Tollys and Gustave Roussy enter into new research agreement

- **Prof. Guido Kroemer's team, from Gustave Roussy, will test Tollys' specific TLR3 agonist, TL-532, to restore deficient chemotherapeutic responses in the context of FPR1 deficiency**

- **FPR1 deficiency affects 30% of world population and is associated with precocious manifestation of breast, colorectal, esophageal, head and neck carcinomas**

Lyon, France, March 7, 2022 — Tollys, a biopharmaceutical company developing TL-532, the first anti-cancer immunotherapy based on a synthetic toll-like receptor 3 (TLR3) specific agonist, today announces that it has entered into a sponsored research agreement with Gustave Roussy, the leading cancer center in Europe.

Professor Guido Kroemer's team will evaluate the effects of TL-532 in the context of FPR1 deficiency using methods similar to those recently published in the original research article entitled '*A TLR3 Ligand reestablishes chemotherapeutic responses in the context of FPR1 deficiency'*. These studies were conducted with polyinosinic:polycytidylic acid (pIC), a research grade TLR3 agonist. In comparison with agonists of TLR 2, 4, 5, 6, 7, 8 and 9, only the TLR3 agonist pIC was able to restore deficient chemotherapeutic responses in mice lacking FPR1, suggesting a personalized strategy for compensating for the FPR1 defect with a TLR3 agonist.

TL-532 is developed by Tollys and is a specific TLR3 agonist with a defined 70 base pair sequence of double-stranded RNA (dsRNA), produced by chemical synthesis, which can meet today's quality manufacturing standards for new molecular entities.

"We are very eager to show that TL-532 can restore deficient chemotherapeutic responses in the model of Prof Kroemer's team, because FPR1 deficiency is a common genetic disorder and there is a good chance that, in the future, patients with FPR1 deficiency may derive critical benefits from a treatment with TL-532," said Vincent Charlon, CEO of Tollys.

About FPR1 Deficiency
For anthracycline-based chemotherapy to be immunogenic, dying cancer cells must release annexin A1 (ANXA1) that subsequently interacts with the pattern recognition receptor, formyl peptide receptor 1 (FPR1), on the surface of dendritic cells (DC). Approximately 30% of individuals bear loss-of-function alleles of *FPR1*, calling for strategies to ameliorate their anticancer immune response. Le Naour et al. (Cancer Discovery 2021;11:408-23), showed that immunotherapy with a ligand of Toll-like receptor-3, polyinosinic:polycytidylic acid (pIC), restores the deficient response to chemotherapy in tumors lacking ANXA1 developing in immunocompetent mice or those of normal cancers growing in FPR1-deficient mice. This effect was accompanied by improved DC- and T-lymphocyte–mediated anticancer immunity. Of note, carcinogen-induced breast cancers precociously developed in FPR1-deficient mice as compared with wild-type controls. A similar tendency for earlier cancer development was found in patients carrying the loss-of-function allele of *FPR1*. These findings have potential implications for the clinical management of FPR1-deficient patients.

About TL-532
TL-532 is the first synthetic specific TLR3 agonist with a proprietary defined double-stranded RNA sequence. As such, TL-532 has the potential to be the best-in-class and first-to-market TLR3 agonist. TL-532 was shown to have a triple mechanism of action inducing 1) death by apoptosis selective to cancer cells - not in normal cells -, leading to the *in-situ* release of tumor specific antigens, 2) activation of the myeloid dendritic cells of the immune system to mount a specific T-cell response against the tumor antigens and 3) a switch of the tumor microenvironment by producing cytokines and chemokines which are

unfavorable to tumor development. The result is the immunogenic cell death of tumor cells, accompanied by an auto-vaccination preventing the recurrence of cancer.

About Gustave Roussy

Classed as the leading European Cancer Center and the sixth on the world stage, Gustave Roussy is a center with comprehensive expertise and is devoted entirely to patients living with cancer. The Institute is a founding member of the Paris Saclay Cancer Cluster. It is a source of diagnostic and therapeutic advances. It caters for almost 50,000 patients per year and its approach is one that integrates research, patient care and teaching. It is specialized in the treatment of rare cancers and complex tumors, and it treats all cancers in patients of any age. Its care is personalized and combines the most advanced medical methods with an appreciation of the patient's human requirements. In addition to the quality of treatment offered, the physical, psychological and social aspects of the patient's life are respected. 3,200 health professionals work on its two campuses: Villejuif and Chevilly-Larue. Gustave Roussy brings together the skills which are essential for the highest quality research in oncology: a quarter of patients treated are included in clinical trials.
www.gustaveroussy.fr

About Tollys

Tollys is a biopharmaceutical company focused on cutting-edge cancer immunotherapy and on the biology and modulation of the TLR3 receptor. Tollys discovered and patented a family of new structurally defined dsRNA sequences able to activate the TLR3 receptor. TL-532 was selected as the lead-candidate for development. TL-532 is a structurally defined double-stranded RNA; produced synthetically and highly specific to the TLR3 receptor. The specificity for the TLR3 receptor and its defined 70 base pair sequence differentiates TL-532 from all other TLR3 agonists tested to date in clinical trials. In 2021, TL-532 was named the 'best-in-class innovation of the year' by the international board of MATWIN, a European oncology innovation acceleration program. Founded in 2015 by pharmaceutical executives and scientists from the Cancer Research Center in Lyon and the Centre Léon Bérard, Tollys offices and research laboratories are based in Lyon, France. The company has raised a total of €7M ($7.9M) from private investors and received a grant of €1.5M ($1.7M) from Bpifrance.
www.tollys.fr

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