

# CAR-T Clinical Trailblazer in AL Amyloidosis and autoimmune diseases

July 2024



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## NXC-201: The only CAR-T in AL amyloidosis

- NXC-201 could transform the treatment of Relapsed/Refractory AL amyloidosis (~30,000 prevalence, ~3,000 annual incidence US patients, \$3bn market)
- NXC-201 CART construct provides barrier to entry
- NEXICART-1: 92% (12/13) overall response rate with 75% (9/12) complete response rate in patients without prior BCMA bispecifics exposure

## Clinical profile ideal for autoimmune

- Established clinical profile across large 76 patient dataset dosed with NXC-201: well-suited to treat autoimmune
- Short duration of cytokine release syndrome
- Lack of neurotoxicity

## Sterically-optimized, proprietary CAR-T construct

- N-GENIUS platform produced NXC-201, our lead, sterically-optimized CAR-T
- 3 key CAR modifications drive unique clinical profile: CD3 $\zeta$  $\gamma$ , CD8 hinge, COBRA binder
- NXC-201 engineered specifically to solve for CAR-T tolerability (cytokine release syndrome, neurotoxicity)

## Significant Near-Term Milestones

Upcoming Milestones	Anticipated Timing
Initial NEXICART-2 clinical data presentation in AL Amyloidosis	4Q 2024
Report interim clinical data readout for NEXICART-2 trial in AL Amyloidosis	2Q/3Q 2025
Report NXC-201 interim clinical data in 2 unaddressed autoimmune indications	4Q 2025
Report final topline clinical data readout for NEXICART-2 trial in AL Amyloidosis	2Q/3Q 2026

Completed	
NASDAQ IPO 2021	✓
Formed Cell Therapy R&D taskforce in 2022	✓
Secured global commercial rights for NXC-201 from Hadassah/Bar-Ilan in 2022	✓
Reported NEXICART-1 AL Amyloidosis interim clinical data at: <b>ASGCT 2023</b>	✓
<b>ASH 2023</b>	✓
<b>ASGCT 2024</b>	✓
Dosed first US patient in NEXICART-2 AL Amyloidosis clinical trial	✓ Met mid-2024 guidance



# Pipeline: Only CAR-T in AL Amyloidosis; Tailor-Made for Autoimmune Indications

## Lead Program: NXC-201, a next-generation BCMA-targeting CAR-T for AL amyloid and autoimmune diseases

Indication	Therapy	Pre-clinical	Phase 1	Phase 2	Upcoming Milestones
Relapsed/Refractory AL Amyloidosis	NXC-201	US FDA and EU EC Orphan Drug Designation (ODD)			<b>4Q 2024:</b> Initial NEXICART-2 clinical data presentation in AL Amyloidosis  <b>2Q/3Q 2025:</b> Report interim clinical data readout for NEXICART-2 trial in AL Amyloidosis  <b>2Q/3Q 2026:</b> Report final topline clinical data readout for NEXICART-2 trial in AL Amyloidosis
Undisclosed Autoimmune Indications	NXC-201	IND enabled			<b>4Q 2025:</b> Report NXC-201 interim clinical data in 2 unaddressed autoimmune indications

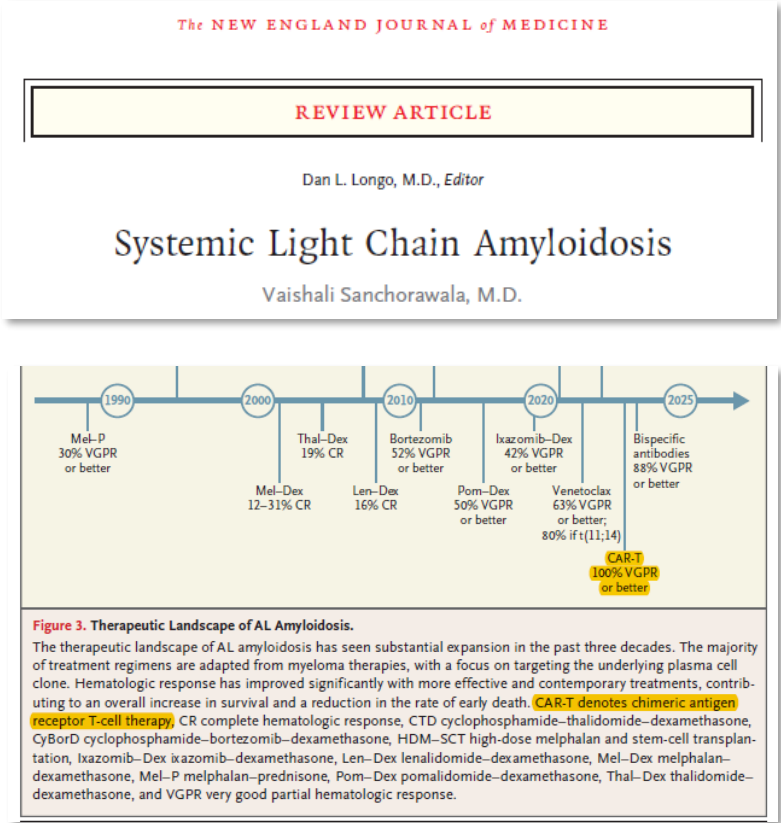
## Other Emerging Pipeline

Preclinical Candidates	Not yet announced				
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TREATMENT OF RELAPSE AND PROGRESSION AFTER INITIAL THERAPY

No consensus has been established on the criteria for commencing second-line therapy in patients with progressive disease after initial therapy.<sup>73,74</sup> Patients with relapsed disease can be treated by repeating first-line therapy if the response lasted for more than a year, although such patients have a shorter time to relapse without a reduction in overall survival than patients who are treated with a different therapy for relapsed disease.

The potential options available for the treatment of relapsed systemic AL amyloidosis include proteasome inhibitors,<sup>75,76</sup> anti-CD-38 monoclonal antibodies,<sup>77,78</sup> immunomodulatory agents,<sup>79</sup> venetoclax for patients with t(11;14),<sup>80</sup> bendamustine,<sup>81</sup> high-dose melphalan with autologous SCT,<sup>82,83</sup> bispecific antibodies,<sup>84,85</sup> and even chimeric antigen receptor T-cell therapy.<sup>86</sup> Although it is not possible to be prescriptive regarding the sequencing of therapies, the two guiding considerations are the depth and duration of the initial response and the choice of a class of agents not previously used. The limitations imposed by a patient's reduced level of fitness or frailty and end-organ damage must also be considered. Enrollment in clinical trials is encouraged.



tory AL amyloidosis: a multinational retrospective case series. Blood 2024;143:734-7.

86. Kfir-Erenfeld S, Asherie N, Grisariu S, et al. Feasibility of a novel academic ECMA-CART (HB10101) for the treatment of relapsed and refractory AL amyloidosis. Clin Cancer Res 2022;28:5156-66.

87. Nuvolone M, Nevone A, Merlini G. Targeting amyloid fibrils by passive immunotherapy in systemic amyloidosis.

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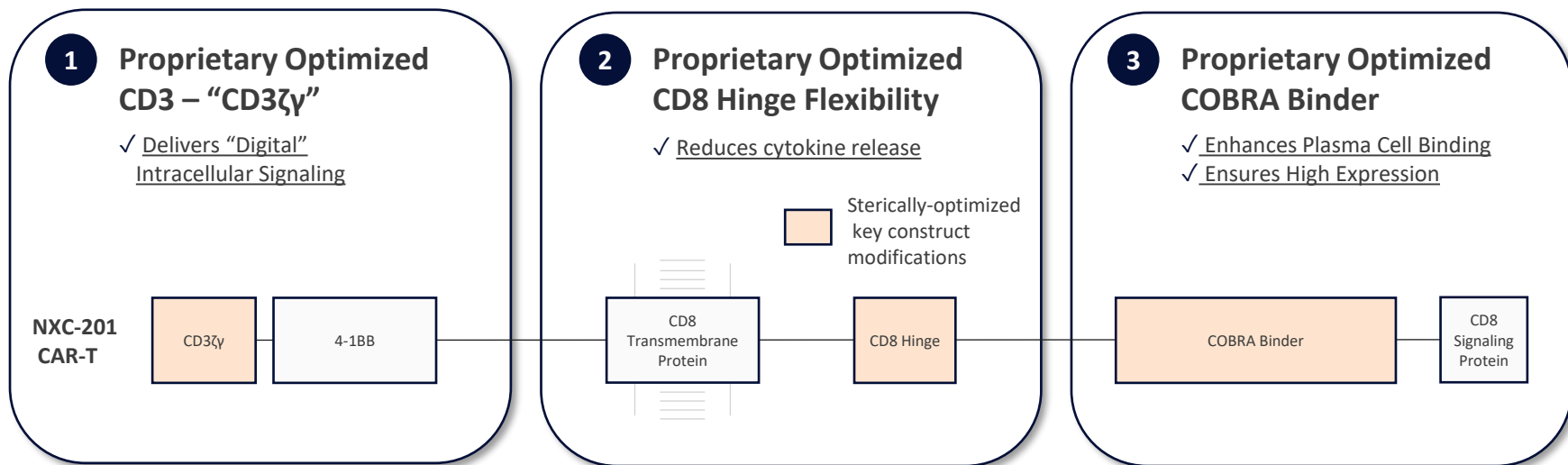


# N-GENIUS Platform: Sterically-Optimized CAR-T Construct Drives Differentiated NXC-201 Clinical Profile

ALL BCMA CAR-TS ARE NOT CREATED EQUAL

## N-GENIUS PLATFORM

Our CAR-T is differentiated based on 3 Key Construct Modifications



Immix's proprietary N-GENIUS Platform can overcome the inherent limitations of conventional CAR-T methodologies that lack the sterically-optimized CD3ζγ (“Digital” Signaling), CD8 hinge flexibility, and COBRA binder, which drive NXC-201's greatly reduced neurotoxicity, minimized CRS duration, and enhanced efficacy in heavily pretreated patients

*“Single amino acid substitutions at key sites can affect CAR-T function over 200-fold range”*

Source: M. Assayag, et al. Academic BCMA-CAR-T cells (HB0101), a promising approach for the treatment of LC Amyloidosis. 27th Annual Meeting of The American Society of Gene and Cell Therapy (ASGCT). Late Breaking Oral Presentation. Baltimore, MD. May, 2024. Feucht, M. Sadelain, et al. Calibration of CAR activation potential directs alternative T cell fates and therapeutic potency. Nature Medicine. 2019 Jan;25(1):82-88. doi: 10.1038/s41591-018-0290-5. Epub 2018 Dec 17. PMID: 30559421 PMCID: PMC6532069. O. Harush C. J. Cohen, et al. Preclinical evaluation and structural optimization of anti-BCMA CAR to target multiple myeloma. Haematologica. 2022 Oct 1;107(10):2395-2407. doi: 10.3324/haematol.2021.280169. PMID: 35354252 PMCID: PMC9521250. Adapted from PEGS 2021.



