supplemental New Drug Application accepted in China for BRUKINSA (zanubrutinib) in Waldenström's Macroglobulinemia

"The sNDA acceptance is welcoming news, and following BRUKINSA's recent NMPA approval for patients with WM in the relapsed or refractory setting, this represents an opportunity to expand access to more WM patients in China, subject to NMPA approval. As demonstrated in the ASPEN trial, BRUKINSA can offer an efficacious treatment option with improved safety in regard to certain

cardiovascular events, such as atrial fibrillation, for patients with WM," commented Jane Huang, M.D., Chief Medical Officer, Hematology, BeiGene. "The ASPEN trial has supported BRUKINSA's approval for patients with WM in the U.S., Canada, Australia, and the European Union. We look forward to continued discussions with the CDE and the opportunity to bring this potential best-in-class therapy to more people in the WM community in China."

Silmitasertib Receives US FDA Orphan Drug Designation for the Treatment of Biliary Tract Cancer

"We are pleased to receive ODD for Silmitasertib for the treatment of Biliary Tract Cancer, a rare, malignant disease for which there are no effective therapies. ODD represents an important regulatory milestone that has the potential to expedite the clinical development of Silmitasertib, which is a potent and selective CK2 inhibitor," said Mei-Hui Kuo, Acting Chief Executive Officer of Senhwa Biosciences.

AO-176, a Next-Generation Anti-CD47 IgG2 Antibody, Receives U.S. FDA Orphan Drug Designation for the Treatment of Multiple Myeloma

"Multiple myeloma is a type of hematological cancer affecting about 35,000 individuals each year in the US. There is currently no cure for multiple myeloma, and while first-line treatment may result in remission, there remains a significant unmet need for patients with r/r MM," said Amit Agarwal, M.D., Ph.D., Senior Vice President of Clinical Development at Arch Oncology. "We believe the multiple unique properties of AO-176, including lower binding to normal cells and negligible binding to red blood cells, enhanced binding to CD47 in acidic environments found in tumors, and induction of programmed and immunogenic cell death, in addition to strong preclinical data in multiple myeloma, could make AO-176 a promising new first-in-class therapeutic approach to improving outcomes for these patients.

Gedatolisib Receives FDA Fast Track Designation in HR+ / HER2- Metastatic Breast Cancer

"There is an urgent need for better treatment options for HR+/HER2- metastatic breast cancer patients whose disease progressed after treatment with a CDK4/6 inhibitor and endocrine therapy," said Brian Sullivan, CEO and co-founder of Celcuity. "We are very encouraged by the clinical data for gedatolisib and believe that Fast Track designation will facilitate our efforts to advance its development for patients as quickly as possible."

Enhertu granted Priority Review in the US for patients with HER2-positive metastatic breast cancer treated with a prior anti-HER2-based regimen

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca said: "This review across geographies and the Priority Review in the US as part of Project Orbis is so important because it speaks to the transformative potential of Enhertu based on the unprecedented progression-free survival benefit in this setting. The news reinforces the importance of bringing this potential new option to patients as quickly as possible."