TECHNOLOGY OFFER

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Pan-Anti-Histamine: Rapid Inactivation of Excess Histamine in Plasma and Tissue

A modified human diamine oxidase completely degrades anaphylaxis relevant histamine levels in human plasma with a half-life of less than 5 minutes. Modifications increase the area under the curve of the enzyme more than 20-fold and completely prevent higher order aggregate formation. First indications are anaphylaxis, mastocytosis, and anti-histamine resistant chronic urticaria.

BACKGROUND

Human diamine oxidase (DAO) was discovered more than 90 years ago and a pig kidney version was marketed/sold from 1936 to 1967 (Torantil). DAO is the only natural enzyme for the degradation of extracellular histamine (HIS). During pregnancy, plasma DAO levels increase more than 100-fold. Excess HIS plays an important pathophysiological role in several human diseases like anaphylaxis, mastocytosis (orphan disease), mast-cell-activation syndrome (MCAS), chronic urticaria, possibly asthma. Anti-histamines are not effective in severe cases of these diseases since they can only block a 3-5 fold increase in HIS concentrations compared to for example an over 100-fold increase during anaphylaxis.

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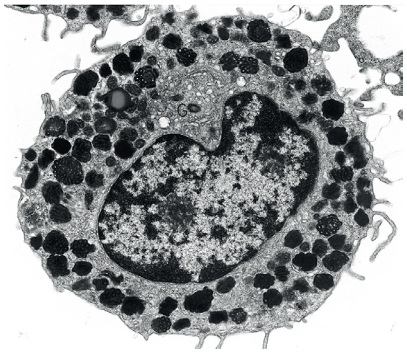

mast cell: not degranulated

Natural human DAO has a short half-life and is therefore unsuitable for drug development. We modified human DAO resulting in dramatically improved pharmacokinetic (PK) but unaffected pharmacodynamic (PD) properties. An additional modification inhibits natural tetramerization and higher order aggregate formation. Our modified DAO is forming only “natural” dimers, which greatly simplifies protein expression, purification but also lowers immunogenicity and increases safety. The next steps are generation of a GMP high expression cell line and a suitable GMP manufacturing process, Toxicity and Phase 1 studies. Approval under exceptional circumstances (EC) is possible with Phase 1 data (Discussions with EMA during orphan designation scientific advice). Expedited review programs of the FDA are very likely also applicable.

ADVANTAGES

- Rapid elimination of circulating (and tissue) HIS
- Reduction of HIS signaling irrespective of the involved HIS receptor
- Modified natural enzyme with strongly improved PK parameters
- Low cost of goods (COG)
- Orphan Drug Designation granted by EMA
- Marketing approval in anaphylaxis with Phase 1 data possible (Approval under Exceptional Circumstances EMA and Expedited Programs FDA)
- Additional “attractive” diseases for DAO with high unmet medical need

REFERENCE:
DAO

AVAILABLE FOR:
- Development partnership
- Licence
- Investment into Spin-off

INDICATIONS:
Anaphylaxis, mastocytosis, MCAS, chronic Urticaria

DEVELOPMENT STATUS:
IProduct ready for GMP cell line development and manufacturing

IPR:
PCT application filed Feb2019

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