# Proprietary Sterically-Optimized CD3ζ + CD8 Delivers “Digital” Intracellular Signaling, Eliminates Neurotoxicity, Reduces CRS Duration

## CD3ζ

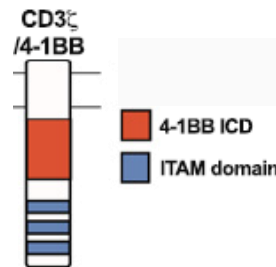
CARs rely on activation of CAR-T cells through CD3ζ derived immunoreceptor tyrosine-based activation motifs (ITAMs), typically 3 ITAM motifs per CAR

NXC-201 adds a positively charged amino acid (lysine) next to a tyrosine phosphorylation site, therefore:

- ✓ Impeding phosphorylation of ITAM1 (by affecting protein folding dynamics which block the tyrosine site), thus reducing intracellular reactivity
- ✓ Adding an additional site for ubiquitination, allowing the CAR to be marked for degradation more rapidly than a traditional CAR

The combined effect of these modifications is to drive a “digital” signaling of extracellular activity, that is on when antigen is present and off when not

Modification of ITAMs is a common theme in third-generation CAR design, with publications in Nature Medicine and by Memorial Sloan Kettering on the topic



## nature Signal Transduction and Targeted Therapy

“In activated T cells, the CD3ζ chain gets ubiquitinated by CBLB at its multiple lysine residues and induces degradation of surface TCRs”

doi: 10.1038/s41392-021-00823-w

nature  
medicine



Memorial Sloan Kettering  
Cancer Center

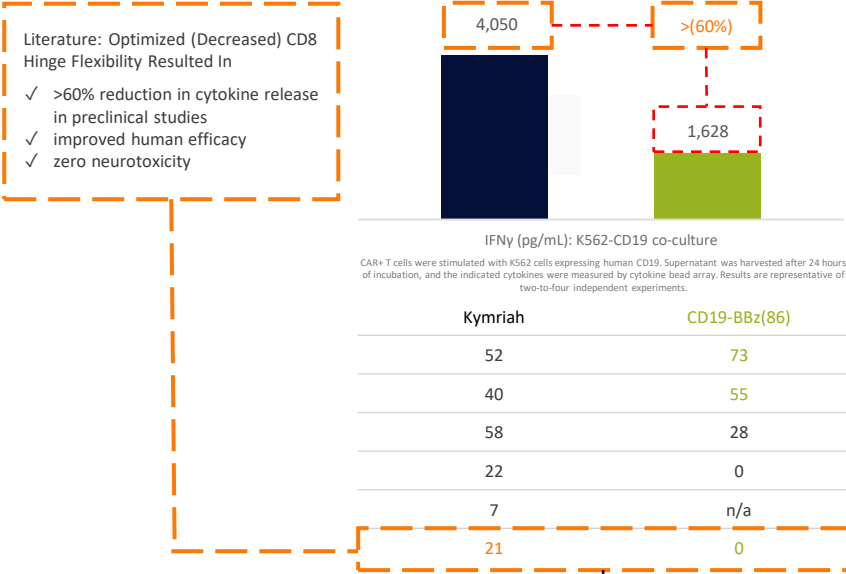
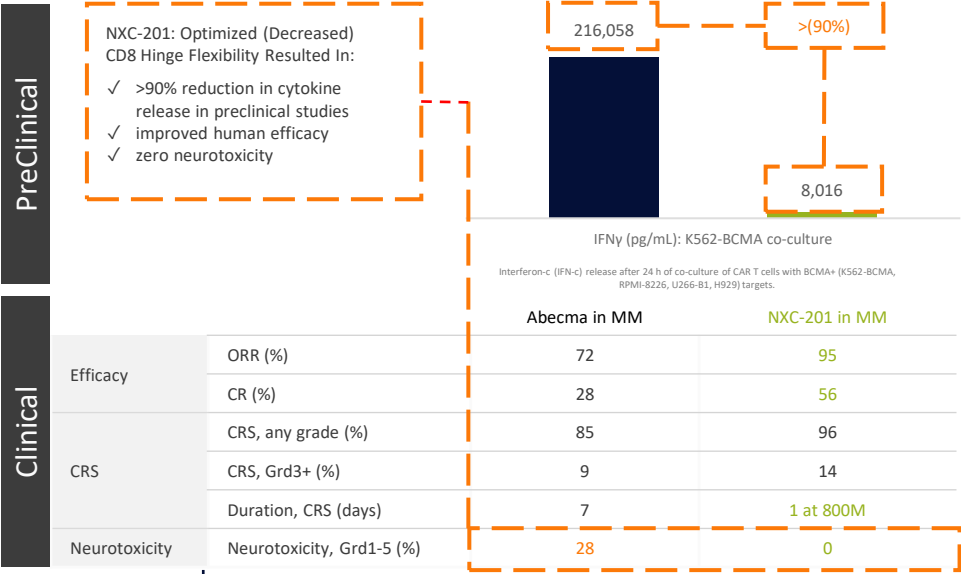
“We hypothesized that the redundancy of CD28 and CD3ζ signaling in a chimeric antigen receptor (CAR) design incorporating all three CD3ζ immunoreceptor tyrosine-based activation motifs (ITAMs)<sup>11,13</sup> may foster counterproductive T cell differentiation and exhaustion. Therefore, we calibrated ITAM activity by mutating tyrosine residues to impede their phosphorylation and downstream signaling”

doi: 10.1038/s41591-018-0290-5

# Proprietary Sterically-Optimized CD3ζ + CD8 Delivers “Digital” Intracellular Signaling, Eliminates Neurotoxicity, Reduces CRS Duration



## CD8 Hinge



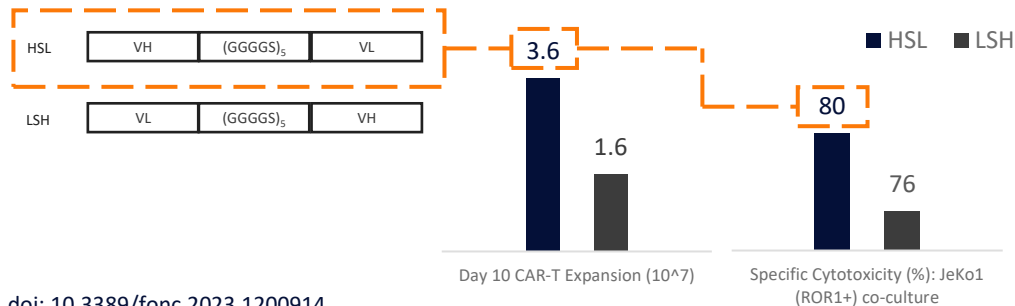
Sterically-optimized (Decreased) CD8 Hinge Flexibility Results in Zero Neurotoxicity, Improved Human Efficacy, and reduction in CRS duration

MM: multiple myeloma  
 Source: E. Lebel, et al. Safety And Efficacy of a Locally Produced Novel Anti-BCMA Chimeric Antigen Receptor T-Cell (CAR-T) (HB101) for the Treatment of Relapsed and Refractory Multiple Myeloma. 65th ASH Annual Meeting and Exposition, San Diego, CA. December 2023. Ying Z, et al. Nat Med. 2019; Schuster SJ, et al. N Engl J Med. 2019; Assayag, M., et al EBMT 2023; Abecma FDA label; Harush O, et al. Haematologica. 2022; Friedman KM, et al. Hum Gene Ther. 2018. Kymriah: Predelineal is an average of CD8+ and CD4+ T-cells, source: Milone MC, et. Al. Mol Ther. 2009 Aug;17(8):1453-64. doi: 10.1038/mt.2009.83. Epub 2009 Apr 21. Erratum in: Mol Ther. 2015 Jul;23(7):1278. PMID: 19384291; PMCID: PMC2805264. \*1 Day CRS occurred in high dose MM cohort as of EBMT 2023. NXC-201 in multiple myeloma data from ASH 2023 95% ORR in patients without prior anti-BCMA therapy exposure

### 3 Sterically-Optimized COBRA Binder Ensures High Expression And Binding Affinity

#### COBRA Binder

COBRA Binder  
Leads with  
Heavy Chain



doi: 10.3389/fonc.2023.1200914

#### Biomarker Research

Proven Linker of Heavy  
and Light Chain  
Employed

“Glycine (Gly) and serine (Ser) residues provide the flexibility necessary for antigen-binding sites to change conformation and maintain good stability in aqueous solutions... prevent[ing] formation of secondary structures and reduc[ing] likelihood of the linker interfering with the folding and function of the scFv”

September 19, 2022

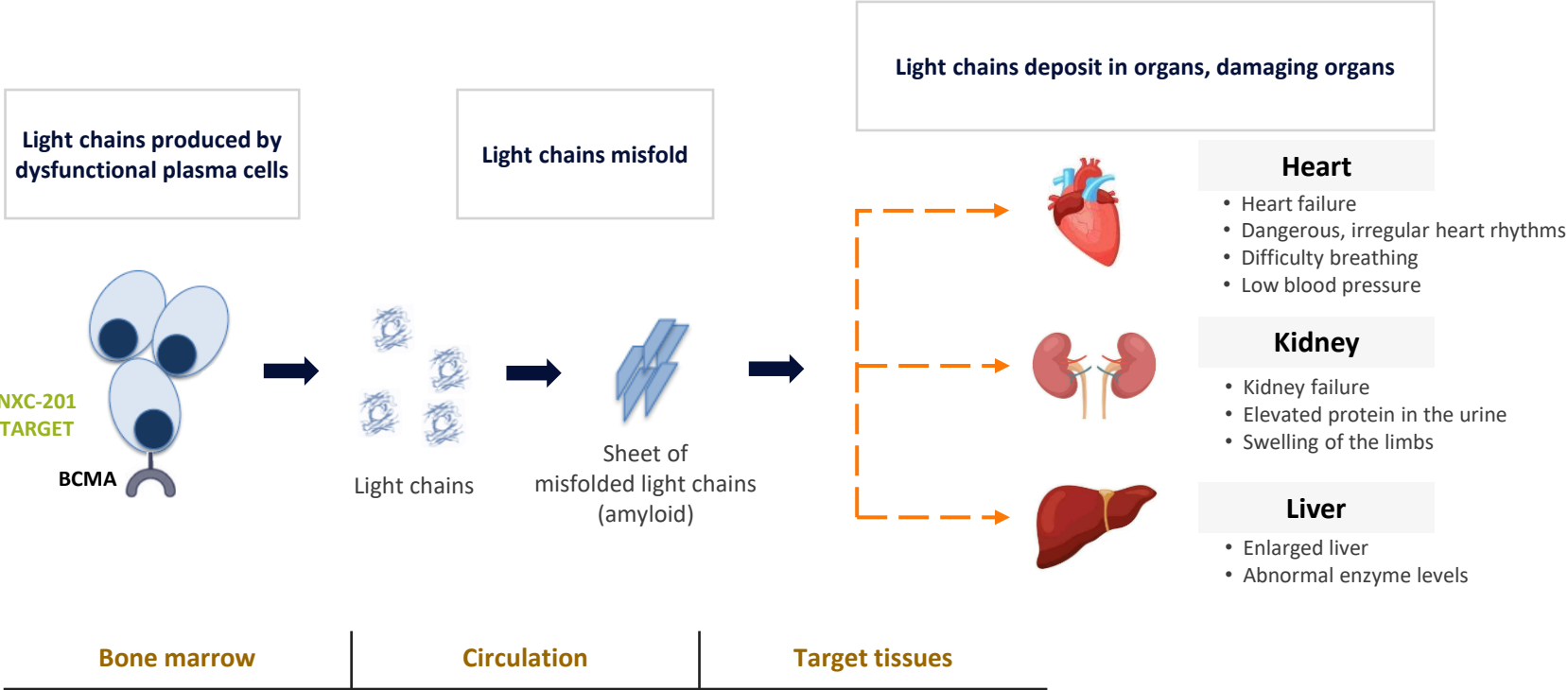
doi: 10.1186/s40364-022-00417-w

NXC-201  
COBRA Binder: Heavy  
Chain – Proven Linker –  
Light Chain Configuration,  
enabling:

