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)

Heather J. Landau, MD[1], Charlotte Hughes, MD[1], Aaron Seth Rosenberg, MD[2], Mehrdad Abedi, MD[2], Shahzad Raza, MD[3], Jeffrey A. Zonder, MD[4], Eugene Brailovski, MD[1], Sergio Giralt, MD[1], Sham Mailankody, MBBS[1], Jae H. Park, MD[1], Miguel-Angel Perales, MD[1], Saad Z Usmani, MD[1], David Marks, MBBS, PhD[5], Raymond Comenzo, MD[6], Sridevi Rajeeve, MD[1], Jennifer Liu, MD[1]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]University of California Davis, Davis, CA; [3]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH; [4]Barbara Ann Karmanos Cancer Institute, Detroit, MI; [5]Immix Biopharma, Los Angeles, CA; [6]Department of Hematology-Oncology, Tufts Medical Center, Boston, MA

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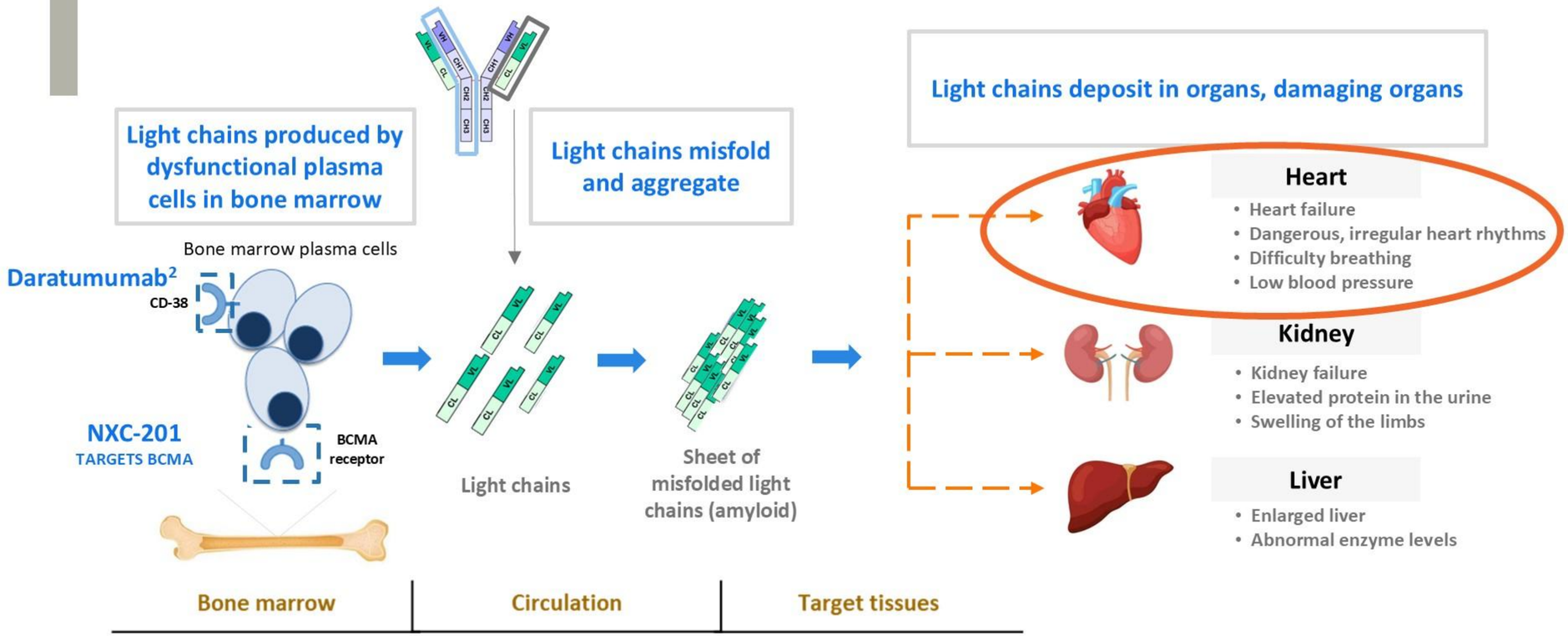
Overview / Conclusion

