Novartis Shows Growing Strength in Lung Cancer Innovation with New Capmatinib Investigational Data and Novel Canakinumab Clinical Trials

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- - Primary analysis of investigational capmatinib (INC280) in the GEOMETRY mono-1 study demonstrates promising efficacy in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring MET exon-14 skipping mutation
- - Overall response rate among patients receiving capmatinib was 68% for treatment-naive and 41% for previously treated patients; median duration of response was also clinically meaningful irrespective of prior line of therapy
- - The U.S. Food and Drug Administration (FDA) recently granted capmatinib Breakthrough Therapy Designation for the treatment of patients with metastatic NSCLC harboring MET exon-14 skipping mutation with disease progression on or after platinum-based chemotherapy; discussions with global health authorities are underway
- - Additional Novartis lung cancer research presented at the American Society of Clinical Oncology (ASCO) 2019 Annual Meeting include Phase III CANOPY clinical trial designs, evaluating canakinumab (ACZ885) monotherapy in patients with mid- to late-stage NSCLC

BASEL, Switzerland, June 3, 2019 /PRNewswire/ -- Novartis announced today new data and clinical trial updates in NSCLC at the ASCO 2019 Annual Meeting. This includes primary efficacy results from the GEOMETRY mono-1 Phase II clinical trial demonstrating that investigational MET inhibitor capmatinib (INC280) shows promise as a potential treatment option for patients with locally advanced or metastatic NSCLC that harbor MET exon-14 skipping mutation. There are currently no approved targeted therapies to treat this particularly aggressive form of NSCLC. Results of the Phase II study will be presented at an oral session today at ASCO, June 3, 2019, at 8:00 a.m. CDT (Abstract #9004)[1].

GEOMETRY mono-1 is an international, prospective, multi-cohort, non-randomized, open-label study evaluating 97 adult patients with locally advanced or metastatic NSCLC harboring MET exon-14 skipping mutation who received capmatinib tablets 400 mg orally twice daily. Primary efficacy results among treatment-naive patients (Cohort 5b: 28 patients) were a 68% overall response rate (ORR) based on the Blinded Independent Review Committee (BIRC) assessment per RECIST v1.1 (95% CI: (47.6 - 84.1)). Forty-one percent of previously treated NSCLC patients (Cohort 4: 69 patients) also responded (95% CI: (28.9 - 53.1)). Data on median duration of response (DOR), a key secondary endpoint, was 11.14 months (95% CI: (5.55 - NE)) and 9.72 months (95% CI: (5.55 - 12.98)), respectively. Intracranial activity in 54% (n=7/13) of patients, including some cases of complete resolution of brain lesions, was also observed by ad hoc neuro-radiologist review in patients with brain lesions. All results were based on independent assessment by the BIRC, and all tumor CT scans were evaluated in parallel by two radiologists to confirm the response.

The most common treatment related adverse events (AE) (≥10% all grades) across all cohorts (n=334), were peripheral edema (42%), nausea (33%), creatinine increase (20%), vomiting (19%), fatigue (14%), decreased appetite (13%) and diarrhea (11%); the majority of the AEs were grades 1/2.

"New lung cancer treatment options are critical, as this deadly disease affects more than 2 million new patients

around the world each year," said John Tsai, MD, Head of Global Drug Development and Chief Medical Officer, Novartis. "The GEOMETRY mono-1 results are encouraging, and we look forward to discussing these results with health authorities with the hope of bringing this targeted treatment option to people with this aggressive type of lung cancer."

Capmatinib Granted Orphan Drug and Breakthrough Therapy Designation Status

The U.S. Food and Drug Administration recently granted capmatinib Breakthrough Therapy Designation for patients with metastatic NSCLC harboring MET exon-14 skipping mutation with disease progression on or after platinum-based chemotherapy. Previously, both the U.S. FDA and Japan's Pharmaceuticals and Medical Devices Agency recognized capmatinib with Orphan Drug status. It is estimated that 3% to 4% of all patients with NSCLC have an identified MET mutation[3].