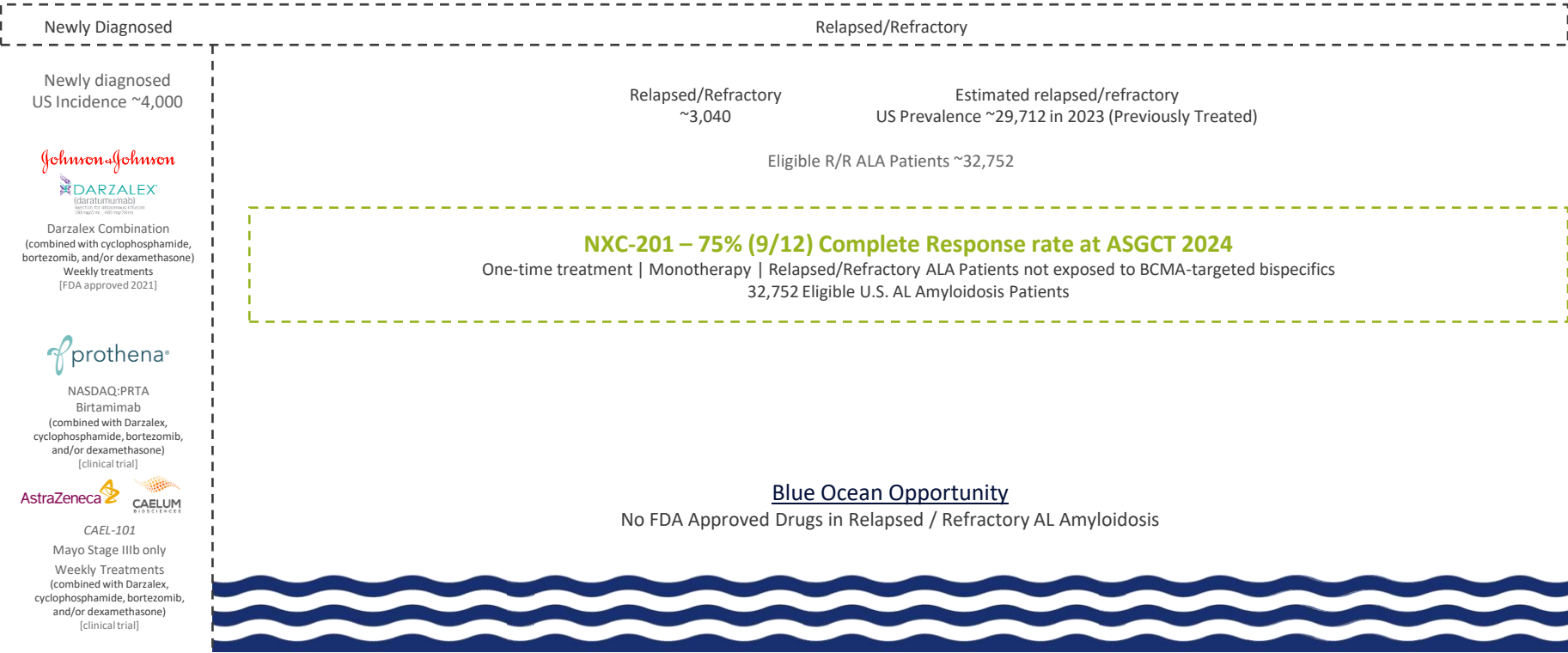
- ✓ Rapid, Sustained CAR-T Expansion
- ✓ Improved Cytotoxicity in the presence of antigen

# AL Amyloidosis: ~30,000 relapsed/refractory U.S. Patients With No FDA approved drugs

NXC-201 TARGETS AL AMYLOIDOSIS PLASMA CELLS THAT EXPRESS BCMA ON CELL SURFACE



# NXC-201 Addresses Sizable U.S. Relapsed/Refractory AL Amyloidosis Patient Population (1/2)



Blue Ocean Opportunity  
No FDA Approved Drugs in Relapsed / Refractory AL Amyloidosis

Note: Public information development plans as of 2023. Dara-CyBorD: Daratumumab, Bortezomib + cyclophosphamide + dexamethasone. BMD: bortezomib, melphalan, and dexamethasone. Source: Dima D, et al. Diagnostic and Treatment Strategies for AL Amyloidosis in an Era of Therapeutic Innovation. JCO Oncol Pract. 2023; Jimenez-Zepeda VH, et al. Understanding real-world treatment patterns and clinical outcomes in AL amyloidosis patients diagnosed in Canada: A population-based cohort study. EJHaem. 2022; Bou Zerdan M, et al. Systemic AL amyloidosis: current approach and future direction. Oncotarget. 2023; Kumar S, et al. Revised prognostic staging system for light chain amyloidosis incorporating cardiac biomarkers and serum free light chain measurements. J Clin Oncol. 2012; Browning S, et al. Hematologic relapse in AL amyloidosis after high-dose melphalan and stem cell transplantation. Blood. 2017; Palladini G, et al. Presentation and outcome with second-line treatment in AL amyloidosis previously sensitive to nontransplant therapies. Blood. 2018; Quock TP, Yan T, Chang E, Guthrie S, Broder MS. Epidemiology of AL amyloidosis: a real-world study using US claims data. Blood Adv. 2018 May 22;2(10):1046-1053. doi: 10.1182/bloodadvances.2018016402. PMID: 29748430; PMCID: PMC5965052. Staron A, et al. Marked progress in AL amyloidosis survival: a 40-year longitudinal natural history study. Blood Cancer J. 2021;11(8):139; Lu R, Richards TA. AL Amyloidosis: Unfolding a Complex Disease. J Adv Pract Oncol. 2019;10(8):813-825.

# NXC-201 Addresses Sizable U.S. Relapsed/Refractory AL Amyloidosis Patient Population (2/2)



## Prevalence

## Incidence

## Standard of Care

**1<sup>st</sup> Line**

Newly diagnosed AL Amyloidosis  
US Incidence ~4,000

75% Relapsed/Refractory

Relapsed/Refractory ~3,040

US Total Relapsed/Refractory patient  
population ~32,752

8% long-term  
remission from SCD

26% Mayo  
Stage 3b

**21,616 US Relapsed/Refractory AL  
Amyloidosis patients eligible for  
treatment with NXC-201 in 2023**

Estimated Relapsed/Refractory  
US Prevalence ~29,712 in 2023

+

**Relapsed/  
Refractory**

**Autologous stem cell transplant or  
*daratumumab* + *CyBorD***  
(± clinical development candidates Birtamimab / CAEL-101)

**1<sup>st</sup> Line**

**No FDA approved treatments for Relapsed/Refractory AL  
Amyloidosis**

**Relapsed/  
Refractory**

Note: 8% long-term remission estimated based on 20% eligible for SCT x 40% achieving CR (associated with superior long survival)

Source Quock TP, Yan T, Chang E, Guthrie S, Broder MS. Epidemiology of AL amyloidosis: a real-world study using US claims data. *Blood Adv*. 2018 May 22;2(10):1046-1053. doi: 10.1182/bloodadvances.2018016402. PMID: 29748430; PMCID: PMC5965052. Staron A, et al. Marked progress in AL amyloidosis survival: a 40-year longitudinal natural history study. *Blood Cancer J*. 2021;11(8):139; Lu R, Richards TA. AL Amyloidosis: Unfolding a Complex Disease. *J Adv Pract Oncol*. 2019;10(8):813-825. Santhorawala V, Sun F, Quillen K, Sloan JM, Berk JL, Seldin DC. Long-term outcome of patients with AL amyloidosis treated with high-dose melphalan and stem cell transplantation: 20-year experience. *Blood*. 2015 Nov 12;126(20):2345-7. doi: 10.1182/blood-2015-08-662726. Epub 2015 Oct 6. PMID: 26443620. Kumar S, Dispenzieri A, Lacy MQ, Hayman SR, Buadi FK, Colby C, Laumann K, Zeidenrust SR, Leung N, Dingli D, Greipp PR, Lust JA, Russell SJ, Kyle RA, Rajkumar SV, Gertz MA. Revised prognostic staging system for light chain amyloidosis incorporating cardiac biomarkers and serum free light chain measurements. *J Clin Oncol*. 2012 Mar 20;30(9):989-95. doi: 10.1200/JCO.2011.36.5724. Epub 2012 Feb 13. PMID: 22331953; PMCID: PMC3675680.

# NXC-201 May Be a Curative Treatment for AL Amyloidosis

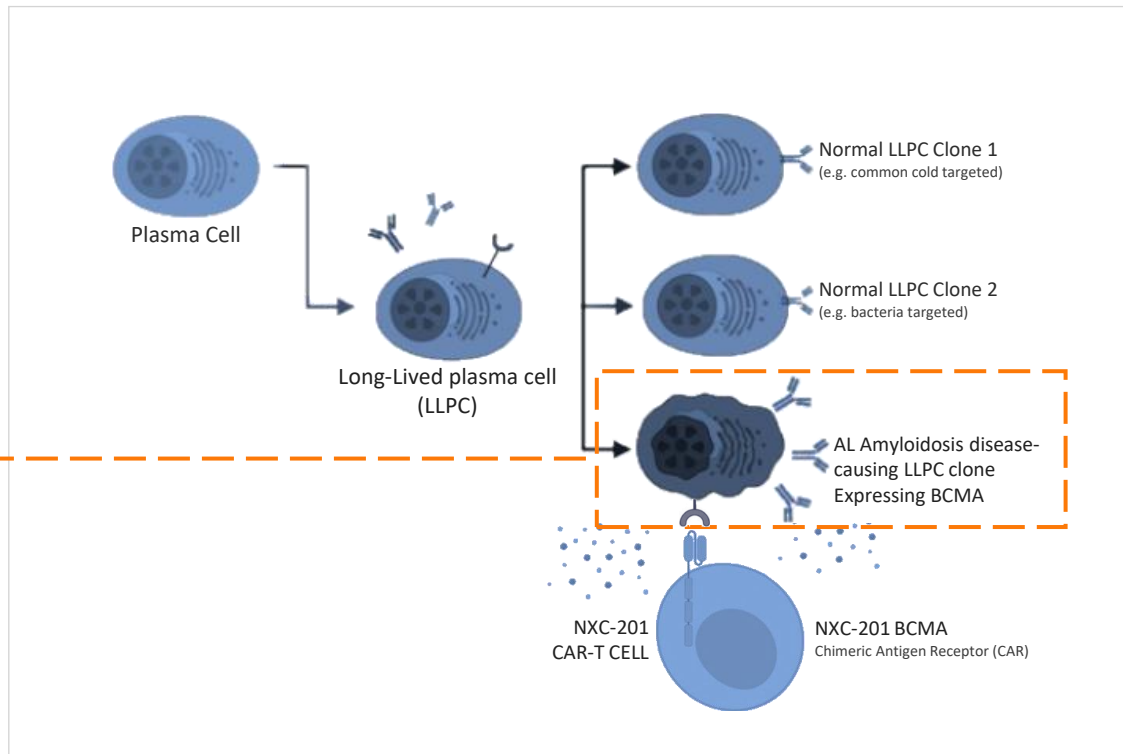
ALL BCMA CAR-TS ARE NOT CREATED EQUAL

AL amyloidosis is caused by dysfunctional plasma cells that can live for years, continuously producing toxic, misfolded amyloid light chain antibody fragments

## AL Amyloidosis disease-causing plasma cells:

- Are a minority of total plasma cells
- Are 1 of thousands of antibody-specific plasma cells, each of which produces 1 antibody, specific to 1 target (e.g. common flu, cold, a type of bacteria...)
- Are eliminated by NXC-201 treatment

Then healthy plasma cells regenerate in the months after NXC-201 treatment, potentially preventing disease relapse



# NXC-201 Designed for High Activity Against Disease-causing AL Amyloidosis Plasma Cells

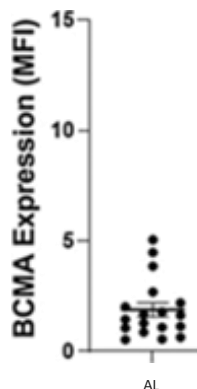
ALL BCMA CAR-TS ARE NOT CREATED EQUAL



a) Uneven BCMA expression and b) frail patient condition has historically prevented conventional, approved CAR-T use in AL Amyloidosis  
NXC-201 was designed and tested for human AL Amyloidosis treatment, with preclinical testing revealing that:

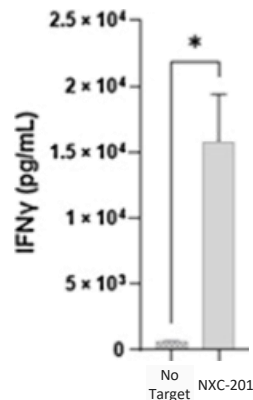
1

BCMA is expressed in 18 AL Amyloidosis patients at a low-medium level...

