# Initial Safety and Efficacy Data from Nexicart-2, the First U.S. Trial of a CAR-T (NXC-201) in Relapsed or Refractory (R/R) Light Chain (AL)

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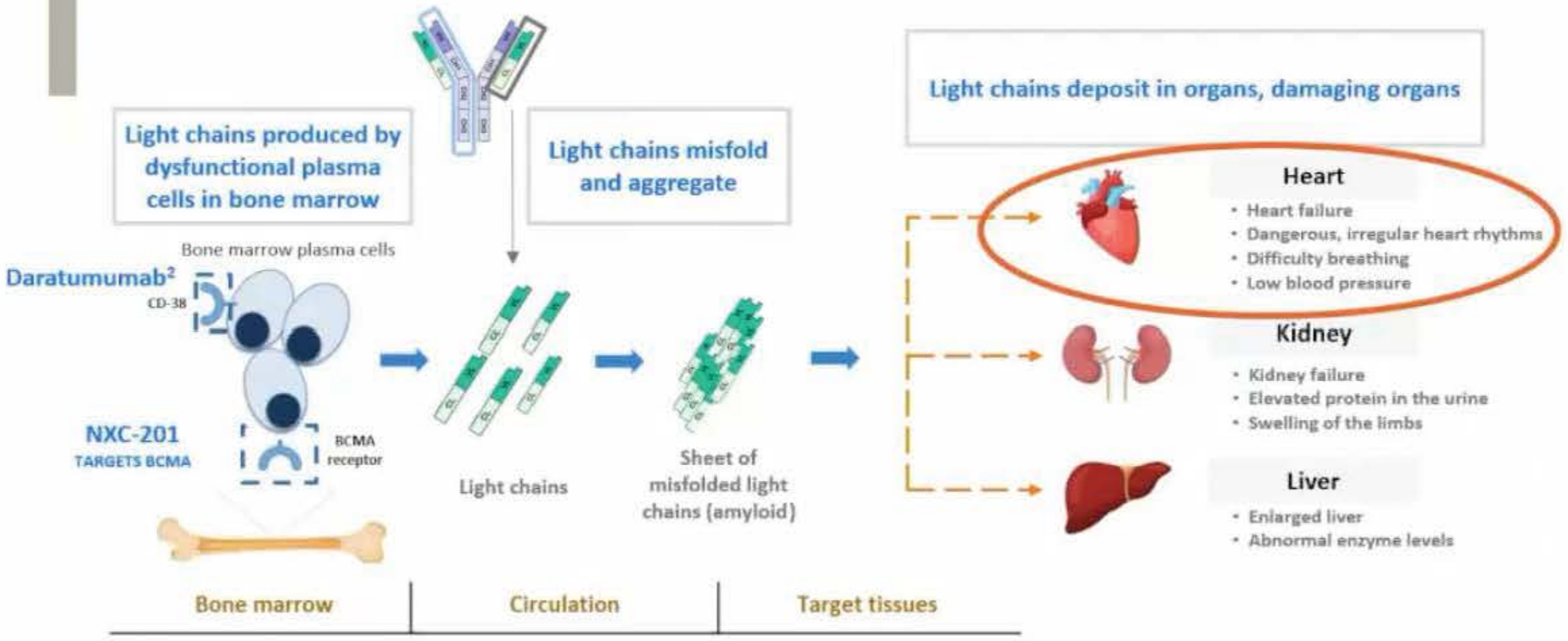
# Overview / Conclusion

- Initial results from Nexicart-2 suggest NXC-201 can be administered safely & efficiently to patients with relapsed/refractory (R/R) AL amyloidosis
  - mild + manageable CRS and no neurotoxicity
- 100% experienced rapid and deep hematologic responses
  - Organ responses in 80% evaluable patients
- To date, no hematologic relapse or progression observed

