TL-532
The first rationally designed specific TLR3 agonist

THERAPY

CONTEXT & BACKGROUND

We are a preclinical stage company stemming from 20 years of research in innate immunity and TLR3 receptor biology and modulation. Unlike other Pattern Recognition Receptors and Toll-Like Receptors, specific TLR3 agonists have unique properties including direct antitumoral effects through apoptosis and activation of myeloid dendritic cells, leading to a specific immune response against the myriad of tumor-associated antigens released by the apoptotic process. As a result, the tumor is eliminated by immunogenic cell death and cancer recurrence is prevented by a mechanism of in situ autovaccination.

TLR3 is a validated cancer target since the studies of Institut Gustave Roussy with polyAU (Lacour, 1984) and posthoc analyses by Salaun et al. 2011, demonstrating that the treatment benefit in these studies was observed only in women with TLR3 expressing tumors.

TLR3 has been extensively studied with various dsRNA of undefined length in the past decades. PolyIC is a potent TLR3 agonist in vitro but it lacks specificity and presents toxicities at efficacious doses. PolyAU was clinically efficacious in breast cancer but was made of a mix of RNA sequences which were never registered. TL-532 is superior to PolyIC and its derivatives in specificity and tolerability, superior to PolyAU in anti-tumoral activity, and superior to PolyAU and PolyIC (and derivatives) as a defined sequence dsRNA produced chemically to meet current pharmaceutical manufacturing standards.

> *"TLR3 agonist is of interest and appealing since it has less tox concerns and a larger therapeutic window compared to other TLRs"*
> Senior Oncology Director Pharma - Nov 2020

INNOVATIVE COMPONENT & TECHNOLOGY

We rationally designed and patented a family of dsRNA sequences with TLR3 agonist properties and selected TL-532 as its lead candidate for its balanced potency to induce selective apoptosis in cancer cells and efficient activation of the immune cells. These properties are unique and superior to any other previous TLR3 agonist.

We demonstrated the anti-tumoral and autovaccination properties of TL-532 in vitro on cancer cells, in vivo in animal models of cancer and on human tumor biopsies.

TL-532 has the potential to be the first specific TLR3 agonist to reach the market and to be best-in-class as a single agent cancer immunotherapy treatment. Its market potential across multiple cancer indications could reach several billions per year. In addition, by triggering a new in situ immune response, TL-532 reverses resistance to checkpoint inhibitors and could thus derive significant further potential as combination therapy.

KEYWORDS

Cancer immunotherapy, TLR3 agonist, ds RNA, proof-of-concept, biomarker, TL-532, Best-in-class

OBJECTIVES

We expect to start clinical trials with local administration of TL-532 to establish the clinical proof of concept in patients with solid tumors (bladder and/or cutaneous tumors).

A systemic version of TL-532 will be progressed to clinical stage as well. TL-532 has already been chemically conjugated in proof-of-concept experiments and various options of vectorization are being studied currently.

We are interested to evaluate opportunities of collaboration with companies and scientific groups with expertise in antibody-oligonucleotide-conjugates.

DEVELOPMENT & MATURATION STAGE

Full preclinical proof-of-concept established
Ready to proceed to clinical stage by local administration
Lead-optimization in progress for optimal systemic use

TARGET POPULATION

Patients with solid tumors expressing TLR3
TLR3 expression is the expected biomarker to be used as a predictor of response to TL-532

TARGET PROFILE

Injectable compound developed for local and for systemic use

INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S

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STRENHGTS & COMPTETIVE ADVANTAGES

Proprietary specific TLR3 agonist, with a fully defined double-strand RNA sequence
Reproducibly manufactured by chemical synthesis
Specificity for TLR3
Best-in-class recognition and first-in-class potential
Conjugable as payload to antibodies or to other carriers
Well tolerated

INDUSTRIAL APPLICATIONS & OPPORTUNITIES

Treatment of multiple cancers as stand-alone and in combination with existing anti-cancer agents
Very broad market opportunities including potential reversal of checkpoint inhibitor resistance