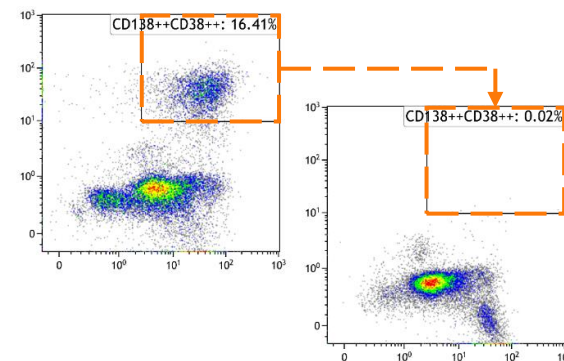


2

...NXC-201 CAR-Ts are activated in presence of the AL Amyloidosis target cells...



...completely eliminating AL Amyloidosis aberrant plasma cells from patient bone marrow.



NXC-201's uniquely favorable tolerability profile (no neurotoxicity + “Single-day CRS”) combined with proven preclinical and clinical efficacy make NXC-201 uniquely suited to treat AL Amyloidosis.

Note: NXC-201 (formerly NB10101). Infy TNFa for two patients, AL1, AL2. Far right top right quartile selected diseased AL Amyloidosis plasma cell elimination. Far right graph after 33 days co-incubated with NXC-201.

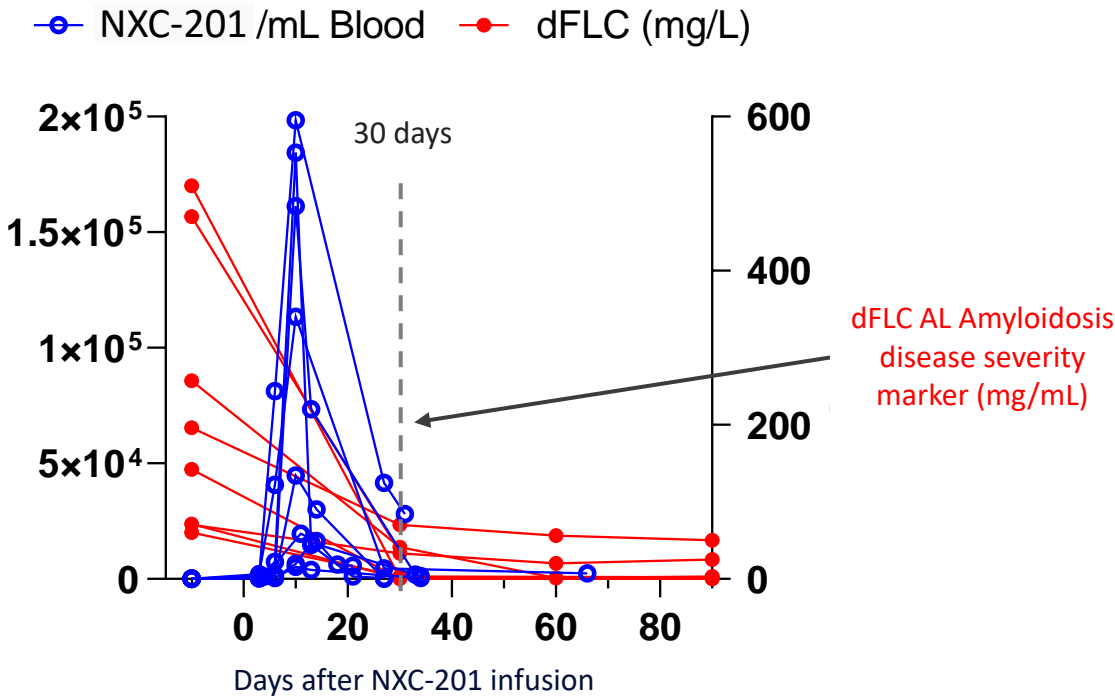
Source: Kfir-Erenfeld S, et al. Feasibility of a Novel Academic BCMA-CAR-T (HB10101) for the Treatment of Relapsed and Refractory AL Amyloidosis. Clin Cancer Res. 2022; Raju N, et al. Anti-BCMA CAR-T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2019;



# Primary Efficacy Endpoint for NEXICART-2: Normalization of Diseased Free Light Chains 30 Days after Dosing



NXC-201 RAPIDLY ELIMINATES DISEASED AL AMYLOIDOSIS PLASMA CELLS AND EXITS WITHIN ~30 DAYS

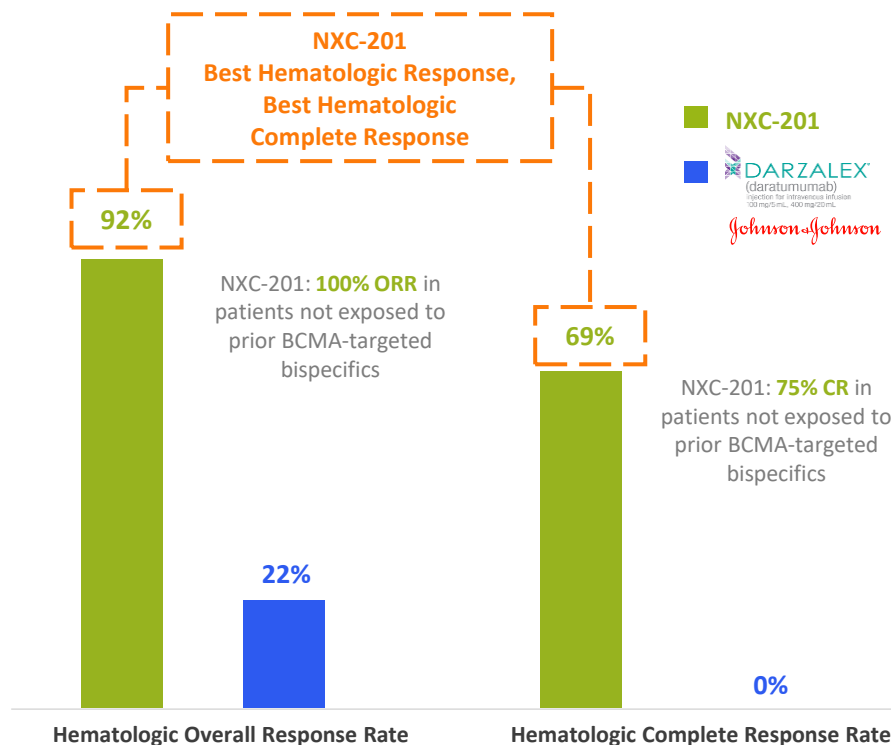


NEXICART-1 Clinical Trial Data. Each line represents 1 patient clinical data readout after NXC-201  
\*dFLC (=involved free light chain - uninvolved free light chain), an AL amyloidosis disease severity marker

# NXC-201: High Hematologic Responses in R/R AL amyloidosis (\$3bn market) at ASGCT 2024



APPROVAL OF DARZALEX CyBORd IN FRONT-LINE AL AMYLOIDOSIS BASED ON HEMATOLOGIC RESPONSE RATE



## NXC-201 – NEXICART-1 Clinical Data

Only CAR-T in AL Amyloidosis

100% Overall Response Rate and 75% Complete Response Rate in Relapsed/Refractory AL amyloidosis for patients without prior BCMA-targeted bispecifics exposure

(median 4 lines of prior therapy prior to NXC-201 – all including Darzalex)

Zero Neurotoxicity of any grade in AL Amyloidosis

# Ongoing NEXICART-2 Trial to Target Relapsed/ Refractory AL Amyloidosis Patients Most Likely to Benefit



NXC-201 clinical data indicate that R/R Amyloidosis patients with better baseline cardiac status and no prior BCMA-targeted bispecifics exposure are more likely to benefit from treatment

Relapsed/Refractory AL Amyloidosis NXC-201 trial	Allows severe cardiac patient enrollment?	Allows patients with prior BCMA-targeted therapy exposure?
NEXICART-1: ongoing Israel trial	X Yes	X Yes
NEXICART-2: ongoing US trial	✓ No	✓ No

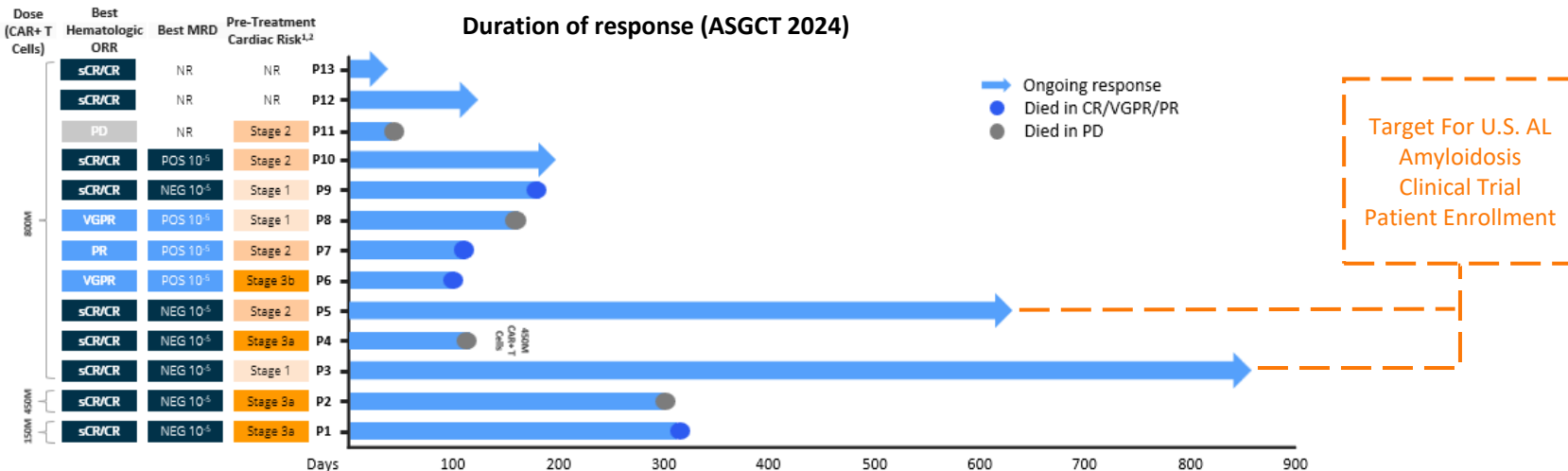
40 patient, single-arm, open-label US trial → submit data to FDA

# NEXICART-1: Durable Responses in NXC-201 AL Amyloidosis Clinical Trial

ONGOING U.S. TRIAL TARGETING R/R AL AMYLOIDOSIS PATIENTS MOST LIKELY TO BENEFIT FROM DURABLE RESPONSES



- Complete hematologic response (CR) of 69% (9/13), and CR 75% (9/12) in patients without prior exposure to BCMA-targeted bispecific, a precedent approval endpoint based on the only commercial treatment for AL amyloidosis
- Ongoing NEXICART-2 US trial targeting patients reflective of durable responders



<sup>1</sup>All but one (patient 9) had multi-organ involvement

<sup>2</sup> MAYO staging

sCR: strict complete response, CR: complete response

Darzalex FDA label. Assayag, et al. Academic BCMA-CART cells (HB0101), a promising approach for the treatment of LC Amyloidosis. 27th Annual Meeting of The American Society of Gene and Cell Therapy (ASGCT). Late Breaking Oral Presentation. Baltimore, MD. May, 2024. E. Lebel, M.E. Gatt et al. Feasibility of a Novel Academic Anti-BCMA Chimeric Antigen Receptor T-Cell (CART) (HB0101) for the Treatment of Relapsed and Refractory AL Amyloidosis, 65th ASH Annual Meeting and Exposition, San Diego, CA. October 2023.

