PRESS RELEASE

NERVIANO MEDICAL SCIENCES

PART OF NMS GROUP

# Nerviano Medical Sciences Announces Phase 1 Clinical Trial Data for NMS-03592088 in Patients with FLT3 positive Relapsed or Refractory Acute Myeloid Leukemia

*Nerviano 16 April 2023*_Nerviano Medical Sciences Srl, a member of NMS Group and a clinical stage company discovering and developing innovative therapies for the treatment of cancer, today announced that data from the First-In-Human study of NMS-03592088, a novel, potent inhibitor of FLT3, KIT and CSF1R were presented during an oral scientific session at the American Association for Cancer Research 2023 Annual Meeting in Orlando, Florida.

NMS-03592088 is an orally available compound that showed superior preclinical activity with respect to first and second generation FLT3 inhibitors and demonstrated a good potency on resistance mutation F691L identified as cause of relapse in patients treated with selective FLT3 inhibitors. NMS-03592088 is currently being explored in MKIA-088-001 trial, a multi-center Phase 1/2 study to evaluate safety, tolerability and efficacy in patients with relapsed or refractory (R/R) acute myeloid leukemia (AML) or chronic myelomonocytic leukemia (CMML).

The Phase 1 portion of the study was a 3+3 design dose escalation with NMS-03592088 administered daily for 21 of 28 days (schedule A) or continuously (schedule B). As of January 26, 44 R/R AML or CMML patients were treated across doses from 20 to 360 mg/day in schedule A or from 120 to 250 mg/day in schedule B. 41 patients had AML and 3 patients had CMML. 24 AML patients were FLT3 positive with FLT3-ITD mutations representing the most common genetic alteration and the majority of them had received at least one prior FLT3 inhibitor (87.5%).

NMS-03592088 showed manageable safety with no maximum tolerated dose characterized. Overall, the most frequent treatment-emergent related adverse events were nausea (any grade, 20.5%), vomiting (13.6%), asthenia (11.4%). A dose-dependent trend of reversible myasthenic syndrome was also characterized.

In terms of clinical benefit, the data showed a dose-dependent trend for response. 5 out of 12 evaluable patients with FLT3 positive AML treated at dose ≥ 300 mg achieved an investigator-assessed response. All these patients had received prior midostaurin and 2 had received prior midostaurin and prior gilteritinib. Two patients with response were able to withdraw from study to receive HSCT. Overall, the duration of response ranged from 1.3-7.9 months.

In summary, NMS-03592088 showed clinical efficacy in patients with FLT3 positive R/R AML, including patients who have failed prior FLT3 inhibitors. These results, together with the manageable safety observed, warrant further development which is now being explored in Phase 2 trial.

*"We are pleased to see that NMS-03592088 demonstrates antileukemic activity in FLT3 positive AML patients since these patients are at high risk for poor outcomes" was noted by Lisa Mahnke, MD, PhD, Chief Medical Officer for Nerviano Medical Sciences.*

*"We believe that despite availability of FLT3 targeted agents there is still need for more effective treatments, including those for patients that have failed current FLT3 inhibitors" according to Hugues Dolgos, PharmD, CEO, Nerviano Medical Sciences.*

A copy of today's presentation "NMS-03592088, a novel, potent FLT3, KIT and CSF1R inhibitor with activity in FLT3 positive acute myeloid leukemia patients with prior FLT3 inhibitor experience" is available at this link: https://www.nmsgroup.it/wp-content/uploads/2023/04/NMS03592088_AACR-2023_CURTI.pdf

## About Acute Myeloid Leukemia

Acute Myeloid Leukemia (AML) is a rapidly progressing hematologic malignancy that most frequently develops in older adults. FLT3 mutations occur in approximately 30% of AML patients and are associated with aggressive disease, higher relapse rates and worse survival. Despite the approval of FLT3 inhibitors midostaurin and gilteritinib the prognosis of patients with relapsed or refractory disease is poor.

**About NMS-03592088**

NMS-03592088 is a novel, potent inhibitor of FLT3, KIT and CSF1R, all relevant targets in AML. NMS-03592088 showed superior preclinical activity compared with approved FLT3 inhibitors in different FLT3-driven models. In addition, NMS-03592088 is active on FLT3 gatekeeper mutation F691L causing resistance to first generation FLT3 inhibitors. NMS-03592088 is being developed in AML with two studies currently recruiting (MKIA-088-001 and MKIA-088-002)

**About Nerviano Medical Sciences**

Nerviano Medical Sciences S.r.l. (NMS Srl) is focused on discovery and clinical development of small molecule NCEs for oncology. We take innovative approaches on novel mechanisms of action and drug targets to bring first- and best-in-class personalized medicines to cancer patients. Our current pipeline consists of NCEs, which all originate from our well validated kinase platform that span from early preclinical to clinical stage projects and which are being developed both in house and with partners.

NMS Srl combines the flexibility of a biotech with the quality of a big pharma. Here, an experienced management team leads a highly skilled staff of professionals with global vision and a broad range of expertise in research, drug discovery and clinical development. We cover the whole range of additional aspects of drug development through the NMS Group affiliate companies, Accelera (AdMet) and NerPharMa (manufacturing). A key strength is our industrially renowned kinase inhibitor drug discovery platform which comprises an ever-evolving chemical collection with broad intellectual property coverage, discovery know-how and technologies which enabled us to out-license IP rights on recently approved innovative medicines such as encorafenib and entrectinib.

We collaborate with academia and clinical investigators as well as with industrial partners worldwide to advance our programs from early discovery to clinical development of new drugs. We seek further strategic collaborations to develop and commercialize our products in different territories as well as in-licensing opportunities of promising assets for clinical development.

**About NMS Group**

NMS Group is the largest oncological R&D company in Italy. With more than 400 employees of whom more than half are highly educated individuals dedicated to innovative research, development and manufacturing. The NMS kinase inhibitor discovery platform as well as the antibody-conjugating payload platform are the driving forces of the group's innovation, securing global recognition of NMS in personalized therapy. Recently entrectinib, originally discovered by NMS, is a targeted kinase inhibitor to treat NTRK1/2/3 and ROS1 dependent solid tumors that was licensed to Ignyta, now a member of the Roche Group, gained approvals for commercialization in all major markets. This is further evident of the competitiveness of the drug discovery platform of NMS Group.

NMS Group has three subsidiaries. NMS S.r.l. is a FIC / BIC focused drug research and development company with a robust pipeline of more than a dozen of anti-cancer projects, and three of the projects are currently in early clinical development. The other two subsidiaries are Accelera, which is a preclinical CRO company, and NerPharMa which manufactures API and drug product supporting clinical developments and commercialization.

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