

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 10, 2022

Century Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

001-40498
(Commission File Number)

84-2040295
(I.R.S. Employer
Identification No.)

3675 Market Street
Philadelphia, Pennsylvania
(Address of principal executive offices)

19104
(Zip Code)

Registrant's telephone number, including area code: **(267) 817-5790**

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol	Name of Exchange on Which Registered
Common Stock, par value \$0.0001 per share	IPSC	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure

On November 10, 2022, Century Therapeutics, Inc. (the “Company”) updated information reflected in a slide presentation, which is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. Representatives of the Company will use the updated presentation in various meetings with investors from time to time.

The information contained in this Item 7.01 (including Exhibit 99.1) is being furnished and shall not be deemed “filed” for purposes of Section 18 of the Exchange Act, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section and shall not be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

The following exhibit is being furnished herewith:

Exhibit No.	Document
99.1	Investor Presentation of Century Therapeutics, Inc., dated November 10, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CENTURY THERAPEUTICS, INC.

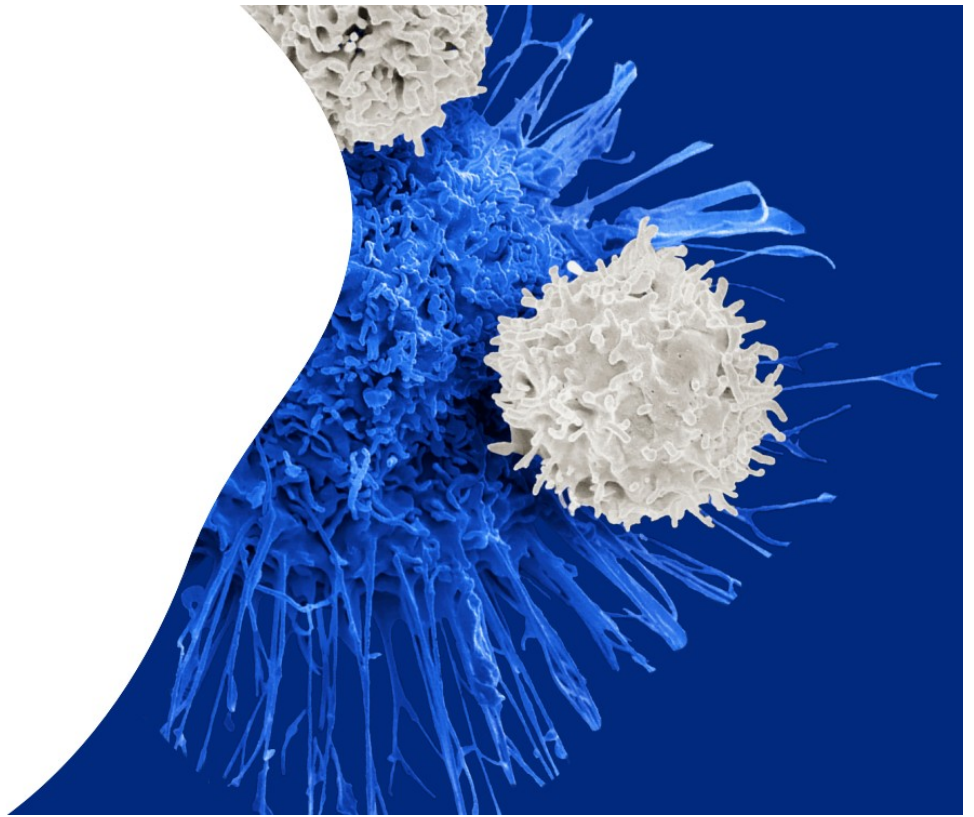
By: /s/ Osvaldo Flores, Ph.D.
Name: Osvaldo Flores, Ph.D.
Title: President and Chief Executive Officer