- 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**

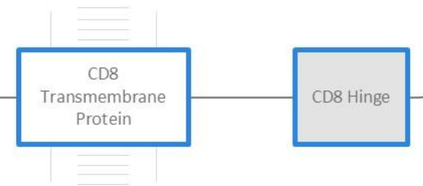
Sterically-optimized key construct modifications

1 Proprietary Optimized CD3 – "CD3ζγ"

✓ **Delivers "Digital" Intracellular Signaling**

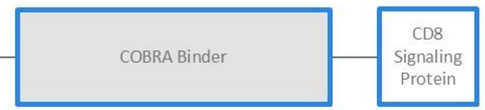
2 Proprietary Optimized CD8 Hinge Flexibility

✓ **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 • Measurable hematologic disease, defined by one of the following: - dFLC* >50 mg/L (or 5 mg/dl) - M-spike > 0.5 g/dl - dFLC* >20 mg/L (or 2 mg/dl) with abnormal k/l ratio[1]
Exclusion	• Prior anti-BCMA directed therapy • Cardiac: Mayo stage 3b, NYHA class III/IV • 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.

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NEXICART-2: Status

Open to accrual June 2024

Phase 1 ✓

Dose Escalation

- 150 x 10^6 (n=3)
- 450 x 10^6 (n=7*)

No DLTs

Phase 2 Ongoing → 25 more patients planned

Dose Expansion

- 450 x 10^6 (n=5*)

* 12 patients dosed at 450 x 10^6 including 7 + 5 from Phase 1 and 2, respectively

Data available as of cut-off April 11, 2025.