**Multicenter trial is ongoing and continuing to accrue**

# Relapsed/Refractory AL Amyloidosis: ~23,000 U.S. Patients with No FDA Approved Drugs[1]




1. Quock et al. Blood Adv. 2018.
2. Kastritis et al. NEJM 2021.

# NXC-201: Sterically-Optimized CAR-T construct

**N-GENIUS PLATFORM**

**"Digital Filter"....** **...decrease nonspecific activation**

Sterically-optimized key construct modifications

**1 Proprietary Optimized CD3 – "CD3ζγ"**

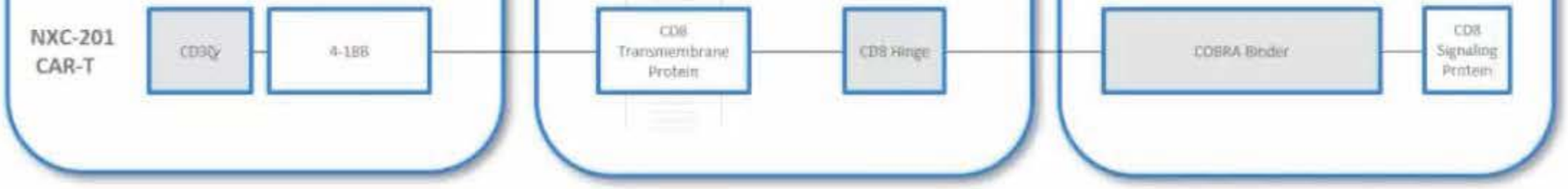
✓ Delivers "Digital" Intracellular Signaling

**2 Proprietary Optimized CD8 Hinge Flexibility**

✓ Reduces cytokine release

**3 Proprietary Optimized COBRA Binder**

✓ Enhances Plasma Cell Binding
✓ Ensures High Expression




**Manufacturing time: 10 days**

1. Harush O et al. Haematologica 2022.
2. Lebel E et al. JCO 2024.

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# NEXICART-2: First CAR-T Trial Designed For R/R AL Amyloidosis (NCT06097832)

## Study design

- Open-label, single-arm, multi-site phase 1/2 study
- n=40 patients

## Key criteria

| | |
|---|---|
| **Inclusion** | • Exposed to at least 1 line of therapy, including CD38 monoclonal antibody + proteosome inhibitor<br>• Measurable hematologic disease, defined by one of the following:<br>- dFLC* >50 mg/L (or 5 mg/dl)<br>- M-spike > 0.5 mg/dl<br>- dFLC* >20 mg/L (or 2 mg/dl) with abnormal k/l ratio[1] |
| **Exclusion** | • Prior anti-BCMA directed therapy<br>• Cardiac: Mayo stage 3b, NYHA class III/IV<br>• Concomitant Symptomatic Multiple Myeloma |

* dFLC = difference between the involved and uninvolved free light chain

## Outcome measures

### Phase 1

- Safety
- Efficacy: Complete hematologic response (CR) based on validated criteria[2,3]