Date: November 10, 2022



R&D Day

November 11, 2022



Forward-looking statements

This presentation contains forward-looking statements within the meaning of, and made pursuant to the safe harbour provisions of, The Private Securities Litigation Reform Act of 1995. All statements contained in this document, other than statements of historical facts or statements that relate to present facts or current conditions, including but not limited to, statements regarding possible or assumed future results of operations, business strategies, research and development plans, regulatory activities, market opportunity, competitive position and potential growth opportunities are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "might," "will," "should," "expect," "plan," "aim," "seek," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "forecast," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this presentation are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this presentation and are subject to a number of risks, uncertainties and assumptions, some of which cannot be predicted or quantified and some of which are beyond our control, including, among others: our ability to successfully advance our current and future product candidates through

development activities, preclinical studies, and clinical trials; our reliance on the maintenance on certain key collaborative relationships for the manufacturing and development of our product candidates; the timing, scope and likelihood of regulatory filings and approvals, including final regulatory approval of our product candidates; the impact of the COVID-19 pandemic on our business and operations; the performance of third parties in connection with the development of our product candidates, including third parties conducting our future clinical trials as well as third-party suppliers and manufacturers; our ability to successfully commercialize our product candidates and develop sales and marketing capabilities, if our product candidates are approved; and our ability to maintain and successfully enforce adequate intellectual property protection. These and other risks and uncertainties are described more fully in the "Risk Factors" section of our most recent filings with the Securities and Exchange Commission and available at www.sec.gov. You should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in a dynamic industry and economy. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that we may face. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Agenda

Delivering on a Next-Generation iPSC Platform

Lalo Flores, PhD, CEO

Nectin-4 directed therapies: Urothelial Cancer and Beyond

Jonathan Rosenberg, MD, Chief Genitourinary Oncology Service, Division of Solid Tumor Oncology; Enno W. Ercklentz Chair, Memorial Sloan Kettering Cancer Center

Rationale for iPSC-derived $\gamma\delta$ CAR-T cells

Hy Levitsky, MD, President of Research & Development

Century's Gamma Delta iT Cell Platform

Mark Wallet, PhD, Vice President, Head of Immuno-Oncology

CNTY-107, our $\gamma\delta$ iT Product Candidate for the Treatment of Solid Tumors Expressing Nectin-4

Luis Borges, PhD, CSO

Q&A



Delivering on a Next-Generation iPSC Platform

Lalo Flores, PhD | CEO

Positioned to Deliver Next-Generation Cell Therapies



First IND (CNTY-101) deemed eligible to proceed by FDA, Poised to initiate Phase 1 imminently



Advances with next generation iNK 3.0 and gamma delta iT cell platforms



Foundational investment to establish in-house manufacturing



Maintaining financial strength with cash runway into 2025

Century's Key Areas of Internal Focus



B cell malignancies

CNTY-101: Lead product candidate, CD19 targeted CAR-iNK

CNTY-102: First $\gamma\delta$ iT candidate, multi-specific (CD19 + CD79b) CAR-iT

Designed to increase proportion of patients achieving durable responses through multi-dosing regimens enabled by key Allo-Evasion™ edits



Glioblastoma

CNTY-103: CD133 CAR iNK for recurrent GBM

Address heterogeneity via multi-tumor antigen targeting and safety and technical trafficking challenges with locoregional delivery