# NEXICART-1: NXC-201 N-GENIUS Platform “Single-Day CRS” Drives AL Amyloidosis Leadership



ALL BCMA CAR-TS ARE NOT CREATED EQUAL

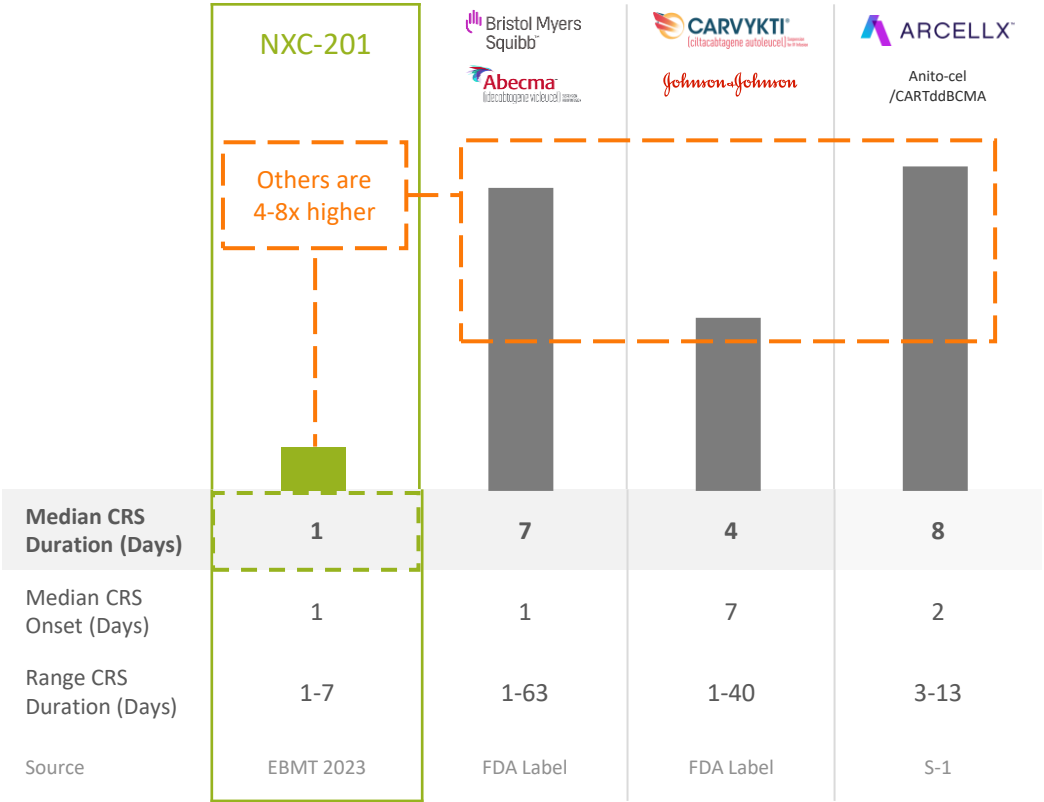
NXC-201’s short CRS duration makes it **uniquely suitable to treat ALA patients** (in whom the #1 source of mortality is heart failure)

Cardiovascular stress is the key determinant for ability to treat relapsed/refractory ALA patients

- Long CRS duration causes extended cardiovascular stress
- Other CARTs have 4-8x longer CRS duration

“The biggest challenge ... has been applicability of these therapies in amyloidosis **when the patients are particularly frail and have organ dysfunction** ... where the key lies in the safety rather the efficacy in a low-volume disease setting is going to be key ... ”

— Dr. Susan Bal, MD  
Assistant Professor, Hematology  
University of Alabama at Birmingham



Source: M. Assayag, et al. Point-of-care CART manufacture and delivery for the treatment of multiple myeloma and AL amyloidosis: the experience of Hadassah Medical Center. European Society for Blood and Marrow Transplantation 49th Annual Meeting. Poster Presentation. April 2023. Nov 2023 KOL discussion <https://livesciencetalk.com/event/immixbio/NXC-201> (formerly HB10101) American Society of Hematology Presentation, Abecma FDA approval label, Carvykti FDA approval label, Arcellx S-1.

Data in Multiple Myeloma

# NEXICART-1: Overcoming Neurotoxicity

ALL BCMA CAR-TS ARE NOT CREATED EQUAL



## LOW VOLUME DISEASE

**NXC-201**  
AL Amyloidosis

**Others**  
Low volume autoimmune diseases

Others are  
>10x higher



Patients 13 30

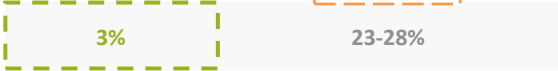
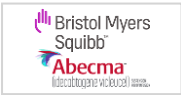
Source ASGCT 2024 EULAR 2024

## HIGH VOLUME DISEASE

**NXC-201**  
Multiple Myeloma

**Abecma/Carvykti**  
Multiple Myeloma

Others are  
8-10x higher



Patients 63 31-127

Source ASH 2023 Abecma label, Carvykti label, Arcellx S-1

Source: Carvykti and Abecma FDA labels, Arcellx S-1. Assayag, et al. Academic BCMA-CAR-T cells (HB10101), a promising approach for the treatment of LC Amyloidosis. 27th Annual Meeting of The American Society of Gene and Cell Therapy (ASGCT). Late Breaking Oral Presentation. Baltimore, MD. May, 2024 Assayag, N., et al. European Society for Blood and Marrow Transplantation 49th Annual Meeting. Lebel E, et al. Efficacy and Safety of a Locally Produced Novel Anti-BCMA Chimeric Antigen Receptor T-Cell (CAR-T) (HB10101) for the Treatment of Relapsed and Refractory Multiple Myeloma, International Myeloma Society 20th Annual Meeting. 2023. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies. Figures reflect cross-trial comparison and not results from a head-to-head study. Kyverna corporate presentation June 14, 2024. Accessed through <https://www.sec.gov/edgar/data/0001994702/000095017024073312/kytx-20240614.htm>. Low volume diseases refers to ANCA vasculitis, autoimmune encephalitis, anti-synthetase syndrome, CIDP, DGLA encephalitis, IgG4 related disease, Lambert-Eaton myasthenic syndrome, lupus nephritis, myasthenia gravis, multiple sclerosis, rheumatoid arthritis, systemic sclerosis, Stiff Person syndrome

# NEXICART-2 US Relapsed/Refractory AL Amyloidosis Trial (NCT06097832)

NEXICART-2 NXC-201 US TRIAL INITIATED IN MID-2024



## Study design

- Open-label, single-arm Phase 1/2a study
- n=40 patients

## Key criteria

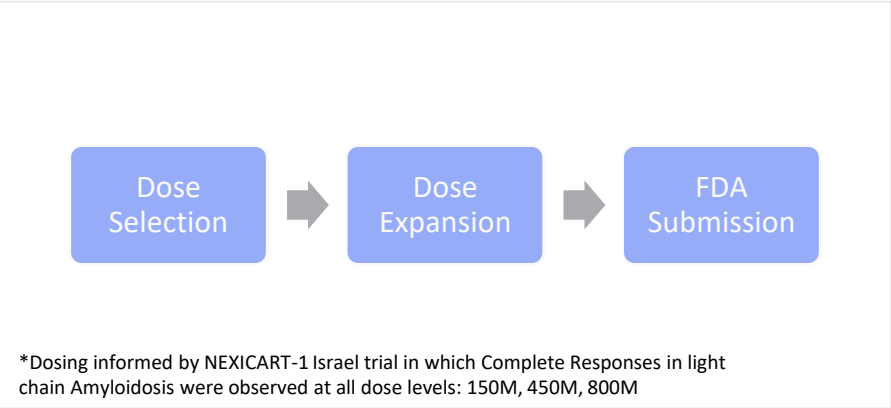
Inclusion	<ul style="list-style-type: none"><li>• AL Amyloidosis patients exposed to at least 1 line of therapy including a CD38 monoclonal antibody</li></ul>
Exclusion	<ul style="list-style-type: none"><li>• Prior anti-BCMA directed therapy</li><li>• Cardiac: Mayo stage 3b, NYHA stage III/IV</li></ul>

## Outcome measures

- Phase 1b dose escalation/expansion
  - Safety
  - Hematologic response according to consensus recommendations in AL amyloidosis

## Status as of July 2024

- Lead site Memorial Sloan Kettering and other US sites started mid-2024



Relapsed/Refractory AL Amyloidosis NXC-201 trial	Allows severe cardiac patient enrollment?	Allows patients with prior BCMA-targeted therapy exposure?
NEXICART-1: ongoing Israel trial	<b>X</b> Yes	<b>X</b> Yes
NEXICART-2: ongoing US trial	<b>✓</b> No	<b>✓</b> No

Could enrich ongoing NEXICART-2 US trial for patients more likely to benefit from therapy

Note: Hematologic response according to consensus recommendations in AL amyloidosis (Palladini, et al. 2012. "Consensus guidelines for the conduct and reporting of clinical trials in systemic light-chain amyloidosis." Leukemia 26(11): 2317-2325.)

