NETRIS Pharma: data published in 2 Nature papers confirm netrin-1 blockade as significant clinical strategy in oncology

Netrin-1 blockade with NP137 confirmed as a clinical strategy in oncology to alleviate resistance to standard treatments

LYON, FRANCE, August 30, 2023 /EINPresswire.com/ -- > Anti-netrin-1 monoclonal antibody, NP137, demonstrates objective response and disease stabilization as monotherapy in Phase 1 study of patients with advanced endometrial carcinoma (EC); effective in inhibiting tumor growth in several different preclinical mouse models.

> Given its impact on EMT and excellent safety profile, NP137 is perfectly positioned for combination trials in indications with poor immune and chemotherapy responses.”” *Patrick Mehlen, CEO and Founder*

> Paired biopsies, pre-and-on NP137 treatment, highlight a statistically significant reduction of tumor epithelial-to-mesenchymal transition.

> Netrin-1 blockade with NP137, is confirmed as a clinical strategy to alleviate resistance to standard treatments, in multiple clinical indications, including EC.

NETRIS Pharma, a clinical-stage biopharmaceutical company developing first-in-class anticancer drugs, today announced data showing that its lead compound, NP137, is effective in reducing tumor growth and inhibiting tumor epithelial-to-mesenchymal transition (EMT). These data were published in Nature as two back-to-back papers titled “Pharmacological targeting netrin-1 inhibits EMT in cancer” and “Netrin-1 blockade inhibits tumor growth and EMT features in endometrial cancer,” as well as a clinical briefing: “Blockade of netrin-1 is a promising strategy against endometrial cancer”.

Preclinical studies were conducted by Prof. Cédric Blanpain, Professor of developmental biology and genetics, and Director of the Stem Cell and Cancer Laboratory of the Medical School at the Université Libre de Bruxelles (ULB), who stated: “In preclinical settings, we found that netrin-1 is upregulated during tumor EMT in a primary mouse model of skin squamous cell carcinoma (SCC). Pharmacological inhibition of netrin-1 by administrating NP137 decreased the proportion

EMT tumor cells in skin SCC, as well as decreased the number of metastases and increased the sensitivity of tumor cells to chemotherapy. Altogether, our results identify a unique pharmacological strategy to target EMT in cancer, opening novel avenues for therapeutic intervention."

The mode of action of NP137 was also investigated in patients with endometrial carcinoma during a Phase1 study by performing bulk and single cell RNA sequencing analysis and spatial transcriptomic on paired, pre and on NP137 treatment, biopsies.

"Although patients were at a late stage the disease with multiple lines of previous treatment, we noted a statistically significant reduction of tumor EMT that was associated with a net decrease of neoplastic cells," indicated Philippe Cassier, Medical Oncologist at Centre Léon Bérard and Principal Investigator of the Phase1 study. "This EMT inhibition was associated with changes in the immune infiltrate, with general increased interaction between cancer cells and the tumor microenvironments."

Despite the advanced disease status of Phase 1 patients, NP137 showed preliminary signs of efficacy as measured by objective responses and disease stabilization at 3 months. "Given the increasing literature describing EMT as a major player in the resistance to chemotherapy and immune checkpoint inhibitors, the observation that treatment with NP137 inhibits features of tumor EMT argues for the clinical assessment of combinations of this anti-netrin-1 mAb with conventional therapies to interfere with tumor progression," added Dr. Cassier.

"The confirmation of NP137 mode of action in preclinical and clinical settings with benefits for patients, now published in the journal Nature, have raised significant interest from clinicians to further conduct proof-of-concept trials in various cancer indications where (i) netrin-1 is significantly upregulated and (ii) EMT is documented as a key mechanism for cancer resistance," said Patrick MEHLEN, Co-founder and CEO of NETRIS Pharma. "Given its impact on EMT and excellent safety profile, NP137 is perfectly positioned for combination trials in indications with poor immune and chemotherapy responses."

NETRIS Pharma is delivering on a large clinical development plan for NP137, enrolling patients in four clinical trials, including:

1. GYNET trial (NCT04652076), a sponsored, randomized trial over 240 patients evaluating NP137 in combination with carbotaxol and/or pembrolizumab in endometrial carcinoma and squamous cervical cancer;
2. IMMUNONET (NCT05605496), which is targeting resistance to immunotherapy in patients stratified according to their response to treatments in several indications, including head & neck, melanoma, non-small cell lung cancer;
3. Liver-NET1 (NCT05546879), in hepatoCellular carcinoma patients, which is evaluating NP137 as a first line treatment on top of standard of care (atezo-bev);
4. Lap-NET1 (NCT05546853), a study in pancreatic cancer patients (PDAC), assessing NP137 as a

first line treatment over standard-of-care (Folfirinox).

“Both papers and the clinical briefing published in Nature emphasize the value of targeting netrin-1 as a novel and differentiated approach against cancer,” added Jean-Pierre Bizzari, Chairman of the NETRIS Pharma Board of Directors. “As part of our strategic clinical development plan for NP137, we now intend to have discussions with the European and US regulatory authorities to determine the most appropriate path forward to potentially gain approval.”

About NETRIS Pharma
NETRIS Pharma, a clinical-stage company, designs and develops anti-cancer therapeutic molecules, particularly monoclonal antibodies, to block the interaction between dependence receptors and their ligands. NETRIS Pharma, based in Lyon, has the world’s most advanced product candidates targeting netrin-1.
Further information can be found at: https://www.netrispharma.com.

About NP137
NP137 is a humanized monoclonal antibody of isotype IgG1 directed against netrin-1. Netrin-1 is overexpressed in a large number of human cancers. Expression of netrin-1 often correlates with disease severity and no therapy has ever been tested against this new pathway. Preclinical studies show NP137 has an anti-cancer effect as a monotherapy as well as synergistic effects in combination with chemotherapy or immune checkpoint inhibitors. After confirmation of the excellent safety profile in human, NETRIS Pharma is currently actively recruiting into four clinical trials testing NP137 in several cancer indications.

Contacts @ NETRIS Pharma

Patrick MEHLEN, CEO, patrickmehlen@netrispharma.com
Christophe GUICHARD, CFO and IR, christopheguichard@netrispharma.com
Mike Sinclair, Halsin Partners (for NETRIS Pharma) msinclair@halsin.com

NETRIS Pharma
NETRIS Pharma
email us here
Visit us on social media:
LinkedIn