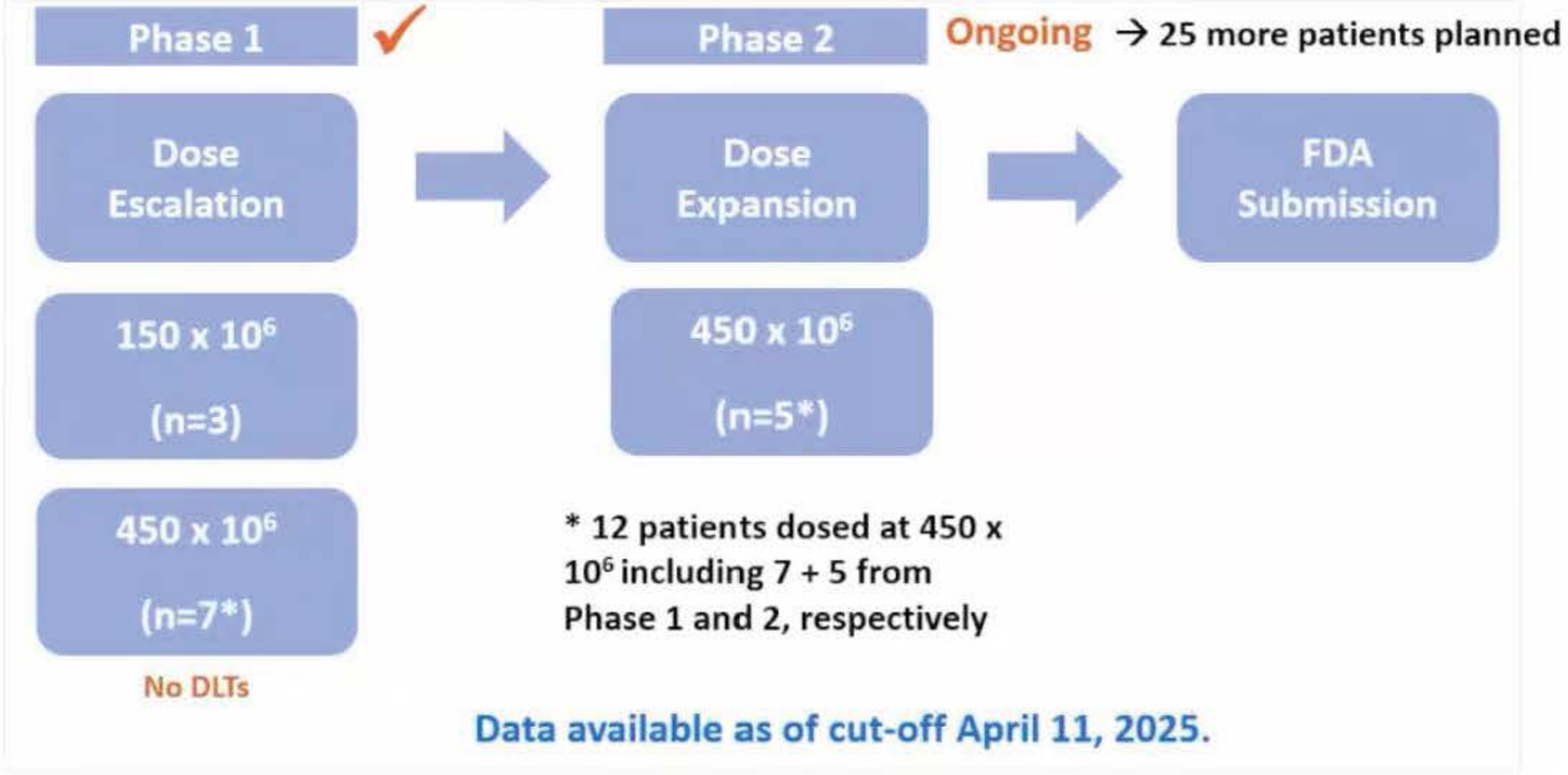
### Phase 2

- Efficacy: CR based on validated criteria in AL amyloidosis[2,3]
- Safety

1. Milani et al. Blood 2017.
2. Palladini G et al. JCO 2012.
3. Palladini G et al. Amyloid 2021.

# NEXICART-2: Status

**Open to accrual June 2024**





Palladini G et al. JCO 2012.
Palladini G et al. Amyloid 2012.
Milani et al. Blood 2017.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# NEXICART-2: Patient Characteristics

| | NX2-001 | NX2-002 | NX2-003 | NX2-004 | NX2-005 | NX2-006 | NX2-007 | NX2-008 | NX2-009 | NX2-010 | Median (range) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Age | 56 | 67 | 82 | 64 | 62 | 72 | 77 | 66 | 63 | 80 | 67 (56-82) |
| Gender | Female | Female | Male | Female | Female | Male | Male | Male | Male | Male | - |
| Prior lines of therapy | 4* | 6** | 2 | 4 | 4* | 3 | 12* | 4* | 4* | 3* | 4 (2-12) |
| dFLC (mg/L) | 65 | 24 | - | 86 | 42 | 26 | 47 | 121 | 84 | - | 56 (24-121) |
| M-spike (g/dL) ¥ | - | - | 0.79 | - | - | - | - | - | - | 0.65 | - |
| Organ involvement | Heart | Heart/GI/ nerve | Kidney | Heart/GI | Kidney | Heart | Nerve | Heart | Heart | Kidney/ Heart | - |
| NYHA stage | I | II | I | I | I | I | I | II | I | II | - |
| NT-ProBNP (ng/L) | 146 | 560 | 1,297 | 218 | 805 | 989 | 143 | 909 | 289 | 290 | 425 (143-1,297) |
| hs-Troponin-I (ng/L) | 7 | 6 | 42 | 7 | 9 | 31 | 14† | 47 | 6 | 52 | 9 (6-52) |
| Mayo Stage At Diagnosis | II | II | II | IIIa | I | IIIa | I | II | IIIb | IIIa | |
| At Enrollment | I | II | - | I | - | IIIa | - | IIIa | I | II | - |
| Creatinine (mg/dL) | 0.7 | 1.1 | 2.2 | 1.8 | 2.7 | 0.8 | 1.3 | 0.8 | 0.9 | 0.9 | 1.0 (0.7-2.7) |
| Albuminuria (mg/24 hrs) | 143 | 0 | 3,032 | 10 | 10,274 | 0 | 135 | 360 | 13 | 2,153 | 143 (0-10,274) |

