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Novimmune doubles down in HLH; second $31M round this year

By Cormac Sheridan
Staff Writer

Thursday, May 12, 2016

DUBLIN – Novimmune SA closed a CHF30 million (US$31 million) funding round, taking the total cash it has raised this year to CHF60 million and its lifetime total to more than CHF300 million.

The Geneva-based firm is doubling down on its lead program in primary hemophagocytic lymphohistiocytosis (HLH), a rare and devastating dysfunction of the immune system, which has a fatality rate of about 50 percent. Novimmune gained FDA breakthrough therapy designation in March for NI-0501, a fully human antibody that targets interferon gamma, the pleiotropic pro-inflammatory cytokine that modulates innate and adaptive immune responses. It is now close to completing recruitment in a pivotal phase II/III trial.

"Our current expectation is we can file in 2017 – most likely early in the second quarter. If it goes very well, maybe in the first quarter," Chairman and CEO Ed Holdener told *BioWorld Today*.

The company had been considering an IPO back in January, but, given the weakening market conditions, its investors decided to build the company's value by funding the generation of more clinical data. Partnering discussions are ongoing – and a trade sale is "always a possibility," Holdener said – but the company is not actively working on an IPO at present.

Gaining the FDA designation boosted investor confidence in the company. Seeking it involved a certain amount of risk, Holdener said, as rare disease programs at small, unlisted companies do not match the typical profile for breakthrough therapies. Oncology programs – or infectious disease programs – at larger, quoted firms are the norm.

HLH is, he said, "an ultra-rare disease." It has a prevalence of about one in 50,000. It can be caused by mutations in several genes involved in regulating immune cell functions, including PRF1, UNC13D, STX11 and STXBP2. The gene involved in a fifth subtype, designated HLH subtype 1, has yet to be identified, according to the NIH's Genetic and Rare Diseases Information Center.

There are no drugs approved for HLH. Current regimens involve highly toxic cytotoxic and immunosuppressive therapy, which are administered with the aim of achieving remission so that patients can undergo bone marrow transplant. "Bone marrow transplant in mutation-driven primary HLH is the only potentially curative approach, ultimately," Holdener said.

A long-term study of the HLH-94 treatment protocol, which involves co-administration of etoposide and dexamethasone, in 249 patients with primary or acquired HLH achieved a five-year survival rate of 54 percent (± 6 percent). The survival rate for patients with familial HLH was 50 percent (± 13 percent). No patient who did not undergo bone marrow transplant survived. The data appeared in the Oct. 27, 2011, issue of *Blood*, in a paper, titled "Chemoimmunotherapy for hemophagocytic lymphohistiocytosis: long-term results of the HLH-94 treatment protocol."

Novimmune reported promising preliminary data from an open-label phase II study of NI-0501 at the American Society for Hematology meeting in December. Of 13 patients with advanced disease, 10 responded to therapy – seven underwent bone marrow transplant and two more were scheduled to do so, once suitable donors were identified. A 10th patient – the only one to receive NI-0501 as a first-line therapy – also attained good disease control but was not designated to receive a bone marrow transplant owing to the absence of a causative genetic mutation. Eleven of the 13 remained alive at eight weeks.

In familial disease, NI-0501 has the potential to reduce the toxic burden on patients and enable them to progress to bone marrow transplant more easily. It also has potential – yet to be explored in the clinic – in managing acquired HLH, which can arise from complications following infection, autoimmune disease or hematological malignancy.

The company has three other clinical-stage programs, two of which are out-licensed. The Genentech arm of Roche AG, of Basel, Switzerland, is developing NI-1401, an anti-interleukin-17 antibody, for autoimmune indications. London-based Tiziana Life Sciences plc has in-licensed foralumab (NI-0401), which targets the epsilon chain of the T-cell receptor CD3, for autoimmune indications. An unpartnered antibody targeting Toll-like receptor 4 is ready to enter a phase II proof-of-concept study in rheumatoid arthritis. Novimmune is seeking a deal for that program.

Its most advanced bispecific molecule, NI-1701, which targets CD19 and CD47, is in development for B-cell leukemia and lymphoma and is ready to enter the clinic next year.