Boehringer Ingelheim Snaps Up Lupin's MEK Inhibitor For Difficult-To-Treat Cancers

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Executive Summary

Boehringer Ingelheim intends to combine Lupin's MEK inhibitor with its own KRAS inhibitors to target the oncogenic KRAS-RAF-MEK-ERK pathway, mutations in which drive many difficult-to-treat cancers.

CELLULAR SIGNALING PATHWAY MUTATIONS ARE LINKED TO CANCER *Source: Shutterstock*

In its second major out-licensing R&D deal of the past 12 months, Lupin Ltd. has signed a pact with Boehringer Ingelheim GmbH. The German group is to collaborate on the development of Lupin's clinical-stage MEK inhibitor, LNP3794, for the treatment of difficult-to-treat KRAS-driven cancers.

The licensing, development and commercialization agreement, under which Lupin will receive an upfront of $20m, potential total milestones of $700m, and sales royalties, will involve the two companies evaluating LNP3794 in combination with Boehringer Ingelheim's investigational KRAS inhibitors for the treatment of gastrointestinal and lung cancers with oncogenic KRAS mutations.

KRAS-mutated cancers have no targeted treatments and monotherapy has been tried but, to date, has not been successful. "We've actually seen synergy using combinations in the relevant models, and our compound has shown efficacy in a small number of patients in a UK trial, and now combining with their (BI's) agent will enhance the probability [of success]," said Raj Kamboj, president of Lupin's novel drug discovery and development (NDDD) unit, speaking at a press briefing in India.

The KRAS gene is the most frequently mutated cancer-causing gene, with mutation rates of more than 90% in pancreatic cancers, more than 40% in colorectal cancers and more than 30% in lung adenocarcinomas. KRAS mutations occur in one in seven of all human metastatic cancers.

Lupin believes LNP3794 can be effectively combined with chemotherapy and other targeted agents, such as RAF, PI3K, KRAS, BTK and EGFR inhibitors, for the treatment of BRAF and RAS mutant cancers. "Combining LNP3794 with other targeted agents is expected to provide high response rates," the company said.

Boehringer Ingelheim and Lupin reported on 4 September that preclinical studies show a combination of a KRAS inhibitor with a MEK inhibitor can keep KRAS-driven tumors in check. They target different parts of the intracellular signaling KRAS-RAF-MEK-ERK pathway. In early clinical studies, Lupin's MEK inhibitors have already shown benefits in a small subset of patients, and MEK inhibitors such as Novartis AG's Mekinist (trametinib) and Pierre Fabre Group's Mektovi (binimetinib) are already marketed for the treatment of melanoma containing the BRAF V600 mutation.

Lupin reckons LNP3794 stacks up favorably with existing MEK inhibitors and may have significant advantages over other MEK agents in terms of both efficacy and safety. With regard to potential competitors in development, another KRAS inhibitor, Amgen Inc.'s AMG-510, has a different target, KRAS G12C mutations, Kamboj told *Scrip*. (Also see "Amgen's KRAS Inhibitor AMG 510 Leans Toward Tumor-Dependent, Not Agnostic, Approach" - Scrip, 3 Jun, 2019.)

Lupin is transitioning from a pure-play generics company – it is the third largest pharmaceutical company in the US in terms of the volume of prescriptions – to having a more diversified business strategy involving generics, complex generics, biosimilars, manufacturing and drug discovery. At the end of 2018, the Mumbai-headquartered company out-licensed its MALT1 (mucosa-associated lymphoid tissue lymphoma translocation protein 1) inhibitor program to AbbVie Inc. for a $30m upfront and more than $900m in potential milestone payments, significant amounts for a preclinical asset.

Other companies, including Novartis AG and Galapagos NV, are interested in developing MALT1 inhibitors, for inflammatory and oncological diseases (see sidebar).

For Boehringer Ingelheim, the development of inhibitors to the KRAS oncogene is part of a concerted research and business development effort into new anticancer medicines, particularly those targeting lung and gastrointestinal cancers with novel modes of action. Two months ago, it acquired the Swiss biotech Amal Therapeutics SA whose candidate therapeutic cancer vaccine ATP128 is being evaluated in stage IV colorectal cancer. (Also see "Boehringer Ingelheim To Boost Cancer Immunology Portfolio with Novel Cancer Vaccines " - Scrip, 16 Jul, 2019.)

Lupin Ends 2018 On High, Strikes Large MALT1 Deal With AbbVie

By Anju Ghangurde

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AbbVie has in-licensed Lupin's MALT1 (mucosa-associated lymphoid tissue

A potential first-in-class myeloid checkpoint inhibitor, BI 765063, entered Phase I in June at Boehringer Ingelheim, in its partnership with the French biotech OSE Immunotherapeutics SA. BI 765063 is also being combined with Boehringer Ingelheim's T-lymphocyte checkpoint inhibitor BI 754091. (Also see "OSE Immunotherapeutics Adds Boehringer Ingelheim To Its Pharma Partnering List " - Scrip, 9 Apr, 2018.)

lymphoma translocation protein 1) inhibitor program for over $900m in potential milestone payments, bringing Christmas cheer for the Indian firm. The deal terms for the preclinical asset are rather striking.

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The German multinational already has some experience in the oncology field, as a marketer of Giotrif (afatinib) for non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) mutations, and Vargatef (nintedanib) for NSCLC combination therapy.