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DNTH103, a potentially safer and more convenient novel, investigational therapy for generalized Myasthenia Gravis

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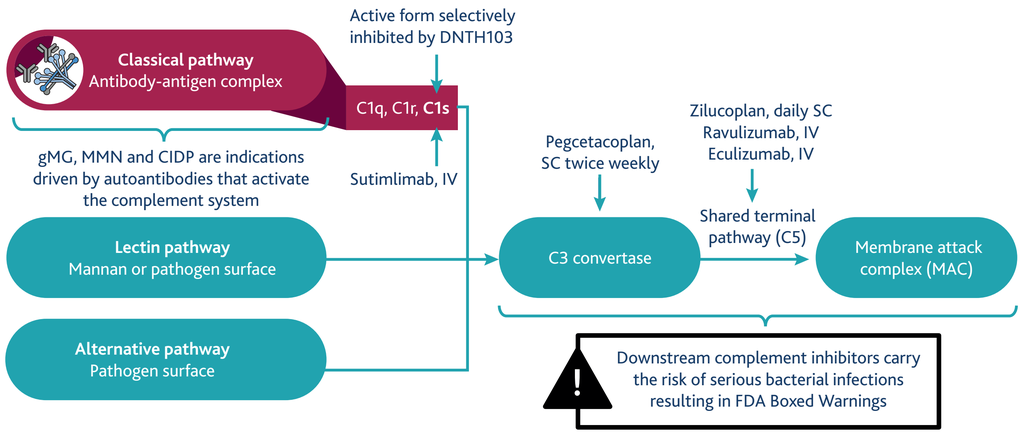
BACKGROUND

Complement inhibitors are well established in gMG and other severe autoimmune disorders

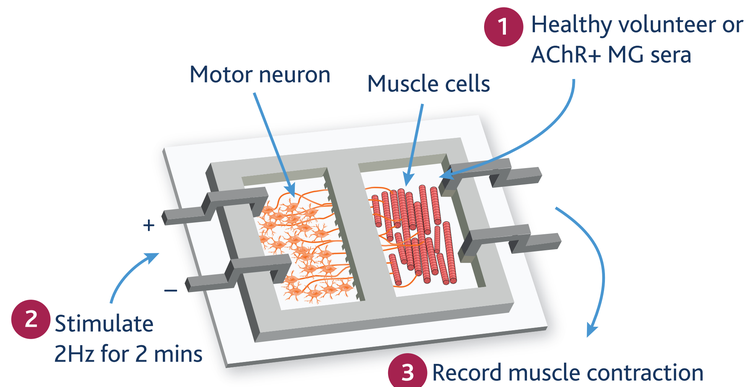
Targeting C1s preserves immune activity of the lectin and alternative pathways, with the aim to provide a safe therapeutic option



DNTH103 – a picomolar-potent monoclonal antibody selectively targeting active C1s

- DNTH103 is a fully human immunoglobulin G (IgG4) monoclonal antibody binding to active C1s, allowing low-volume SC self-administration
- Alternative and lectin pathways are left intact
- In a Phase 1 clinical trial in healthy volunteers, DNTH103 demonstrated an extended half-life of 60 days and potent complement inhibition, supporting potential for infrequent, low-volume SC dosing

Preclinical evaluation of DNTH103 in an established *in vitro* model of MG



- Serum from three acetylcholine receptor-positive (AChR+) MG patients used in a validated commercially available humanized *in vitro* MG model[1,2,3]
- Endpoint: Fatigue index in response to anti-C5 antibody* or DNTH103
  - A reduction in fatigue index indicates improvement in neurotransmission and muscle contraction

Global Phase 2 studies in generalized Myasthenia Gravis (gMG) and Multifocal Motor Neuropathy (MMN) are ongoing, and a global Phase 2 trial in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is planned to start in 2024

*Engineered using the ravulizumab patent sequence
gMG, generalized Myasthenia Gravis; MMN, Multifocal; Motor Neuropathy; CIDP, Chronic Inflammatory Demyelinating Polyneuropathy; IV, intravenous; SC, subcutaneous; FDA, Food and Drug Administration; MG, Myasthenia Gravis; AChR+, acetylcholine receptor-positive

