

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

Jun 03, 2019

- - 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) ($\geq 10\%$ 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 mutation³.

"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 patients¹.

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-1 β 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/IIIC-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 year². 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 therapies⁶. To determine the most appropriate treatment, medical organizations recommend genomic testing for patients with lung cancer⁷.

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.

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch" or similar terms or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches; or disruptions of our information technology systems and other risks and factors referred to in Novartis AG's current Form 20-F on file with the U.S. Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

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.

Novartis is on Twitter. Sign up to follow @Novartis at <http://twitter.com/novartis>

For Novartis multimedia content, please visit www.novartis.com/news/media-library

For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Juergen Wolf. Capmatinib (INC280) in MET Δ ex14-mutated advanced non-small cell lung cancer (NSCLC): efficacy data from the Phase II GEOMETRY mono-1 study. Abstract #9004. 2019 American Society of Clinical Oncology Annual Meeting (ASCO), May 31-June 4, 2019, Chicago, IL.
2. Globocan. Lung Fact Sheet. Available at <http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf>. Accessed October 9, 2018.
3. Salgia R. MET in Lung Cancer: Biomarker Selection Based on Scientific Rationale. Mol Cancer Ther. 2017;16(4):555-565.
4. Luis Paz-Ares. The CANOPY Program: Canakinumab in Patients (pts) With Non-Small Cell Lung Cancer (NSCLC). Abstract #TPS9124. 2019 American Society of Clinical Oncology Annual Meeting (ASCO), May 31-June 4, 2019, Chicago, IL.
5. Edward B. Garon. CANOPY-A: A phase III study of canakinumab as adjuvant therapy in patients with surgically resected non-small cell lung cancer (NSCLC). Abstract #TPS8570. 2019 American Society of Clinical Oncology Annual Meeting (ASCO), May 31-June 4, 2019, Chicago, IL.
6. Hirsch FR, Suda K, Wiens J, et al. New and emerging targeted treatments in advanced non-small-cell lung cancer. Lancet. 2016;388:1012-1024.
7. Lindeman NI, Cagle PT, Beasley MB, et al. Molecular Testing Guideline for Selection of Lung Cancer Patients for EGFR and ALK Tyrosine Kinase Inhibitors. J Thorac Oncol. 2013;8(7):823-859.

Novartis Media Relations

E-mail: media.relations@novartis.com

Antonio Ligi

Novartis Global Media Relations

+41 61 324 1374 (direct)

+41 79 723 3681 (mobile)

antonio.ligi@novartis.com

Mary Curtin Creaser

Novartis Oncology Communications

+1 862 778 2550 (direct)

+1 862 345 4102 (mobile)

Mary.Curtin_Creaser@novartis.com

Eric Althoff

Novartis US External Communications

+1 646 438 4335

eric.althoff@novartis.com

Novartis Investor Relations

Central investor relations line: +41 61 324 7944

E-mail: investor.relations@novartis.com

Central

North America

Samir Shah

+41 61 324 7944

Richard Pulik

+1 212 830 2448

Pierre-Michel Bringer

+41 61 324 1065

Cory Twining

+1 212 830 2417

Thomas Hungerbuehler

+41 61 324 8425

Isabella Zinck

+41 61 324 7188

SOURCE Novartis Pharmaceuticals Corporation

Source URL: <https://qa1.novartis.us/news/media-releases/novartis-shows-growing-strength-lung-cancer-innovation-new-capmatinib-investigational-data-and-novel-canakinumab-clinical-trials>

1. <https://qa1.novartis.us/news/media-releases/novartis-shows-growing-strength-lung-cancer-innovation-new-capmatinib-investigational-data-and-novel-canakinumab-clinical-trials>
2. <https://c212.net/c/link/?t=0&l=en&o=2484473-1&h=2415010524&u=http%3A//www.novartis.com/&a=www.novartis.com>
3. <https://c212.net/c/link/?t=0&l=en&o=2484473-1&h=2406230774&u=http%3A//twitter.com/novartis&a=http%3A//twitter.com/novartis>
4. <https://c212.net/c/link/?t=0&l=en&o=2484473-1&h=2600744377&u=http%3A//www.novartis.com/news/media-library&a=www.novartis.com/news/media-library>
5. <mailto:media.relations@novartis.com>
6. <http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf>
7. <mailto:media.relations@novartis.com>
8. <mailto:antonio.ligi@novartis.com>
9. mailto:Mary.Curtin_Creaser@novartis.com
10. <mailto:eric.althoff@novartis.com>
11. <mailto:investor.relations@novartis.com>