# Single-arm NEXICART-2 trial designed considering NEXCIART-1 and precedents in AL

		2021 daratumumab (DARZALEX) FDA Approval	NXC-201 NEXICART-2
Patient Characteristics	Line of Therapy	Newly Diagnosed	Relapsed/Refractory
	Standard of Care (SoC) at time of trial	3-drug combination: Cyclophosphamide, bortezomib, dexamethasone	✓ <b>None (no FDA approvals)</b>
	Randomization vs. Standard of Care?	✗ <b>Randomization vs. SoC</b>	✓ <b>No SoC to randomize against</b>
	Lines of therapy prior to receiving study drug	✗ <b>None</b>	✓ <b>At least 1 line of therapy including a CD38 monoclonal antibody</b>
Study Design	Statistical Power	Based on the assumption that the percentage of patients with a hematologic complete response would be 15 percentage points higher in the daratumumab group than in the control group; approximately <b>360 patients were required</b> to provide 85% power to detect this difference (two-sided alpha level of 0.05).	Based on NEXICART-1 complete response (CR) rates, with a sample size of <b>40 patients</b> , there is a >99% probability that the lower limit of 95% CI for the NXC-201 CR rate is statistically significantly higher compared to historical controls based on the Clopper-Pearson exact method.
	Primary Endpoint	✓ <b>Hematologic complete response rate for both studies</b>	

Single-arm, open-label FDA approval precedents include: Abecma/BMS (single arm study 100 patients in efficacy results population, FDA approved 2021); Carvykti/J&J (single arm study 97 patients in efficacy results population, FDA approved 2022); Elrexfio/Pfizer (single arm study 97 patients in efficacy results population, FDA approved 2023)



# Advantages of CAR-T NXC-201 in Relapsed/Refractory AL Amyloidosis

	NXC-201	Antibody-drug conjugates	Bispecifics
One-time treatment	✓	✗	✗
High Complete Response Rates	✓	✗	✗
Low rates of severe infection	✓	✓	✗
No ICANS/Neurotoxicity	✓	✓	✗

NXC-201  
uniquely suited for  
Relapsed/Refractory  
AL Amyloidosis



Note: High complete response rates defined as >50%. Low rates of severe infection refers to <30%  
Source: Feasibility of a Novel Academic Anti-BiCMA Chimeric Antigen Receptor T-Cell (CAR-T) (HBD101) for the Treatment of Relapsed and Refractory AL Amyloidosis, 65th ASH Annual Meeting and Exposition, San Diego, CA, October 2023. R. Chakraborty, et al. Safety and efficacy of teclistamab in systemic immunoglobulin light chain amyloidosis. Blood Cancer Journal. October 2023. N. Forgeard, et al. Teclistamab in relapsed or refractory AL amyloidosis, a multinational retrospective case series. Blood. February 2024. Chakraborty R, Bhutani D, Maurer MS, Mohan M, Lentzsch S, D'Souza A. Safety and efficacy of teclistamab in systemic immunoglobulin light chain amyloidosis. Blood Cancer J. 2023 Nov 27;13(1):172. doi: 10.1038/s41408-023-00950-3. PMID: 38012151; PMCID: PMC10682473. One NXC-201 relapsed/refractory AL amyloidosis patient died of COVID-19. Kastritis, et al. Efficacy And Safety Of Belantamab Mafodotin Monotherapy In Patients With Relapsed Or Refractory Light-chain Amyloidosis: A Phase 2 Study By The European Myeloma Network. Abstract. EHA 2024.

# Differentiated NXC-201 Clinical Profile Enables Autoimmune Expansion

## POTENTIAL NXC-201 AUTOIMMUNE EXPANSION INDICATIONS

### Neurology

- Myasthenia Gravis
- Neuromyelitis Optica Spectrum Disorder

### Dermatology

- Pemphigus Vulgaris
- Dermatomyositis

### Gastroenterology

- Ulcerative Colitis
- Celiac disease

### Rheumatology

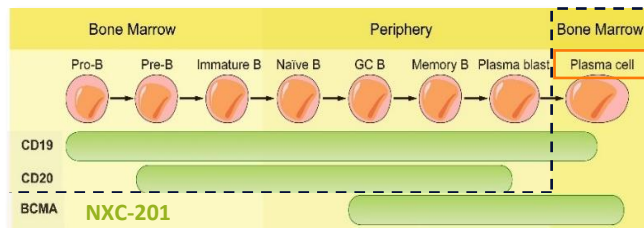
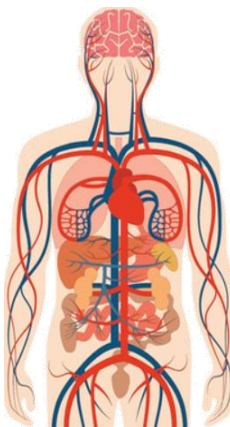
- Systemic Lupus Erythematosus
- Rheumatoid Arthritis

### Hematology

- ✓ **AL Amyloidosis**
- Waldenström macroglobulinemia

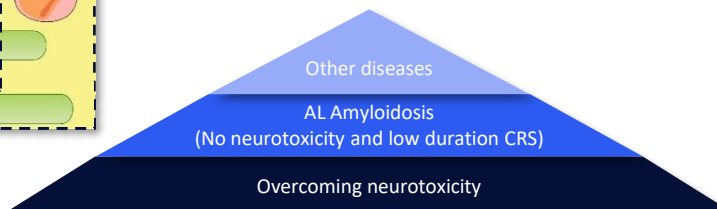
### Nephrology

- IgA nephropathy
- IgM nephropathy



...frequently contributing to autoimmunity

~80% of all auto-antibodies in autoimmune disease are produced by plasma cells...

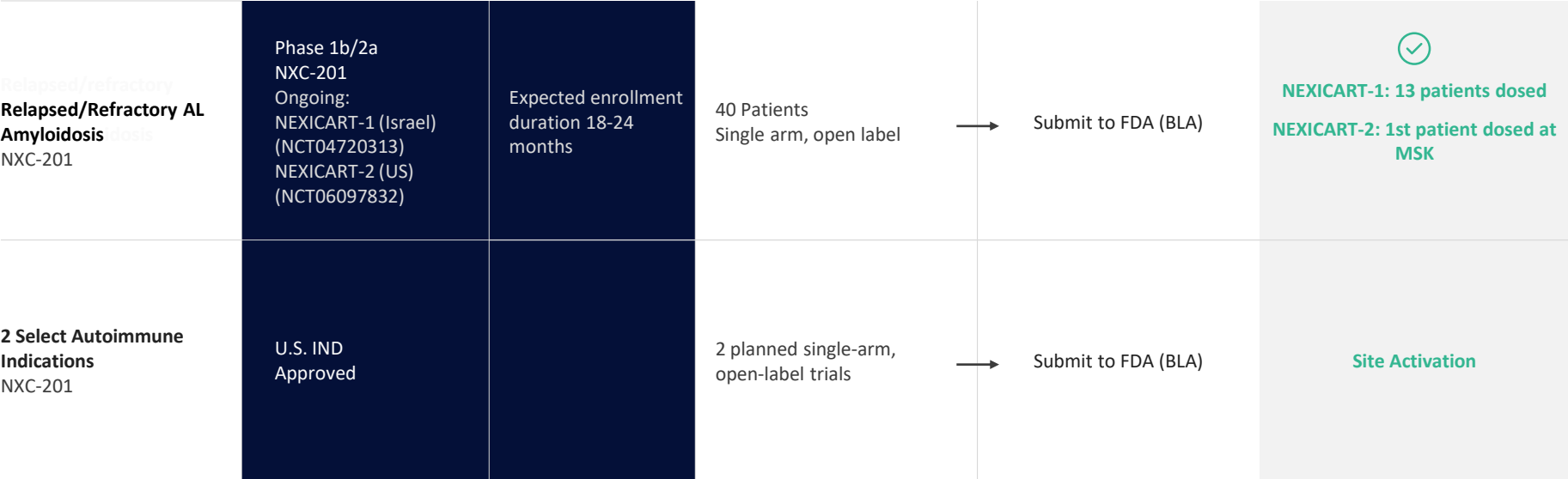


\*Illustrative list of autoimmune diseases where B cells may play a role in initiating or maintaining disease, and where NXC-201 may provide a potential treatment

Source: Medscape. Lee, J. et al. Antigen-specific B cell depletion for precision therapy of mucosal pemphigus vulgaris. J. Clin. Invest. 2020. Mackensen, A. et al. Anti-CD19 CAR T-cell therapy for refractory systemic lupus erythematosus. Nat. Med. 2022. Qin C, et al. Anti-BCMA CAR T-cell therapy CT103A in relapsed or refractory AQP4-IgG seropositive neuromyelitis optica spectrum disorders: phase 1 trial interim results. Signal Transduct Target Ther. 2023. Grant V, et al. Safety and clinical activity of autologous RNA chimeric antigen receptor T-cell therapy in myasthenia gravis (MG-001): a prospective, multicentre, open-label, non-randomised phase 1b/2a study. Lancet Neurol. 2023. Shaker OG, et al. Expression of TNF-α, APRIL and BCMA in Behcet's disease. J Immunol Res. 2014. Shimanovsky A, et al. Autoimmune manifestations in patients with multiple myeloma and monoclonal gammopathy of undetermined significance. BMJ Clin. 2016. McGlothlin J, et al. Bortezomib and daratumumab in refractory autoimmune hemolytic anemia. Am J Hematol. 2023. Casadevall N. What is antibody-mediated pure red cell aplasia (PRCA)? [published correction appears in Nephrol Dial Transplant. 2005; Yu TS, et al. Abnormalities of bone marrow B cells and plasma cells in primary immune thrombocytopenia. Blood Adv. 2021. Greenberg SA, et al. Plasma cells in muscle in inclusion body myositis and polymyositis [published correction appears in Neurology. 2006. Wilbrink R, et al. B Cell Involvement in the Pathogenesis of Ankylosing Spondylitis. Int J Mol Sci. 2021. Uzzan M, et al. Ulcerative colitis is characterized by a plasmablast-skewed humoral response associated with disease activity. Nat Med. 2022. Zhang Z, Xu Q, Huang L. B cell depletion therapies in autoimmune diseases: Monoclonal antibodies or chimeric antigen receptor-based therapy? Front Immunol. 2023. Pioli PD. Plasma Cells, the Next Generation: Beyond Antibody Secretion. Front Immunol. 2019

# NXC-201 Clinical Development Plan Through FDA BLA Submissions

RELAPSED/REFRACTORY AL AMYLOIDOSIS CLINICAL TRIAL TO ENROLL 40 PATIENTS PRIOR TO FDA BLA SUBMISSION



Note: 63 Relapsed/Refractory multiple myeloma patients have been dosed with NXC-201 in the ex-US NEXICART-1 clinical trial. Immix Biopharma is not actively pursuing US commercial approval in Relapsed/Refractory multiple myeloma at this time.

FDA approval precedents include: Abecma/BMS (single arm study 100 patients in efficacy results population, FDA approved 2021); Carvykti/J&J (single arm study 97 patients in efficacy results population, FDA approved 2022); Elrexfio/Pfizer (single arm study 97 patients in efficacy results population, FDA approved 2023)

# Appendix

July 2024



# CAR-T NXC-201 Targets Plasma Cells (antibody factories of the body)

ANTIBODY FACTORY PLASMA CELLS PRODUCE ANTIBODIES THAT DRIVE AUTOIMMUNE DISEASES

## AL Amyloidosis



Infiltrates and damages heart

AL amyloid antibody deposits

## Neurology



- Myasthenia Gravis
- NMO Spectrum Disorder

## Hematology



- Thrombotic thrombocytopenic purpura
- Immune Thrombocytopenia

## Rheumatology



- Systemic Lupus Erythematosus
- Rheumatoid Arthritis

## Vascular



- ANCA vasculitis

Auto-antibodies

Disease causing antibodies

**ANTIBODY FACTORY PLASMA CELL**  
(NXC-201 therapeutic target)



Note: select indications noted above are for illustrative purposes only.