* Prior autologous stem cell transplantation (ASCT)

** Two prior ASCT

¥ M-spike value if used as measurable disease

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# NEXICART-2: Safety

## CRS and ICANS reported according to ASTCT Consensus Grading

| Subject | | NX2-001 | NX2-002 | NX2-003 | NX2-004 | NX2-005 | NX2-006 | NX2-007 | NX2-008 | NX2-009 | NX2-010 | Median (Range) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dose | CART Cell Dose ($x10^6$) | 150 | 150 | 150 | 450 | 450 | 450 | 450 | 450 | 450 | 450 | - |
| | CRS | None | None | Grade 2 | Grade 1 | Grade 1 | Grade 1 | Grade 1 | Grade 1 | Grade 1 | Grade 1 | 1 (1-2) |
| | CRS Onset (days) | None | None | 3 | 3 | 1 | 1 | 1 | 1 | 1 | 3 | 1 (1-3) |
| | CRS Duration (days) | None | None | 1 | 1 | 1 | 1 | 1 | 4 | 1 | 2 | 1 (1-4) |
| | Neurotoxicity | None | None | None | None | None | None | None | None | None | None | - |
| Other | Neutropenia | Grade 3 | Grade 3 | Grade 3 | Grade 4 | Grade 4 | Grade 2 | Grade 4 | Grade 4 | Grade 4 | Grade 2 | 4 (2-4) |
| | Febrile Neutropenia | None | None | None | None | None | None | None | Grade 3 | None | None | - |
| | Anemia | Grade 1 | Grade 2 | Grade 3 | Grade 1 | Grade 3 | Grade 1 | Grade 1 | Grade 2 | Grade 1 | Grade 1 | 1 (1-3) |
| | Thrombo-cytopenia | Grade 1 | Grade 1 | Grade 1 | Grade 1 | Grade 3 | Grade 2 | None | Grade 4 | Grade 3 | Grade 1 | 1 (1-4) |
| | Acute kidney injury | None | None | None | None | Grade 4* | None | None | None | None | None | - |
| | LFT Abnormalities | Grade 2 | None | None | None | None | None | None | Grade 1 | None | None | - |
| | ≥ Grade 3 Infections | None | Grade 3 | Grade 3 | None | Grade 5* | None | None | None | None | None | - |
| | Fatigue | None | Grade 2 | Grade 2 | Grade 2 | None | Grade 1 | None | None | None | None | 2 (1-2) |
| | Cardiac Event | None | None | None | Grade2¥ | None | None | None | None | None | Grade 2¥ | - |

CRS = cytokine release syndrome

*Acute on chronic kidney injury in patient with stage 4 CKD at enrollment

¥ Two patients with pre-existing atrial fibrillation experienced transient arrythmias response to beta-blockers

Lee DW et al. BBMT 2019.