"The efficacy observed with capmatinib in the GEOMETRY mono-1 trial is promising," said Juergen Wolf, MD, University Hospital, Cologne. "In addition to positive overall response rate among first-line patients with the MET mutation, the duration for the responses, including the activity in the brain, and capmatinib's safety profile are important milestones for this patient population. As a group, patients with MET mutated NSCLC often require special clinical considerations, as they are generally older and with poor prognosis further limiting their treatment options."

About GEOMETRY mono-1

GEOMETRY mono-1 is an international, prospective, multi-cohort, non-randomized, open-label Phase II study to evaluate the efficacy and safety of single-agent capmatinib (INC280) in adult patients with EGFR wildtype, ALK-negative rearrangement, advanced NSCLC harboring MET amplification and/or mutations. Patients with locally advanced or metastatic NSCLC harboring MET exon-14 skipping mutation (centrally confirmed) were assigned to Cohorts 4 (previously treated patients) or 5B (treatment-naive), regardless of MET amplification/gene copy number, and received 400 mg capmatinib tablets orally twice daily. The primary endpoint was ORR based on the BIRC assessment per RECIST v1.1. The key secondary endpoint was duration of response (DOR) by the BIRC. The GEOMETRY mono-1 study found an ORR in the treatment-naive patients (n=28) of 67.9% (95% CI: 47.6 - 84.1) and an ORR of 40.6% (95% CI: 28.9 - 53.1) in the previously treated patients (n=69). Median DOR was 11.14 months (95% CI: 5.55-NE) in treatment-naive patients and 9.72 months (95% CI: 5.55-12.98) in previously treated patients[1].

The most common treatment-related AEs included peripheral edema, nausea, creatinine increase and vomiting. Of patients treated with capmatinib, 84% experienced an AE, with 36% having grade 3/4 AEs (only 4.5% were Grade 4)[1].

Capmatinib (INC280) is an investigational, oral and selective MET inhibitor licensed to Novartis by Incyte Corporation in 2009. Under the Agreement, Incyte granted Novartis worldwide exclusive development and commercialization rights to capmatinib and certain back-up compounds in all indications.

Studying Tumor-Promoting Inflammation in Lung Cancer – Ongoing CANOPY Trials

Trials in Progress (TiP) updates on the CANOPY clinical program were also included in the ASCO updates. CANOPY is made up of three randomized, double-blind and placebo-controlled Phase III trials evaluating canakinumab (ACZ885), a selective IL-1β inhibitor (Abstract #TPS9124)[4,5].

- CANOPY-A is a Phase III multicenter, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of canakinumab as adjuvant therapy in adult subjects with stages II-IIIA and NSCLC following complete surgical resection. The primary endpoint is disease-free survival (Abstract #7013).
- CANOPY-1 is a randomized, double-blind, placebo-controlled, Phase III study investigating canakinumab versus placebo in combination with platinum-based chemotherapy (CTx) and pembrolizumab in

previously untreated patients with stage IIIB/IIC-IV squamous and non-squamous NSCLC. The study will evaluate the incidence of dose-limiting toxicity (DLT) in the first 42 days of treatment, as well as PFS and overall survival (OS).
- CANOPY-2 is a randomized, double-blind, placebo-controlled, Phase III study investigating canakinumab or placebo plus docetaxel in stage IIIB-IV NSCLC patients previously treated with PD-1 or PD-L1 inhibitors, as well as CTx. The primary endpoints are incidence of DLT in the first 42 days of treatment and OS.

Novartis Commitment to Lung Cancer

Worldwide, lung cancer causes more deaths than colon, breast and prostate cancer combined, and more than 2 million new cases of lung cancer are diagnosed each year[2]. Despite treatment advances, patients with NSCLC still have a poor prognosis and limited treatment options. This includes the nearly 70% of NSCLC patients who have a genomic mutation that may be targeted with available therapies[6]. To determine the most appropriate treatment, medical organizations recommend genomic testing for patients with lung cancer[7].

Novartis Oncology's research has helped transform treatment approaches for patients living with NSCLC. Novartis continues its commitment to the global lung cancer community through ongoing studies, as well as the exploration of investigational compounds in NSCLC, including those that target genetic biomarkers and tumor promoting inflammation.

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Novartis is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of

great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach more than 750 million people globally, and we are finding innovative ways to expand access to our latest treatments. About 105,000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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