\*Illustrative list of autoimmune diseases where B cells may play a role in initiating or maintaining disease, and where NXC-201 may provide a potential treatment

Source: MedicTests. Lee, J. et al. Antigen-specific B cell depletion for precision therapy of mucosal pemphigus vulgaris. J. Clin. Invest. 2020. Mackensen, A. et al. Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. Nat. Med. 2022. Qin C, et al. Anti-BCMA CAR T-cell therapy CT103A in relapsed or refractory AQP4-IgG seropositive neuromyelitis optica spectrum disorders: phase 1 trial interim results. Signal Transduct Target Ther. 2023. Granit V, et al. Safety and clinical activity of autologous RNA chimeric antigen receptor T-cell therapy in myasthenia gravis (MG-001): a prospective, multicentre, open-label, non randomised phase 1b/2a study. Lancet Neurol. 2023. McGlothlin J, et al. Bortezomib and daratumumab in refractory autoimmune hemolytic anemia. Am J Hematol. 2023. Yu TS, et al. Abnormalities of bone marrow B cells and plasma cells in primary immune thrombocytopenia. Blood Adv. 2021. Zhang Z, Xu Q, Huang L. B cell depletion therapies in autoimmune diseases: Monoclonal antibodies or chimeric antigen receptor-based therapy? Front Immunol. 2023. Pioli PD. Plasma Cells, the Next Generation: Beyond Antibody Secretion. Front Immunol. 2019

# NXC-201 CAR-T cells penetrate tissues and repeat kill disease-causing cells in AL Amyloidosis

AL Amyloidosis pathologic light chains emerge from deep in the bone marrow where they are produced by pathologic antibody factory plasma cells

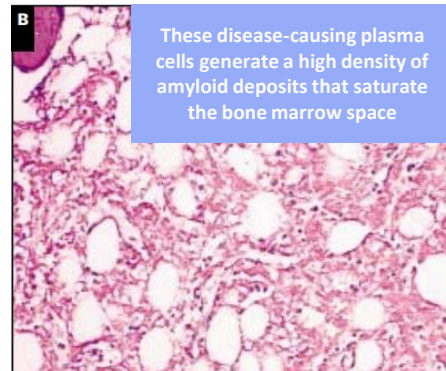
Traditional antibody-based therapies primarily address passively accessible target cells

**NXC-201 is the only AL amyloidosis therapy in clinical development that actively penetrates deep into the bone marrow**



Diseased AL amyloidosis bone marrow contains densely populated disease-causing antibody factory plasma cells

*Immunoperoxidase with hematoxylin counterstain, ×100*



These disease-causing plasma cells generate a high density of amyloid deposits that saturate the bone marrow space

*Periodic acid–Schiff, ×100*

**Antibody-based therapeutics have difficulty penetrating deep into organs where disease causing plasma cells reside**

## Inserm

“Plasma cells (PC) were detected in the [organs] of patients ... up to 6 months after rituximab treatment, and the PC population displayed a long-lived program”

doi:10.1172/JCI65689

# In AL Amyloidosis, NXC-201 Overcomes Limitations of Other Modalities in Performance and Tolerability

Challenges of bispecifics/ T-cell engagers	NXC-201 overcomes these challenges
<ul style="list-style-type: none"> <li>No clinical trials with clinical data available in relapsed/refractory AL amyloidosis</li> <li>Early data from select centers indicates bispecific responses and tolerability are inferior to CAR-T (NXC-201) in relapsed/refractory AL amyloidosis</li> <li>Retrospective study with 17 R/R multiple myeloma + AL Amyloidosis patients: <ul style="list-style-type: none"> <li>✗ 41% CR</li> <li>✗ 35% severe infections including death</li> <li>✗ Grade 3 ICANS neurotoxicity reported</li> </ul> </li> <li>Repeat/ongoing dosing with need for healthcare provider to administer</li> </ul>	<ul style="list-style-type: none"> <li>✓ <b>75% CR in relapsed/refractory AL amyloidosis in patients with no prior BCMA-targeted bispecifics exposure</b></li> <li>✓ <b>0% neurotoxicity (0/13) in relapsed/refractory AL amyloidosis patients</b></li> <li>✓ <b>0 deaths from infection in relapsed/refractory AL amyloidosis</b></li> <li>• <b>One-time dosing with durable responses</b></li> <li>• <b>Ongoing NEXCART-1 relapsed/refractory AL amyloidosis clinical trial with clinical data presented at ASGCT 2024</b></li> </ul>

Advantages of  
NXC-201 CAR-T in  
AL Amyloidosis

# N-GENIUS Sterically-Optimized CARTs Drive Immix's Autoimmune Leadership

## N-GENIUS Platform

Through partnership Hadassah Medical Organization, Jerusalem and Bar-Ilan University, Immix is a pioneer in sterically-optimized CAR-T construct development, driving our next-generation industry-leading CAR-Ts in autoimmune disease.

N-GENIUS developed sterically-optimized CAR-Ts allow for a differentiated safety and efficacy profile through modification of key regions of the CAR-T construct, driving a “digital” intracellular signal and overcoming limitations of current clinical stage and commercial CAR-Ts.

Portfolio of US patents, pending applications, and exclusive patent licenses, which cover our core technology platforms and product





# N-GENIUS Platform has produced sterically-optimized BCMA CAR-T NXC-201 with COBRA binder and EXPAND technology

ALL BCMA CAR-TS ARE NOT CREATED EQUAL



## N-GENIUS PLATFORM

### 3 Key Elements



#### Purpose-Built Cell Therapy Evidence Capture Engine + Relational Database

Relating ImmixBio internal data to external to accelerate therapy design, manufacture, and preclinical



#### Proprietary EXPAND technology

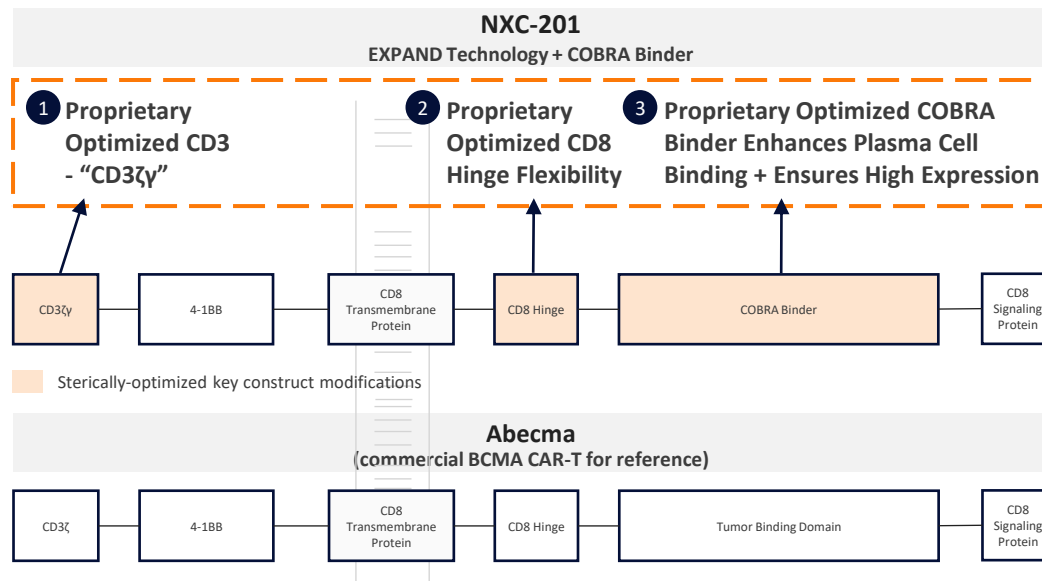
Applied to multiple cell therapy indications, already utilized to create NXC-201, to potentially increase efficacy and tolerability



#### Atomized, Novel Binding Scaffold Generation Engine

Allows us to make the correct binding for every molecule

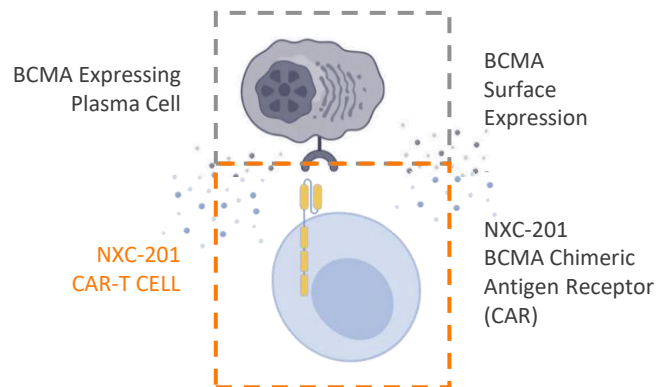
### Produced NXC-201



# NXC-201 MoA: Sterically-Optimized BCMA-targeted CAR-T

## NXC-201: STERICALLY-OPTIMIZED BCMA CAR-T GENERATED BY THE N-GENIUS PLATFORM

### NXC-201



NXC-201 is a next-generation chimeric antigen receptor (CAR) T-cell (CAR-T) produced by our N-GENIUS platform targeting B-cell maturation antigen (BCMA)

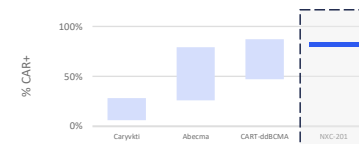
- High Overall Response Rates in AL Amyloidosis and Multiple Myeloma
- First Outpatient CAR-T: Short CRS duration (median 1 days) starting on day 1

### NXC-201 — Key Characteristics



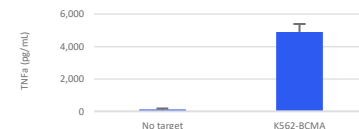
#### High Transduction Efficiency (Ensuring efficient manufacturing)

\*Carvykti data presented at ASH 2019; Abecma data presented at ASH 2017. CART-ddBCMA source Arcellx. Analysis based on cross-trial comparisons of publicly available data reported in ASH 2017 and 2019 and not a head-to-head clinical trial



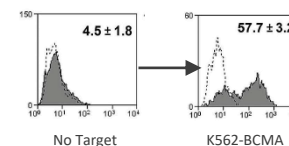
#### Low Tonic Signaling (Lower off-target toxicity may lead to lower toxicity)

NXC-201 was co-cultured with the indicated target T cells and TNFα (B) and IL-2 (C) concentrations secreted in the culture supernatant were determined by ELISA.



#### Anti-Exhaustion Capability (Increased Persistence may lead to efficacy over an extended period of time)

NXC-201 was co-cultured overnight then analyzed by flow cytometry for the expression of 4-1BB

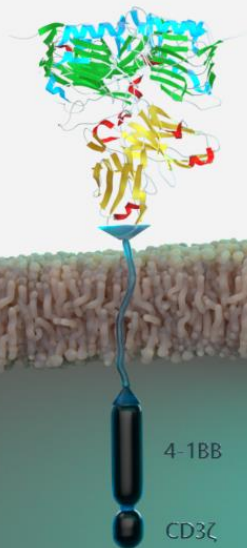


# Proprietary EXPAND Technology and COBRA Binding Domain Are Differentiated Innovations

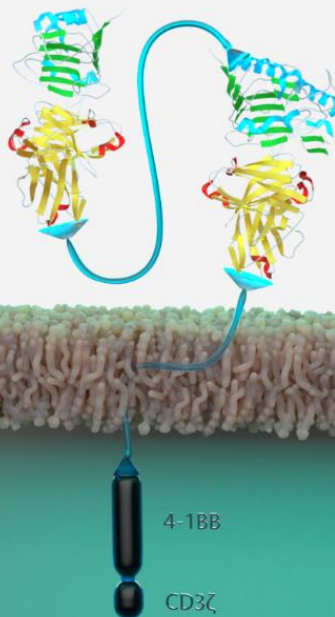
N-GENIUS TECHNOLOGY PLATFORM: STERICALLY-OPTIMIZED BCMA CAR-T NXC-201



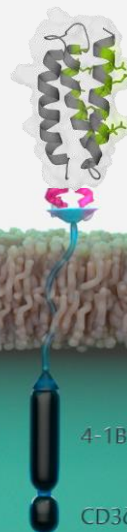
Abecma



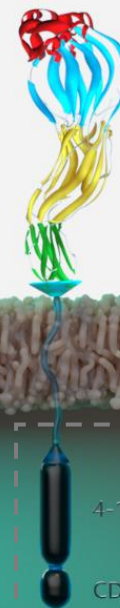
Carvykti



CART-ddBCMA



NXC-201 with  
COBRA Binding Domain



N-GENIUS  
EXPAND Technology

Note: Graphic representation. COBRA = Codon Optimized Binder for Receptor Antigens – Proprietary Binding Domain