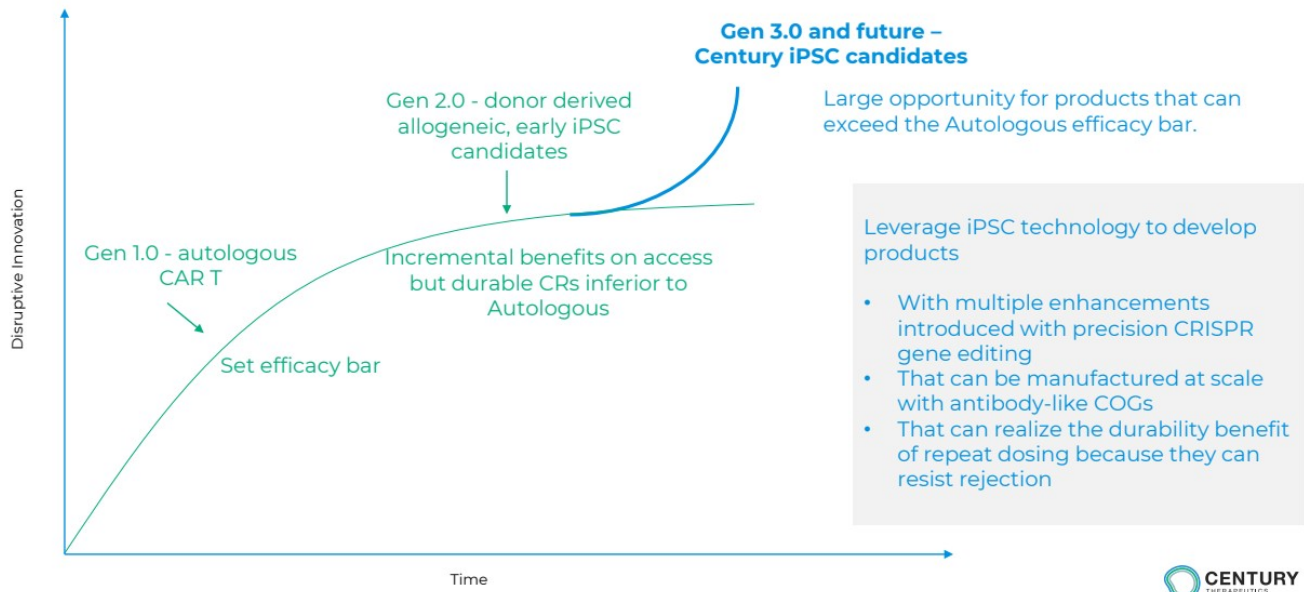


Nectin-4 + Solid tumors

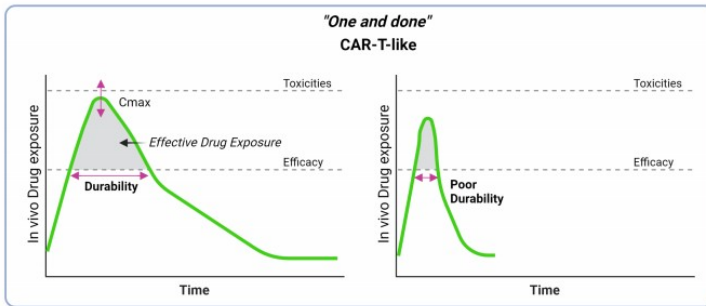
CNTY-107: Nectin-4 targeted CAR GD iT

Leveraging gamma delta iT platform designed to address several solid tumor indications with high expression of Nectin-4 and unmet need

Leapfrogging the Competition in Lymphoma

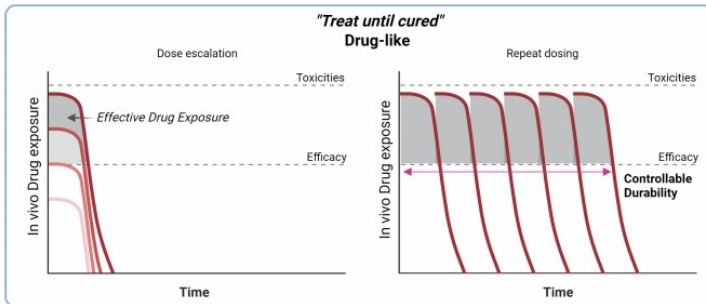


Transforming the cell therapy treatment paradigm



- AUC main predictor of duration of response
- Variable cell expansion/exposure drives toxicity and suboptimal responses

Single dose of allogeneic NK cells unlikely to match $\alpha\beta$ autologous CAR T



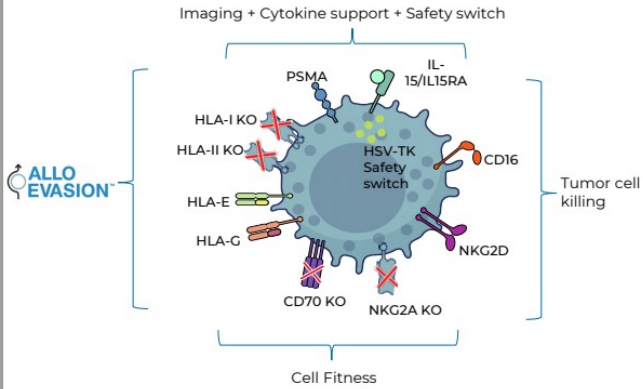
- Finite repeat dosing regimens have the potential to exceed bar set by autologous cell therapy and deliver more durable responses, **if** the cells are engineered to avoid host rejection (Allo-Evasion™)