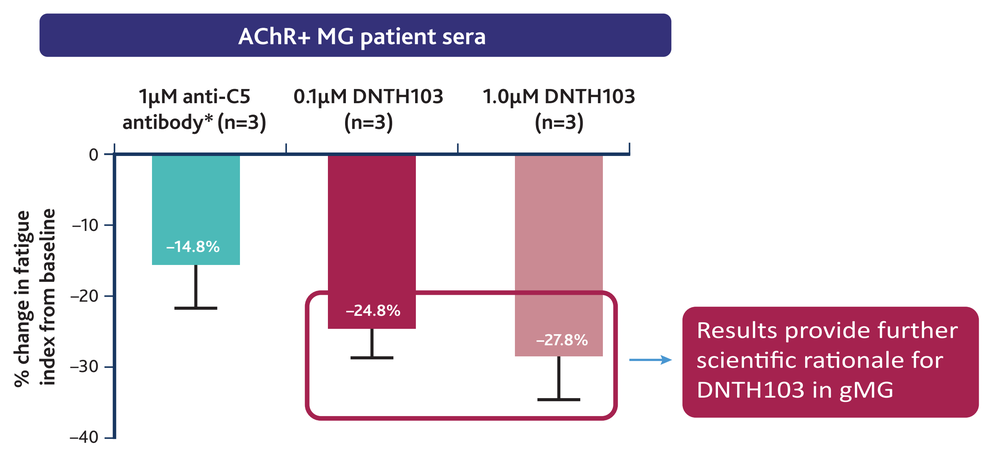
CONCLUSIONS

DNTH103 is a highly potent picomolar inhibitor of active C1s that is as effective in improving neurotransmission and muscle contraction as an anti-C5 antibody in a preclinical model of Myasthenia Gravis

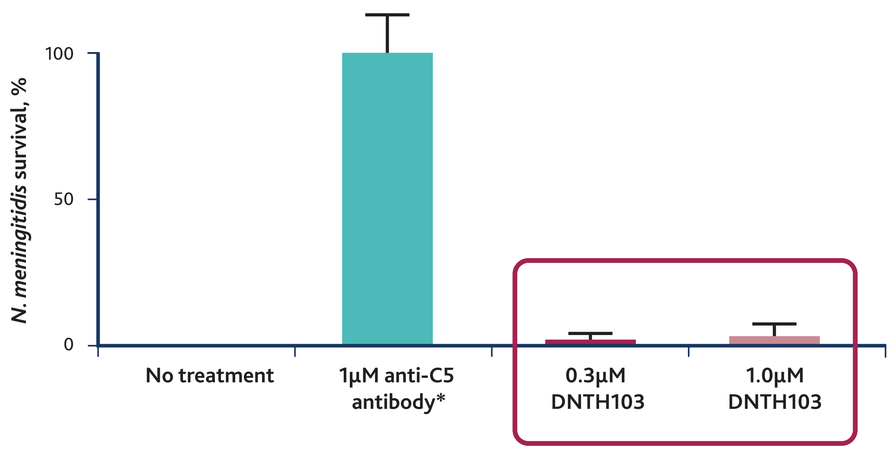
DNTH103 selectively inhibits the classical pathway with the potential to be safer than complement therapies that also block the lectin and/or alternative pathways

RESULTS

DNTH103 improves neurotransmission and muscle contraction in an AChR+ MG model† (change from baseline)



N. meningitidis bacterial killing is unaffected despite inhibition of the classical pathway



In this assay, DNTH103 maintained bacterial killing, potentially leading to a decreased risk of infection vs. anti-C5 antibody*

DNTH103 *in vitro* study demonstrates lower risk of *Neisseria meningitidis* infections

Dianthus Therapeutics data on file
†Validated in healthy volunteer sera; *engineered using the ravulizumab patent sequence; §normal human sera
AChR+ MG, acetylcholine receptor-positive Myasthenia Gravis; MG, Myasthenia Gravis; gMG, generalized Myasthenia Gravis

References

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Acknowledgements

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