Methods

Study Design: Randomized Double-blind Study of Subcutaneous Single-Ampoule Dosing (SAD) of NKTR-358 in Healthy Volunteers

Study Objectives

• Assess the effects of subcutaneous administration of single-ascending doses of NKTR-358 on immune cell populations and functional assays

Study Subjects Follow-Up Completed

No Changes in Numbers of Tcon Cells and Low-level Increases in Numbers of CD56+ NK Cells in

NKTR-358 is Safe and Well Tolerated in Healthy Volunteers

No dose-limiting toxicities, deaths, or AEs occurring at any dose

• No clinically significant virolinks, ECGs, or physical examination abnormalities

Additional adverse events primarily limited to mild nausea, headache, or injection site reactions

1 subject at the highest dose tested (28 µg/kg) experienced mild (Grade 1) signs and symptoms of vomiting, diarrhea, anorexia, and febrile neutropenia, consistent with elevated liver function tests

No anti-drug antibodies detected

NKTR-358 0.3 µg/kg (n=9)

– 1 subject at the highest dose tested (28 µg/kg) experienced mild (Grade 1) signs and symptoms of vomiting, diarrhea, anorexia, and febrile neutropenia, consistent with elevated liver function tests

– No anti-drug antibodies detected

NKTR-358 20.0 µg/kg (n=13)

– No Changes in Numbers of Tcon Cells and Low-level Increases in Numbers of CD56+ NK Cells

– Adverse events primarily limited to mild or moderate (Grade 1 or 2) injection site reactions

– 1 subject at the highest dose tested (28 µg/kg) experienced mild (Grade 1) signs and symptoms of vomiting, diarrhea, anorexia, and febrile neutropenia, consistent with elevated liver function tests

– No anti-drug antibodies detected

NKTR-358 28.0 µg/kg (n=9)

– 4 subjects experienced Grade 1 mild events of headache

– Adverse events primarily limited to mild or moderate (Grade 1 or 2) injection site reactions

– No clinically significant vital sign, ECG, or physical examination abnormalities

References

*All authors are employees of Nektar Therapeutics and have ownership interest (including stock, patents, etc.) in the same. Study funded by Nektar Therapeutics.


1. Langowski J, et al.

• Data provide strong support for studying NKTR-358 in autoimmune and inflammatory diseases

• Tregs induced by NKTR-358 are activated, as measured by flow cytometry and RNA expression analyses

• The induction of Tregs is selective, with no measurable changes in numbers and percentages of CD4+ and CD8+ Tcons at all doses tested

• NKTR-358-dependent differential expression of 13 genes significantly correlated with induction of Tregs as measured by flow cytometry

• 84 genes identified that show consistent trend of dose-dependent changes in expression in response to NKTR-358 administration

• Increase in number and magnitude of differentially expressed genes in response to NKTR-358 administration

• NKTR-358-dependent differential expression of 13 genes significantly correlated with induction of Tregs as measured by flow cytometry

Conclusions

• Safe and well tolerated in this first in human study

• Limited dose-dependent expansion of numbers and proliferating CD25+ Treg cells, as demonstrated by flow cytometric and cytokine/chemokine assays

• The induction of Tregs is selective, with no measurable changes in numbers and percentages of CD4+ and CD8+ Tcons at all doses tested and low-level increases of NK cell numbers at highest doses tested

• Tregs induced by NKTR-358 are activated, as measured by flow cytometric and cytokine/chemokine assays

• Data provide strong support for studying NKTR-358 in autoimmune and inflammatory diseases

• NKTR-358 can also be evaluated in a multiple ascending dose study in patients with systemic lupus erythematosus (CT1558078N) and additional Phase II studies in adults with psoriatic arthritis (CT15165573) and atopic dermatitis (CT15219935)

Post#0098

Selective Induction of Activated Regulatory T-cells in Healthy Volunteers by NKTR-358, a Novel IL-2 Conjugate Treg Stimulator, in Development for Treatment of Autoimmune Diseases

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Background

IL-2 is Critical for Treg Expansion, Function and Control of Immune Responses by Regulatory T-cells (Tregs)

• Tregs are regulatory T cells, including suppressor T cells (Th3), CD4+CD25+ FOXP3+ cells, and associated with

• Reduced Treg numbers

• Impaired Treg function

• Reduced cytokine production

NKTR-358: PEG-conjugated IL-2 Selectively Induces Tregs and Their Suppressive Activity

• Impaired Treg function

• Increased half-life

• Induces Tregs and their suppressive activity

• Selectively cutaneous hypersensitivity

• Treg subpopulation with highest CD25 expression; expected to

• Further characterize their activity following NKTR-358 administration

• Potential for...