Illustrative curves

Advances with iNK and iT Cell Platforms Showcased at SITC

iNK 3.0

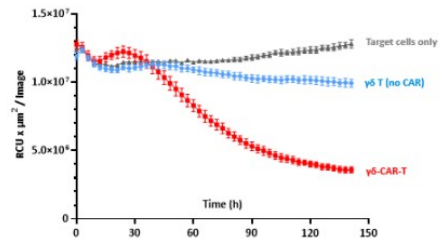
Empowering iPSC-Derived iNK Cells with Multiple Gene Edits to Improve Persistence and Anti-Tumor Efficacy (SITC Abstract 265)



Clonal iPSC line with 11 total genetic modifications show enhanced functionality in iNK 3.0 common progenitor

$\gamma\delta$ iT

Multiple Targeting of Solid Tumors with iPSC-derived Gamma Delta CAR T Cells in Combination with Therapeutic Antibodies (SITC Abstract 262)



$\gamma\delta$ -EGFR-CAR-T cells demonstrate significant CAR-specific killing of ovarian tumor spheroids

Winning in Solid Tumors

Challenges

Trafficking and infiltration

Tumor heterogeneity

Requirement for chemotherapy conditioning

TME / Immunosuppressive environment

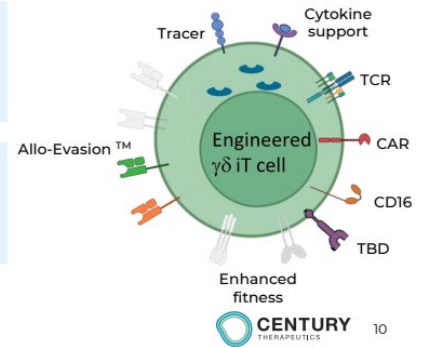
Century's Solution

$\gamma\delta$ iT cells - tissue homing

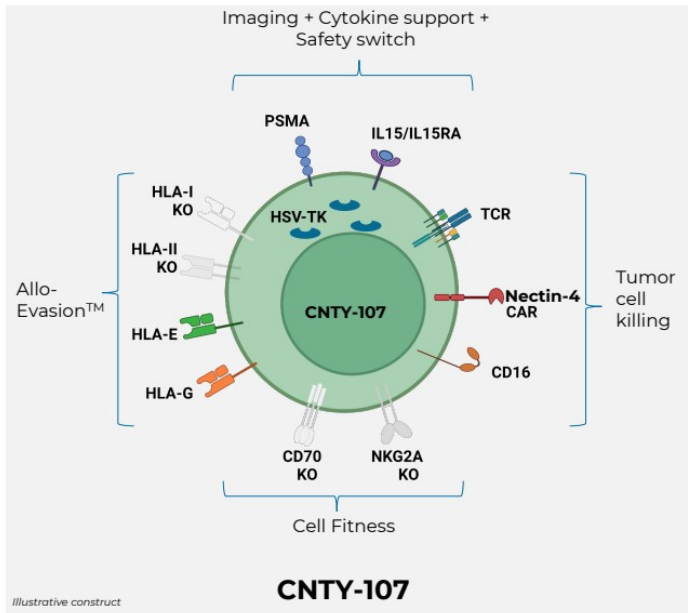
- Engage endogenous immunity
- Multi tumor targeting pathways

- Novel conditioning regimens
- Genetic engineering

Future engineering strategies



CNTY-107: First in Class Nectin-4 Targeted GD iT Cell Therapy



Nectin-4 has been validated by ADC approaches

- Opportunity to address multiple Nectin-4 positive solid tumors
 - Potential indications include bladder, breast, pancreatic, non-small cell lung cancer, esophageal/gastric, head and neck, and/or ovarian cancers

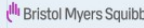

GD iT allogeneic therapies provide potential to improve upon ADC toxicity profile and efficacy

- Intrinsic homing of GD iT cells to tissues and solid malignancies
- Multi-tumor killing modalities to tackle heterogeneity

Pipeline

Product candidate pipeline across cell platforms and targets in solid and hematologic cancers