# NXC-201 Best-in-Class AL Amyloidosis Clinical Results

## Relapsed/Refractory Light chain (AL) Amyloidosis

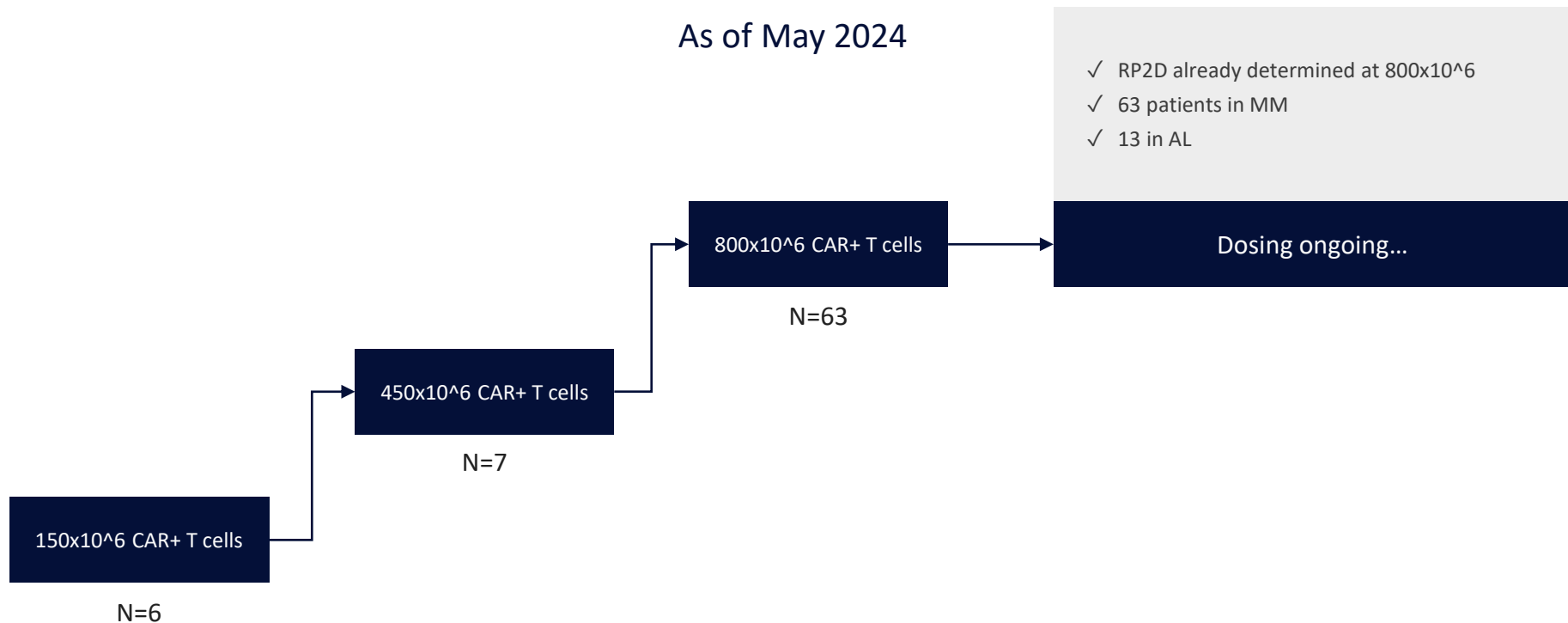
			 	
	NXC-201 Monotherapy	Darzalex Combination (with cyclophosphamide, bortezomib, and/or dexamethasone)	CAEL-101	Birtamimab Combined with SOC CyBorD
Dosing frequency	1X	Weekly	Weekly	Weekly
Patient #s: n=	12	9	10 (renal), 24 (cardiac)	14 (cardiac), 15 (renal)
Hematologic Overall Response Rate	100%	22%	-	-
Hematologic Complete Response Rate	75%	0%	-	-
Hematologic CR + VGPR	92%	22%	-	-
Cardiac response – (NT-proBNP median reduction)	61%		39%	35%
Renal response (%)	67%		20%	60%
Median prior lines of therapy	4	1	2	2
% pretreated with CD38-targeted treatment (Darzalex/other)	100%	100%	?	0%

Birtamimab Source from JCO (Birtamimab development paused + restarted). CAEL-101 source: Edwards CV, et al. Phase 1a/b study of monoclonal antibody CAEL-101 (11-1F4) in patients with AL amyloidosis. Blood. 2021 Dec 23;138(25):2632-2641. doi: 10.1182/blood.2020009039. PMID: 34521113; PMCID: PMC8703360. Darzalex source from Blood. Point-of-care CART manufacture and delivery: Poster. Poster Presentation, ESBMT 2023. Poster ASGCT 2023. Figures reflect cross-trial comparison and not results from a head-to-head study. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies. Poster: IMS 2023. Poster: ASH 2023. Darzalex and Investigator's Choice : Theodorakakou, et al, Blood 2022. Astra Zeneca: Blood 2021 12 NXC-201 patients at ASGCT 2024 with no prior exposure to BCMA targeted bispecifics

# Ongoing Clinical Study Design (NEXICART-1/NCT04720313)

RECOMMENDED PHASE 2 DOSE (RP2D) ALREADY DETERMINED AT  $800 \times 10^6$

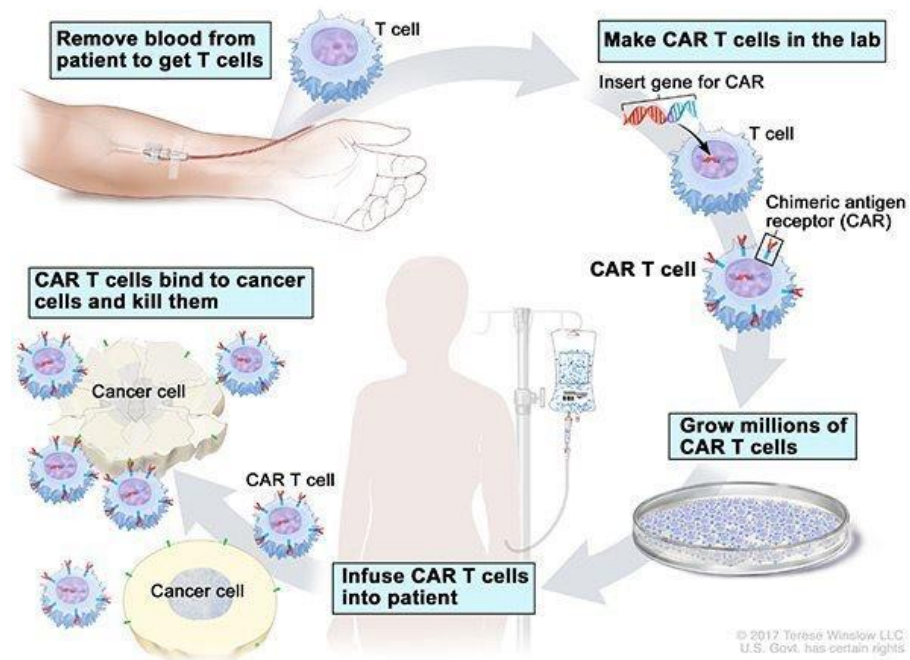
As of May 2024



# What is autologous chimeric antigen receptor (CAR)-T cell therapy?

NXC-201 IS A NEXT-GENERATION BCMA TARGETED AUTOLOGOUS CAR-T CELL THERAPY

## CAR T-cell Therapy



## Patient Specific

Personalized treatment using patient's own T cells

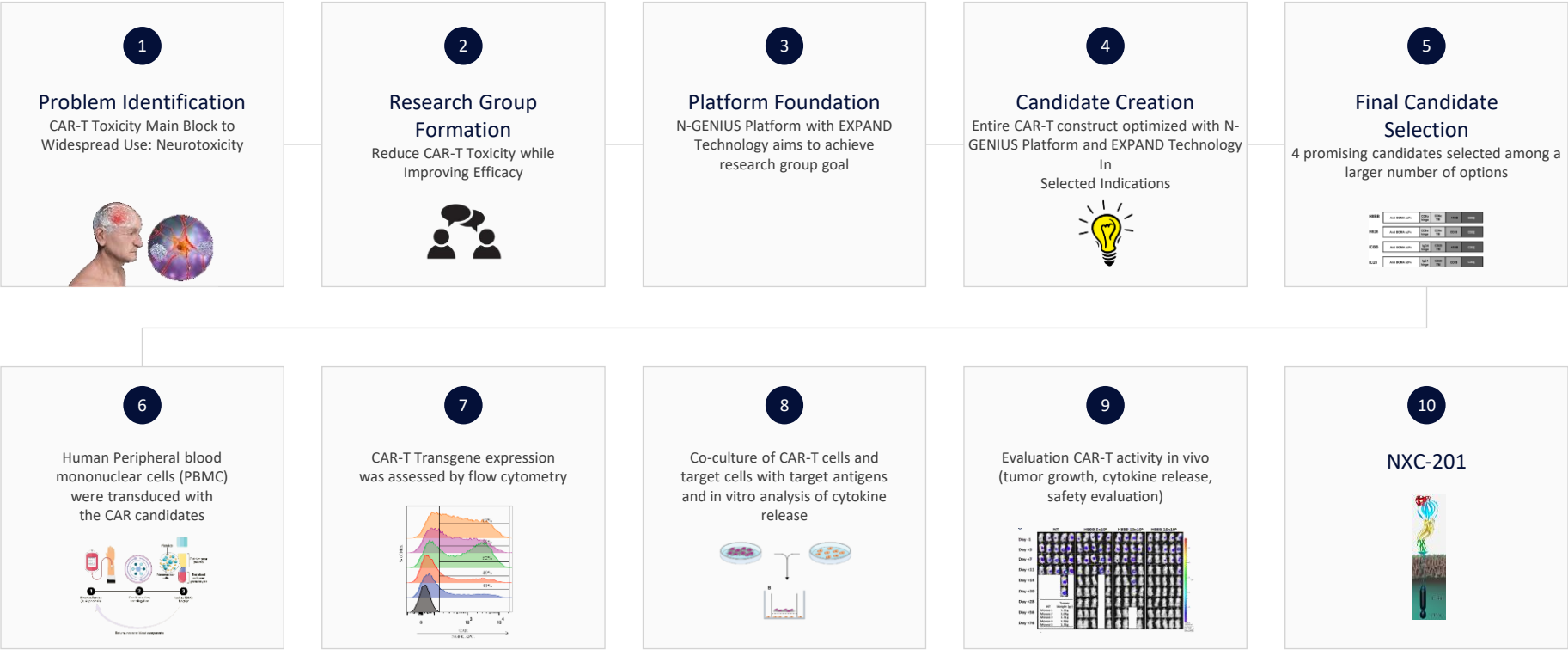
## Genetic Modification

Genetically engineered CARs (chimeric antigen receptors) on T cell surface

## Targeted Therapy

Target cells that express antigens recognized by CARs

# N-GENIUS Platform Process



Source: Harush O, et al. Haematologica. 2022;

# CAR-T Clinical Trailblazer in AL Amyloidosis and autoimmune diseases

July 2024

