A Novel Class of NK-Cell Engagers Targeting NKp30

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Compass Therapeutics’ NK Cell Engager Platform

Functions of NK cells

- Rapid, first responders
- Highly potent
- Versatile target killing ability
- Critical immune system mediators

Compass’ lead NK cell engager demonstrates highly efficient tumor cell killing

Green: live Multiple Myeloma tumor cells

E:T ratio (2:1)

Effectors = primary NK cells
Targets = MM1R cells
Components of Optimized NK Engagers

1. Specifically target 1 or more tumor associated antigens (TAA’s) to localize activity and reduce toxicity

2. Optimally engage CD16a through Fc to drive effective ADCC response

3. Trigger signaling of additional NK activating receptors to synergistically amplify CD16a response or maintain activity after CD16a downregulation

4. Inhibit checkpoint pathways to prevent NK cell suppression
Compass’ Novel Anti-NKp30 Bispecific Platform
Empirical Discovery of Optimal Bispecific NK Engagers

Comprehensive antibody discovery

Panel of StitchMabs™ and CLC bispecifics

Anti-NKp30 bispecific identified as superior
- Better activity than anti-BCMA monoclonal
- Activity does not require CD16a engagement

BCMA [B cell maturation antigen]
- Restricted expression in plasma cells
- Expressed in malignant cells from untreated and relapsed multiple myeloma (MM) patients
- Despite several drugs have improved patient survival, MM remains an unmet medical need

NK-R

Synergistic NK activation

BCMA [B cell maturation antigen]

Restricted expression in plasma cells
- Expressed in malignant cells from untreated and relapsed multiple myeloma (MM) patients
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NK-R

Synergistic NK activation
NKp30 is a Potent Activating Receptor Expressed on NK cells and Other Effector Cells

- NKp30 is a potent activating receptor on NK cells
- Expresses on NK cells and subsets of effector T-cell populations such as γδ T cells
- Known roles in tumor control and pathogen clearance


Compass NK cells engagers activate CD16+ and CD16- NK cells

NKp30 is expressed on γδ T cells in the bone marrow of MM patients
CTX-4419 Induces Potent NK Cell Killing of Target Cells

- Better potency than BCMA-IgG1 mAb
- Potent activity towards targets cells with high, medium & low BCMA
CTX-4419 Does Not Activate NK Cells in the Absence of BCMA Expressing Target Cells

Opportunity for Better Safety Profile Compared to Other Cell Engagers

Primary NK cells, H929 target cells, 10 nM antibody
Single Dose of CTX-4419 Potently Depletes Immunoglobulin-Secreting Cells in Bone Marrow of Cynomolgus Monkeys and Decreases Serum IgM levels

Animal #AK749J

Animal #B6016

CTX-4419 displays IgG-like PK in cynomolgus monkey
Compass’ NK Engager Platform Summary

- **Key properties of CTX-4419, a first-in-class NKp30xBCMA bispecific**
  - *Potent* - Enhances ADCC, cytokine production, and NK-cell proliferation compared to monoclonal antibodies
  - *Large therapeutic window* - Active against target cells with wide range of antigen expression, but no activity in the absence of target
  - *Resistant to CD16a downregulation* - Activates NK cells in the absence of CD16a engagement
  - *Highly manufacturable* - Monoclonal-like drug-like properties and pharmacokinetics
  - *Flexible format* – Common-LC format amenable to multi-TAA or multi-NKR targeting
  - *Potential to target additional effector cell types*

- **CTX-4419 induces potent depletion of plasma cells in cynomolgus monkeys**

- **Compass’ highly modular platform has the potential to tailor TAA and NK cell receptors to target multiple indications**
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**COMPASS THERAPEUTICS**

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Thank you!