TargetSite Therapeutics

Harnessing the power of novel mRNA-targeted oligonucleotide therapeutics
Overview

2018
- Awarded the prestigious Blavatnik funding

2019
- Founding of Targetsite Therapeutics
- Awarded the prestigious Blavatnik funding

2020
- Awarded the prestigious Blavatnik funding

2021
- SBIR Ph1 grant - Autoimmune Uveitis
- R21 Grant - Psoriasis

2022
- Yale grant to support oncology program

TargetSite is a Yale spinout, founded in 2019

Building an mRNA-targeted therapeutics platform company, founded on unique insights into mRNA-stabilizing miRNA

Lead candidate partially de-risked in animal disease models of multiple sclerosis, psoriasis and autoimmune uveitis

Optimization for oral delivery formulations for lead asset in animal diseases models for different autoimmune and inflammatory diseases

Strong IP position

Looking to raise capital & build strategic partnerships
TargetSite Blockers (TSBs) block Enhancing microRNA’s (E-miRNA) interaction with target mRNA

- Destabilizing miRNAs (conventional)
  - mRNA decay and/or translation block

- Novel class of E-miRNAs
  - HuR-miRyyy cooperative mRNA stabilization and/or effective translation

- TSB oligos inhibit E-miRNAs
  - TSB interference with E-miRNA-HuR interaction resulting in mRNA decay

Blocking the cooperative, translation-promoting HuR-miRNA-3’UTR interaction with sequence-specific modified oligonucleotides can greatly and selectively dampen gene expression

Supporting data on both concepts of HuR (Human antigen R) inhibition for mRNA translation block & HuR recruitment for mRNA stabilization
TargetSite Blockers (TSBs) for inhibiting & stabilizing target mRNA: Two pillars

TSB oligos inhibit E-miRNAs

mRNA

miRyyy

HuR

TSB interference with E-miRNA cooperative HuR recruitment results in mRNA decay & translation block

E-miRyyy

Enhancing

mRNA context specific

Autoimmune & inflammatory
Fibrosis
Oncology

R-miRxxx

Repressive

mRNA context specific

Polycystic kidney disease
Wound healing
Heart failure
Keloid
Oncology

TSB oligos inhibit R-miRNAs

mRNA

miRxxy

HuR

TSB interference with conventional R-miRNA HuR-competitive interaction promotes HuR recruitment resulting in mRNA stabilization & effective translation

Gene expression enhancement or repression dependent on precise nature of miRNA influence on HuR recruitment and binding to any given mRNA 3’UTR
IL-17A-miRyyy TSB specifically destabilizes human IL-17 mRNA

Graph showing IL-17A and GM-CSF mRNA decay in human primary T cells

- T cells transfected with 25 nM TSB or CNTA (control) oligo after transcriptional arrest (time 0)

miRyyy-IL17A TSB prevents HuR-dependent protection of IL-17A but not GM-CSF mRNA

CNTA = Control Oligo A (non-specific oligo)
IL-17A-TSB = IL-17A Target site blocker
GM-CSF = granulocyte-macrophage colony-stimulating factor
Complete inhibition of disease in a progressive mouse MS model

IL-17A TSB oligo IP in 2D2 Transgenic
EAE = experimental autoimmune encephalomyelitis

EAE score is a score of MS disease severity

TSB has high therapeutic potential
CEO & Co-founder
Ashoka Madduri, PhD, MBA

Co-founder & SAB Chair
Jeffrey Bender, MD
Professor of Cardiology
Professor of Immunobiology
Director of the Cardiovascular Research Center, Yale

Co-founder & Head of Discovery
Vinod Ramgolam, PhD

BD & Licensing
Morag Grassie, PhD