Over the last several years increasing data on the pivotal role played by interferon gamma (INFγ) in the development and maintenance of HLH has been generated. INFγ is an important molecule of the immune system thought to be responsible for the inflammation and tissue damage observed in HLH. In particular, the interest in the role played by IFNγ in the pathogenesis of HLH is based upon the observation that animals suffering from a disease resembling HLH could survive when IFNγ was neutralized. This observation was of particular interest also because animals with an “HLH-like” disease display not only all the laboratory and clinical features of patients suffering from HLH, but they also carry the same gene mutations responsible for the disease in human beings.

Based on these observations, a research program has been initiated in collaboration with HLH experts around the world with the objective to develop an anti-IFNγ monoclonal antibody as a targeted therapy for the induction treatment of HLH. This research program will determine whether blocking the deleterious effects of IFNγ can get the disease under control with less toxicity and immunosuppressive activity than the treatments currently used, prior to hematopoietic stem cell transplantation.

The research program consists of:

- a pilot study in 10 primary HLH patients in whom the disease has re-activated after initial response (NI-0501-04 study, http://clinicaltrials.gov/ct2/show/NCT01818492?term=ni-0501-04&rank=1). Patients receive an anti-IFNγ antibody on a background therapy of dexamethasone for 8 weeks. This study is being performed in 14 investigational sites distributed in 5 European countries, and in 4 US sites;
- a long-term follow-up study with the objective to monitor all patients who receive at least one dose of the investigational drug. In patients who receive hematopoietic stem cell transplantation, the monitoring continues for the 12 months following transplantation (NI-0501-05 study, http://clinicaltrials.gov/ct2/show/NCT02069899?term=ni-0501-05&rank=1).
- For more information regarding these studies, including eligibility to participate, see the clinicaltrials.gov webpage above, or contact:
  - (USA) Michael Jordan, MD: 513-636-7287, or michael.jordan@cchmc.org
  - (Worldwide) Cristina de Min, MD (Chief Medical Officer, NovImmune SA) +41 22 593 51 16, www.novimmune.com

The future steps of the development of this potential new drug will be decided together with the Regulatory Authorities, both in the US and in Europe (Food and Drug Administration and European Medicinal Agency), and the world Experts in HLH depending on the benefit/risk profile emerging from the ongoing study.

Other parts of this research program, which has received a significant grant from the European Commission (FP7, FIGHT HLH program), are aimed at
- investigating the role of IFNγ in secondary forms of HLH, both in animal models and through the performance of an observational study in HLH patients
- characterizing HLH patients with the search for specific disease markers and disease genotypes through gene profiling.

The anti-IFNγ monoclonal antibody tested in the studies mentioned above is NI-0501, a fully human monoclonal antibody being developed by NovImmune as the first targeted treatment for HLH. NovImmune (www.novimmune.com) is a drug discovery and development company based in Geneva, Switzerland, focused on the creation of therapeutic monoclonal antibodies for the treatment of inflammatory diseases, whose mission is to develop drugs that can directly attack the cause of diseases.