ROTTAPHARM BIOTECH

PRESS RELEASE

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Rottapharm Biotech discloses at ESMO 2023 favourable results from the Phase 1/2 study of the EP4 receptor antagonist CR6086 combined with the anti-PD-1 balstilimab in advanced colorectal cancer

Monza (Italy) – Rottapharm Biotech announces favourable clinical results of CR6086, its potent and selective small molecule antagonist of the prostaglandin EP4 receptor, combined with the anti PD-1 antibody balstilimab (Agenus Inc, Nasdaq: AGEN) in advanced colorectal cancer (CRC). Study results have been presented at the European Society for Medical Oncology (ESMO) annual congress in Madrid, Spain, held from October 20-24, 2023.

Patients with CRC have limited treatment options, given the aggressive behaviour of their tumours. In fact, more than 80% of CRC is classified as mismatch-repair-proficient (pMMR) and microsatellite stable (MSS), which correlates with low tumour mutation burden and poor immune cell infiltration in the tumour microenvironment (TME), and they are therefore classified as immunologically "cold" tumors. These patients generally do not benefit from Immune Checkpoint Inhibitors (ICIs) and combination strategies are needed to address immunosuppression in the TME and improve sensitivity to ICIs.

The involvement of prostaglandin E2 (PGE2) in cancerogenesis has been known for decades. "PGE2, through its EP4 receptor, is a major contributor to immunosuppression in the TME and blockade of this pathway may sensitize cold tumors to ICIs." said Dr. Lucio Rovati, CEO and CSO at Rottapharm Biotech.

"CR6086 is designed to increase the activity and infiltration of several different immune cell types while reversing the immunosuppressive role of PGE2 in the TME. CR6086 is a potential best-in-class EP4 receptor antagonist and has demonstrated a strong safety profile in >250 subjects treated to date." added Dr. Lucio Rovati.

The Phase 1/2 clinical study, conducted at the National Cancer Institute (Istituto Nazionale dei Tumori) in Milan (Italy), evaluated the safety and efficacy of CR6086 combined with balstilimab in 28 patients with advanced pMMR/MSS metastatic CRC.

- The trial met the designated primary endpoint, with a disease control rate (DCR) of 50% associated with good safety.
- A DCR of 25% was observed in the difficult to treat subgroup of patients with liver metastases.
- The overall objective response rate (ORR) was 11%, with 3 patients having partial response (PR): one durable PR is ongoing (>1 year) in a patient with liver metastases.
- Disease control for all the 11 patients with stable disease lasted ≥ 12 weeks, and for 5 patients lasted ≥ 24 weeks.
- At a median follow-up of 8 months, the median progression-free survival (PFS) and overall survival (OS) were 2.6 months (CI 95% 1.7-3.6) and 13.7 months (CI 95% 8.8-not reached), respectively.
- A study expansion in other gastrointestinal tumors is ongoing.

“Given the promising results, we are committed to progress CR6086 development in a randomized Phase 2 study in pMMR/MSS metastatic CRC and we look forward to advancing discussions with potential partners” concluded Dr. Lucio Rovati.
The poster presented at the ESMO 2023 congress is available here.

Rottapharm Biotech

Rottapharm Biotech is a research company dedicated to the discovery and development of innovative drugs. It is located in Monza (Italy). The company expertise in research and development includes medicinal/computational chemistry for small molecules, development of biologics and advanced therapies, new targets validation, pharmacological and pharmacokinetic characterization of new drug candidates, original formulations, and design of innovative clinical trials. The company strategy is to develop its own pipeline independently and then seek partnerships with pharmaceutical companies, as well as investing in alliances on innovative projects of other biotech companies or university spin-offs.

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About Agenus

Agenus is a leading immuno-oncology company targeting cancer and infectious diseases with a comprehensive pipeline of immunological agents. The company's mission is to expand patient populations benefiting from cancer immunotherapy through combination approaches, using a broad repertoire of antibody therapeutics, adoptive cell therapies (through MiNK Therapeutics) and adjuvants (through SaponiQx). Agenus is headquartered in Lexington, MA. For more information, visit www.agenusbio.com or @agenus_bio. Information that may be important to investors will be routinely posted on our website and social media channels.

About balstilimab

Balstilimab (Agenus, Inc.) is an investigational monoclonal antibody inhibitor of programmed cell death 1 (PD-1) protein. It has been evaluated in >900 patients to date and has demonstrated strong clinical activity and an excellent safety profile in several tumour types.

Agenus Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding clinical development and regulatory plans and timelines, anticipated corporate milestones, new clinical data and program updates to be presented. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially. These risks and uncertainties include, among others, the factors described under the Risk Factors section of our most recent Quarterly Report on Form 10-Q or Annual Report on Form 10-K filed with the Securities and Exchange Commission. Agenus cautions investors not to place considerable reliance on the forward-looking statements contained in this release. These statements speak only as of the date of this press release, and Agenus undertakes no obligation to update or revise the statements, other than to the extent required by law. All forward-looking statements are expressly qualified in their entirety by this cautionary statement.

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