An Open-Label, Multicenter Phase 1/2 Dose Escalation and Expansion Study of THOR-707 as a Single Agent and in Combination with Pembrolizumab in Adult Subjects with Metastatic Solid Tumors

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BACKGROUND

Dual Pharmacology of IL-2 is Mediated by Synthorx Expanded Genetic Code Platform: A Synthetic DNA Base Pair and matching X-Y tRNA gene encode product plasmids X and YTPs enter via Intermediate affinity (Kd ~ 10^-9M) (Kd ~ 10^-11M) Type Activated Response ∝ with tRNA displaying anticodon mRNA with X-Y codon matches

Chemistry Into Proteins Improved target selectivity through altered receptor Designed to bioconjugate moieties for improved binding CD4 Th, CD8+ T, and NK cells Broadly expressed Translation machinery decodes X-Y codons Treg

STUDY DESIGN

THOR-707

Dose Escalation (3+3 Design)

STUDY OBJECTIVES

Primary Objectives:
- Evaluate pharmacokinetics, tolerability of THOR-707 as a single agent and in combination with pembrolizumab (Pembrolizumab, Merck) in adult subjects with advanced/unresectable solid tumors
- Define the MTD and OR the RP2D of THOR-707 as a single agent and in combination with a checkpoint inhibitor Secondary Objectives:
- Confirm safety of THOR-707 as a single agent and in combination with a checkpoint inhibitor
- Evaluate efficacy of THOR-707 as a single agent and in combination with pembrolizumab

THOR-707 as a single agent and in combination with pembrolizumab (Pembrolizumab, Merck) in adult subjects with advanced/unresectable solid tumors:

THOR-707 as a single agent and in combination with pembrolizumab

Dose Escalation

Dose Expansion

THOR-707 as a single agent and in combination with pembrolizumab (Pembrolizumab, Merck) in adult subjects with advanced/unresectable solid tumors: 3 mg/kg

Part 1: THOR-707 Single Agent at the MTD


Part 3: Single Agent and Combination Basket Studies in Select Populations

Cohort A: THOR-707 Q2W

Cohort B: THOR-707 Q2W

Cohort C: THOR-707 Q2W

Cohort D: THOR-707 Single Agent RP2D or Q2W

Cohort E: THOR-707 Combo RP2D Q2W

Additional Dose Levels up to the MTD

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Additional Dose Levels up to the MTD

Dose Level

Dose Level N

Dose Level N

Dose Level N

Clinical Sites

Safety

PHASE 1/2 Dose Escalation and Expansion Study of Pembrolizumab and THOR-707 in Solid Tumors

Part 1: THOR-707 at the MTD in combination with pembrolizumab

Part 2: THOR-707 at the MTD in combination with pembrolizumab

Part 3: THOR-707 at the MTD in combination with pembrolizumab

Study enrollment: 9-18 subjects per cohort

Enrollment includes 12-18 subjects per cohort

The study is conducted in four phases:

- Phase 1: Dose Escalation
- Phase 2: Dose Expansion
- Phase 3: Basket Studies
- Phase 4: Combination Studies