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

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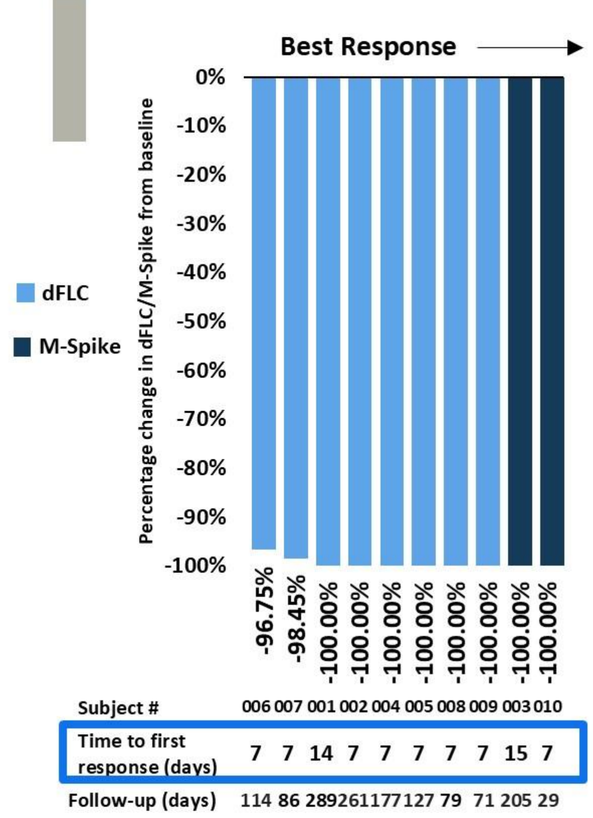
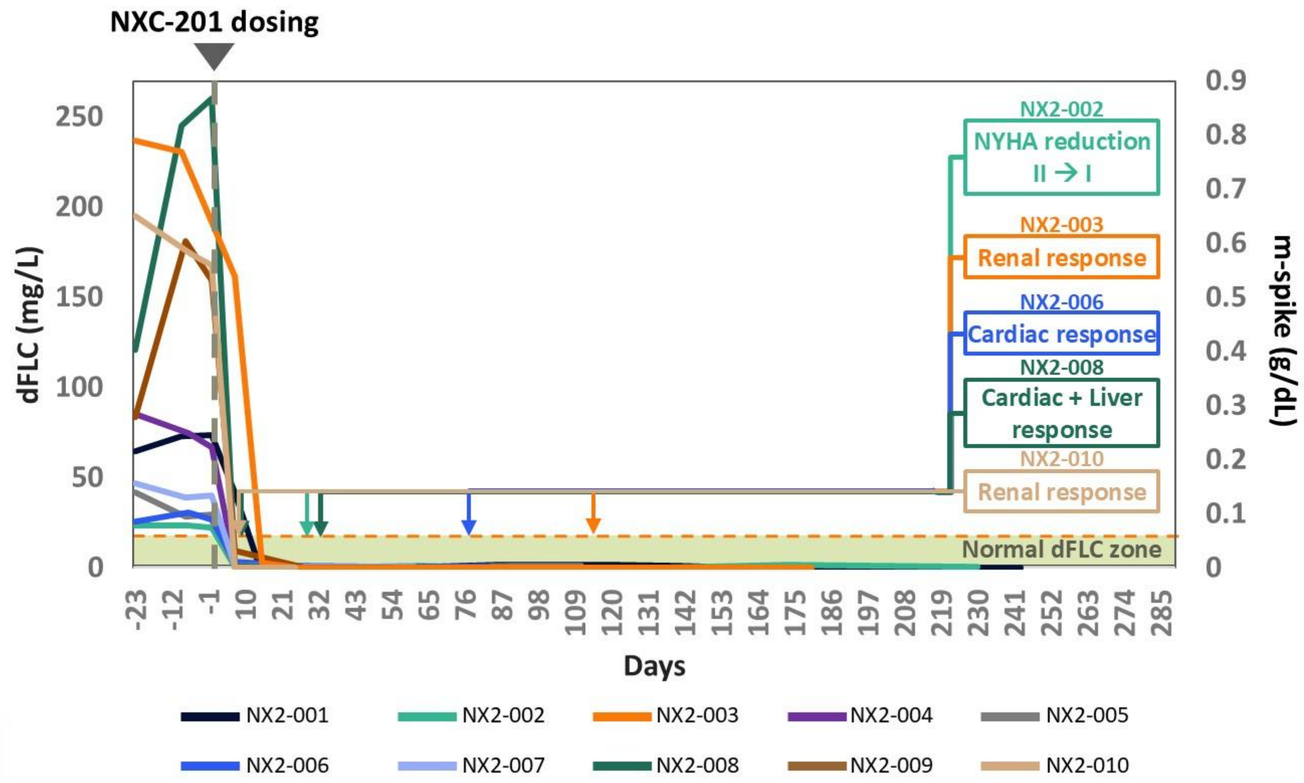
Lee DW et al. BBMT 2019.

