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POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Safety and Efficacy of Bezuclastinib (CGT9486), a Novel, Highly Selective, Potent KIT D816V Tyrosine Kinase Inhibitor, in Patients with Advanced Systemic Mastocytosis (AdvSM): Results from Part 1 of the Phase 2 Apex Trial

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Background: Systemic mastocytosis (SM) is a rare disease characterized by the aberrant proliferation of mast cells (MC). In about 95% of adult patients, SM is driven by a gain-of-function mutation (D816V) in exon 17 of *KIT*. Advanced SM (AdvSM) is a life-threatening form of SM and includes three subtypes: aggressive SM (ASM), SM with an associated hematologic neoplasm (SM-AHN), and Mast Cell leukemia (MCL). Bezuclastinib is an oral, potent, and selective tyrosine kinase inhibitor (TKI) with activity against KIT D816V. Preliminary results from the on-going Apex study in patients with AdvSM (NCT04996875) were presented previously (DeAngelo et al. [abstract] In: Blood (ASH) 2022; 140 (Supplement 1): 1512-13).
Methods: Apex is a randomized Phase 2, open-label, multicenter trial in adult patients diagnosed with AdvSM per 2022 WHO criteria with a baseline serum tryptase of ≥20 ng/mL. In Part 1, patients were randomized 1:1:1:1 to bezuclastinib 50mg BID, 100mg BID, 200mg BID, or 400mg QD. Patients with a history of prior TKI therapy (e.g., avapritinib, midostaurin) are permitted in the trial. Data from Part 1 informed dose selection for Part 2 of the trial. The primary efficacy endpoint for this trial is overall response rate (complete response [CR], CR with incomplete hematologic recovery [CRh], partial response [PR] and clinical improvement [CI]) as assessed by a central review committee based on mIWG-MRT-ECNM response criteria.
Results: As of April 2023, Part 1 was fully enrolled with 33 AdvSM patients. Patients were randomized to 50mg BID (n=8), 100mg BID (n=8), 200mg BID (n=8), or 400mg QD (n=9). Disease subtypes included ASM (n=7), MCL (n=2), and SM-AHN (n=24); AHN subtypes included CMML (n=18), MDS (n=3), MPN (n=1), and MDS/MPN-U (n=2). The majority of patients were male (64%), ECOG PS 0-1 (82%) and KITD816V positive at baseline (91%). At baseline, 67% of patients were TKI-naïve; 33% had prior midostaurin, and 15% had prior avapritinib. Median (range) BM MC burden, serum tryptase, and KIT D816V VAF at baseline were 30% (5-90), 163 ng/mL (35-1578), and 7% (0-47), respectively. Of the 33 patients enrolled, 25 patients (76%) had C-findings evaluable per mIWG-MRT-ECNM criteria; 20 patients (61%) were positive for SRSF2/ASXL1/RUNX1 mutation which are associated with poor survival in SM.

Conclusion: Enrollment in Part 1 of the Apex trial is complete. Patients enrolled in Part 1 of the Apex trial are generally representative of the population of patients with AdvSM based on patient characteristics and markers of disease. Part 1 includes a small subset of patients with prior use of TKIs. Safety, clinical activity, and clinical objective response for all patients in Part 1 will be presented.