● Solid Tumors
 ● Hematologic Tumors

Product	iPSC Platform	Targets	Indications	Expected IND Submission	Discovery	Preclinical	Clinical	Collaborator
CNTY-101	iNK	CD19	B-Cell Malignancies	Cleared to proceed 3Q22	<div style="width: 100%; height: 10px; background-color: blue;"></div>			
CNTY-103	iNK	CD133	Glioblastoma	2024	<div style="width: 50%; height: 10px; background-color: green;"></div>			
CNTY-102	iT	CD19 + CD79b	B-Cell Malignancies	2024	<div style="width: 50%; height: 10px; background-color: blue;"></div>			
CNTY-104	iNK/iT	Multi-specific	Acute Myeloid Leukemia	2024	<div style="width: 50%; height: 10px; background-color: blue;"></div>			 Bristol Myers Squibb
CNTY-106	iNK/iT	Multi-specific	Multiple Myeloma	2024	<div style="width: 50%; height: 10px; background-color: blue;"></div>			 Bristol Myers Squibb
CNTY-107	iT	Nectin-4	Solid Tumors	2025	<div style="width: 30%; height: 10px; background-color: green;"></div>			
Discovery Research Programs								
	iNK	TBD	Hematological Tumors	2023	<div style="width: 50%; height: 10px; background-color: blue;"></div>			
	iT	TBD	Solid Tumors	TBD	<div style="width: 30%; height: 10px; background-color: green;"></div>			

Anticipated Catalysts Over Next 12 Months

Underpinned by strong balance sheet with platform synergies and operational excellence

CNTY-101

- Phase 1 (ELiPSE-1) trial initiation in B-cell malignancies (by YE22)

CNTY-101 Follow On (CNTY-102)

- Present pre-clinical data at major medical meeting (2H23)

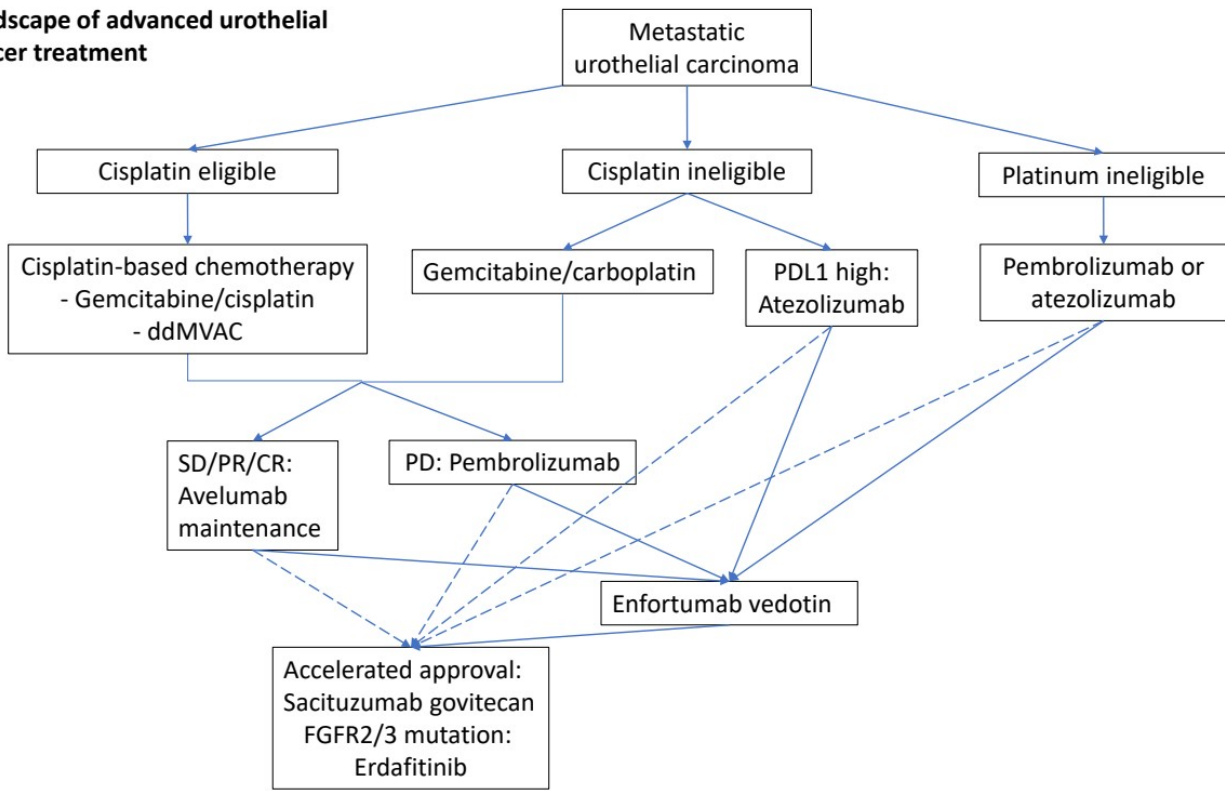
CNTY-103

- Disclose pre-clinical data of development candidate at major medical meeting (2H23)
-