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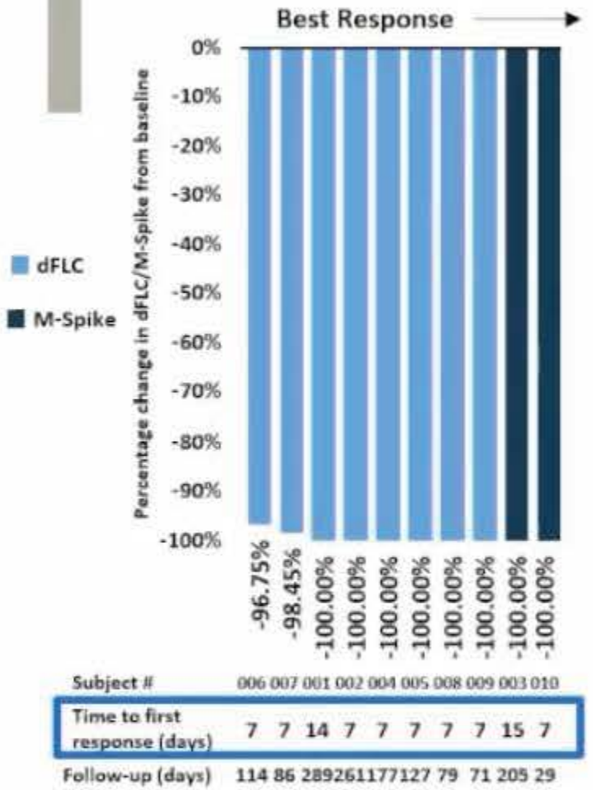
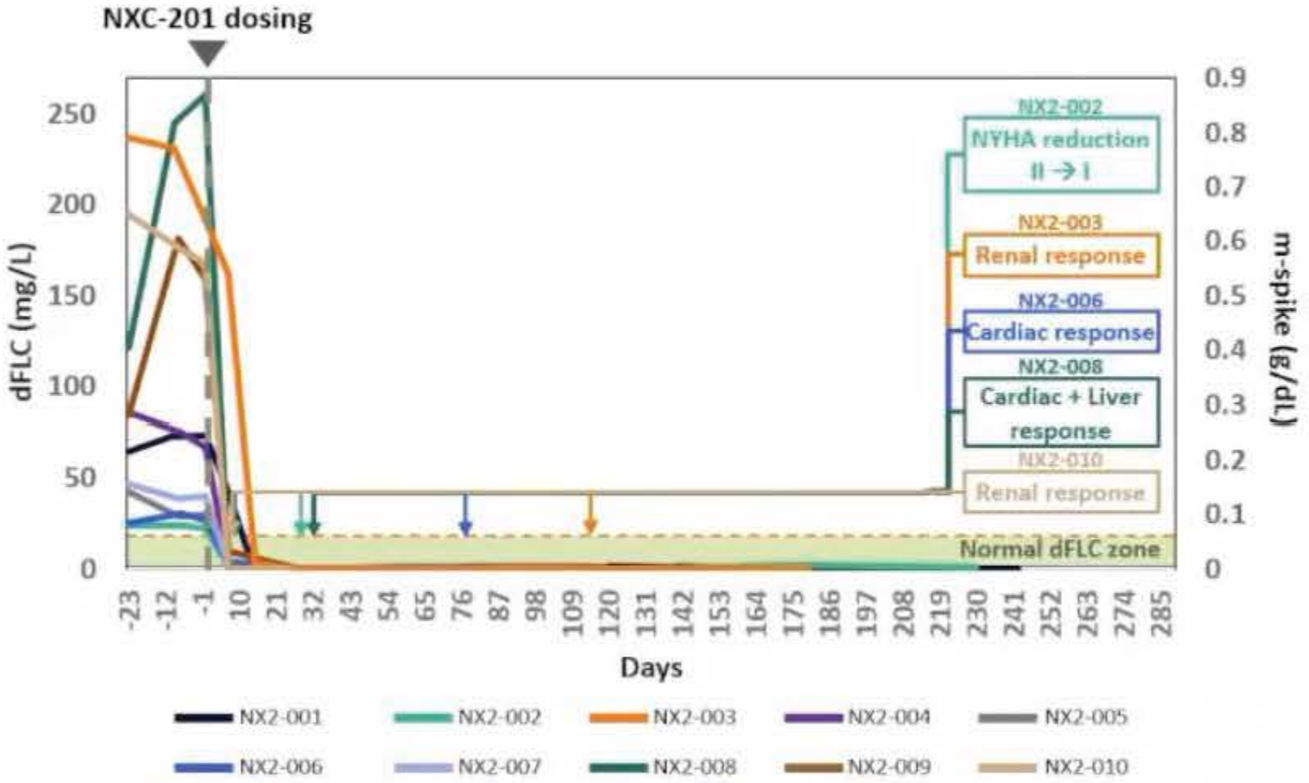
# NEXICART-2: Results