Disclosures Vachhani: *LAVA therapeutics:* Consultancy; *MorphoSys:* Consultancy; *Stemline:* Consultancy; *Servier:* Consultancy; *Genentech:* Consultancy; *Pfizer:* Consultancy; *Novartis:* Consultancy; *Karyopharm:* Consultancy; *GlaxoSmith Kline:* Consultancy; *Daiichi Sankyo:* Consultancy; *CTI BioPharma Corp:* Consultancy, Speakers Bureau; *Incyte:* Consultancy, Speakers Bureau; *Cogent Biosciences:* Consultancy; *Blueprint Medicines:* Consultancy, Speakers Bureau; *Amgen:* Consultancy; *AbbVie:* Consultancy. **Tashi:** *Cogent:* Membership on an entity's Board of Directors or advisory committees; *PharmaEssentia:* Membership on an entity's Board of Directors or advisory committees; *Blueprint:* Membership on an entity's Board of Directors or advisory committees. **Schiller:** *ElevateBio:* Research Funding; *Agios:* Research Funding; *Trovagene:* Research Funding; *Tolero Pharmaceuticals:* Research Funding; *Takeda:* Research Funding; *Stemline Therapeutics:* Research Funding; *Sellas Life Sciences:* Research Funding; *Sangamo Bioscience:* Research Funding; *Samus Therapeutics:* Research Funding; *REGiMMUNE:* Research Funding; *Precog:* Research Funding; *Pfizer:* Research Funding; *Onconova Therapeutics:* Research Funding; *Mateon Therapeutics:* Research Funding; *Geron:* Research Funding; *Genentech/Roche:* Research Funding; *Gamida Cell:* Research Funding; *Fujifilm:* Research Funding; *FORMA Therapeutics:* Research Funding; *Delta-Fly Pharma:* Research Funding; *Deciphera:* Research Funding; *Daiichi Sankyo:* Research Funding; *Constellation Pharmaceuticals:* Research Funding; *Celator:* Research Funding; *Arog:* Research Funding; *Actuate Therapeutics:* Research Funding; *Actinium Pharmaceuticals:* Research Funding; *Karyopharm Therapeutics:* Research Funding, Speakers Bureau; *Sanofi:* Research Funding, Speakers Bureau; *Stemline Therapeutics:* Speakers Bureau; *Kite:* Research Funding, Speakers Bureau; *Astellas Pharma:* Consultancy, Research Funding, Speakers Bureau; *AbbVie:* Consultancy, Research Funding, Speakers Bureau; *Novartis:* Consultancy, Research Funding; *Jazz Pharmaceuticals:* Consultancy, Research Funding, Speakers Bureau; *Incyte:* Consultancy, Research Funding, Speakers Bureau; *Celgene:* Consultancy, Research Funding; *Agios:* Consultancy; *Ono Pharmaceutical:* Consultancy; *Ono Pharmaceutical:* Research Funding; *AVM Biotechnology:* Research Funding; *Syros Pharmaceuticals:* Research Funding; *Kronos Bio:* Research Funding; *Johnson & Johnson:* Current equity holder in publicly-traded company; *Amgen:* Current equity holder in publicly-traded company, Research Funding; *Bristol Myers Squibb:* Current equity holder in publicly-traded company, Research Funding, Speakers Bureau. **Lee:** *Medison:* Consultancy. **Piris Villaespesa:** *Novartis:* Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau; *Blueprint:* Membership on an entity's Board of Directors or advisory committees. **Lividеanu:** *Novartis:* Research Funding; *Lilly, Novartis, UCB:* Consultancy; *Blueprint Medicines Corporation:* Membership on an entity's Board of Directors or advisory committees; *ABScience:* Membership on an entity's Board of Directors or advisory committees. **Lambert:** *Takeda:* Honoraria; *Blueprint:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Honoraria; *Kite-Gilead:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Hunter:** *Sierra Oncology:* Membership on an entity's Board of Directors or advisory committees. **George:** *Blueprint Medicines Corporation:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Celgene/BMS:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Cogent Biosciences:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Incyte Corporation:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *ARUP Laboratories:* Current Employment. **Shoumariyeh:** *Astrazeneca:* Honoraria; *BMS:* Speakers Bureau; *Blueprint:* Consultancy; *Novartis:* Honoraria. **Petroro:** *Cogent:* Current Employment, Current equity holder in publicly-traded company. **Zhang:** *Cogent:* Current Employment, Current equity holder in publicly-traded company. **Pilla:** *Cogent:* Current Employment, Current equity holder in publicly-traded company. **Jolin:** *Cogent:* Current Employment, Current equity holder in publicly-traded company. **Easton:** *Cogent:* Current Employment, Current equity holder in publicly-traded company. **Pullarkat:** *Servier:* Consultancy, Speakers Bureau; *Jazz Pharmaceuticals:* Consultancy, Speakers Bureau; *Amgen:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau; *Pfizer:* Consultancy, Speakers Bureau; *Genentech:* Consultancy, Speakers Bureau; *AbbVie:* Consultancy, Speakers Bureau.

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