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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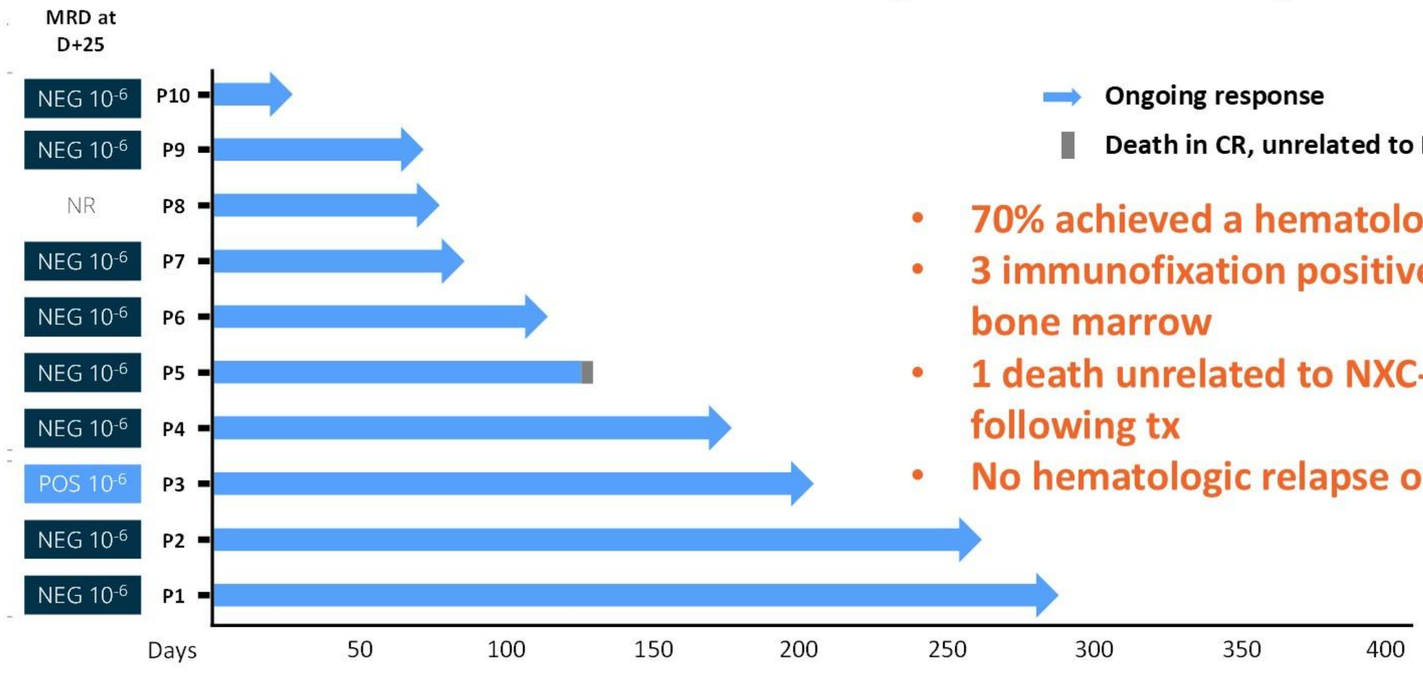
… In Patient's Own Words (day +15)

"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**



Ongoing response

Death in CR, unrelated to NXC-201

- 70% achieved a hematologic CR
- 3 immunofixation positive, MRD – in the bone marrow
- 1 death unrelated to NXC-201 at 5 mos following tx
- No hematologic relapse or progression

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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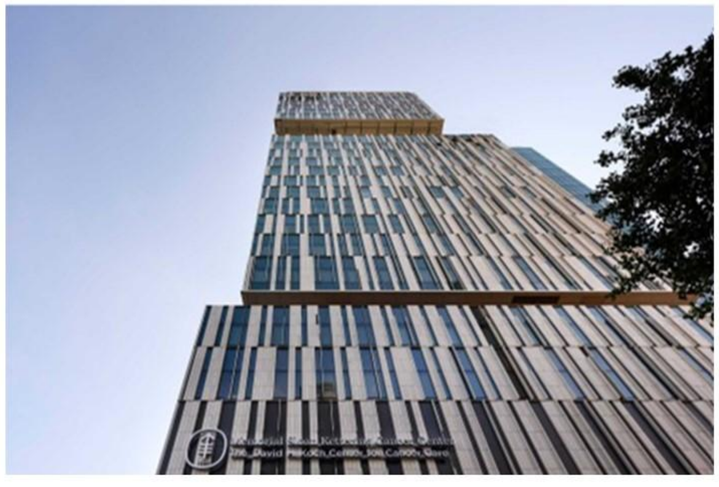
Conclusion

- **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!

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