**Data available as of cut-off April 11, 2025. Median follow up 121 days (range 29-289).**

**Rapid normalization of pathologic paraprotein associated with organ responses**




- All patients' disease marker normalized as of data cut-off or last follow up
- Immunofixation may persist for longer

- 2/2 patients with cardiac evaluable disease achieved a cardiac response (at month 1 and 3)
- 2/3 patients with renal evaluable disease responded (at month 1 and 4)
- Renal progression in 1 patient – within first month; no cardiac progression
- 1 patient improved from NYHA class II to class I at day +15


Palladini G et al. JCO 2012.
Palladini G et al. Amyloid 2012.
Milani et al. Blood 2017.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# … In Patient's Own Words (day +15)

"Hi Dr Landau! Here we are a week tomorrow since I left the hospital (At day 10 after those magic CAR-T cells came on board)! Just had to tell you I've been very happily & comfortably walking 2-3+ miles each day & doing great on the inclines (even the cross overs on the River walk!) as we explore different nooks & crannies & sidewalk cafes of the beautiful Upper East Side!!! (Eating plenty at those cafes too!) I know you said CAR-T should be easier than stem cell transplant, & that has proven to be more accurate than I could have hoped for!! The hospital path was so much smoother & less eventful than the stem cell days! I never thought I'd be feeling this strong & vibrant, just 15 days after my CAR-T cell infusion!! Nor did I ever guess that I'd be feeling stronger & experiencing less of that horrible leg fatigue, shortness of breath & chest tightness, that was ever increasing & weighing me down for the months preceding this!! AMAZING & truly beyond my wildest dreams!! My family & I can never thank you & your teams enough for all you do continuously to bring these amazing treatment options to us, & for the amazing beautiful way you guide us through! I'd be happy to share my experience with other patients considering CAR- T cells, if that's an option at some point. See you soon! 🥰🌼💪"

# NEXICART-2: hematologic responses as reviewed by an independent review committee

**Data available as of cut-off April 11, 2025. Median follow up 121 days (range 29-289).**

| | Subject # | NX2-001 | NX2-002 | NX2-003 | NX2-004 | NX2-005 | NX2-006 | NX2-007 | NX2-008 | NX2-009 | NX2-010 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | NXC-201 Dose (million CAR+T cells) | 150 | 150 | 150 | 450 | 450 | 450 | 450 | 450 | 450 | 450 |
| AL Amyloidosis Disease Markers | Status as of data cutoff | Normal | Normal | Normal | Normal | Normal | Normal | Normal | Normal | Normal | Normal |
| | Time to normalization (days) | 14 | 7 | 15 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
| | Hematologic response | CR | CR | CR | VGPR MRD(-) $10^{-6}$ | CR | CR | Low dFLC PR MRD(-) $10^{-6}$ | CR | VGPR MRD(-) $10^{-6}$ | CR |


- 70% achieved a hematologic CR
- 3 immunofixation positive, MRD – in the bone marrow
- 1 death unrelated to NXC-201 at 5 mos following tx

Minimal residual disease (MRD) negativity was assessed by 10-color flow cytometry or clonoSEQ with sensitivity $10^{-6}$


Palladini G et al. JCO 2012.
Palladini G et al. Amyloid 2012.
Milani P et al. Blood 2017.
Roshal M et al. Blood Advances 2017.


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# Conclusion

- NXC-201 can be administered safely & efficiently to patients with R/R AL amyloidosis – population without a single FDA-approved treatment available – who have a true unmet medical need
  - All (100%) received treatment with a vein-to-vein time 14 days
  - Low grade CRS and no neurotoxicity of any kind
- All (100%) experienced rapid and deep hematologic responses, median time to first & best response 7 + 26 days, respectively
  - At day+25, 8/9 evaluable patients MRD negative ($10^{-6}$ sensitivity)
  - 70% hematologic CR rate at early timepoint, but evolving
  - Organ responses documented in 4/5 evaluable patients
  - At a median follow up 121 days (range: 29-289), no hematologic relapse or progression observed

**Multicenter trial is ongoing and continuing to accrue to the expansion cohort**

# A Giant Thank You....

- The research staff, clinical teams, apheresis units, cell therapy labs and investigators at each participating site
- The patients and their families

## Thank you for your attention!

Study was funded by:

IMMIX BIOPHARMA

NEXCELLA

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