Nectin-4 directed therapies: Urothelial cancer and beyond

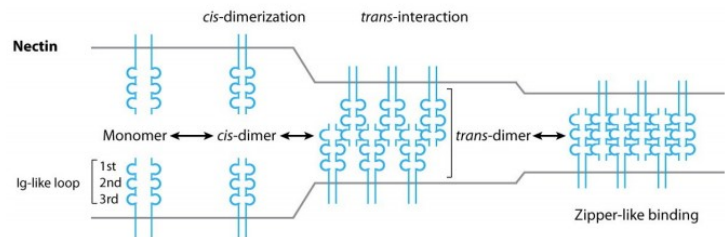
Jonathan Rosenberg, MD
Chief, Genitourinary Oncology Service
Memorial Sloan Kettering Cancer Center
New York, NY

Landscape of advanced urothelial cancer treatment



Nectin-4

- Calcium-independent immunoglobulin-like cell adhesion molecule
- Nectins are cell surface protein involved in polarity, proliferation, differentiation, and migration
 - Expressed during development in multiple cell types (epithelial, immune, neuronal)
- Nectin-4 expression is evident in multiple cancers, although restricted in normal tissues
 - Soluble nectin-4 is potential prognostic biomarker in breast and gastric cancer
 - Overexpression in multiple cancers including breast, gastric, urothelial, biliary, and ovarian cancers
 - Normal tissue expression in skin, cornea (low levels), esophagus



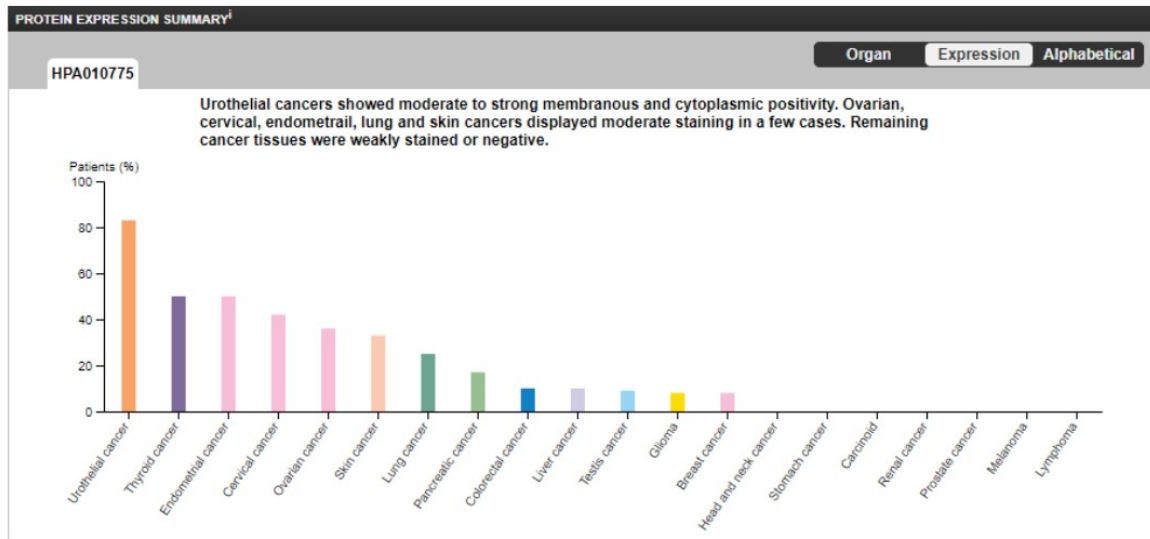
Takai, et al. *Annu Rev Cell Dev Biol.* 2008;24:309-42.

Fabre-Lafay, et al. *BMC Cancer.* 2007;7:73

Okumura et al. *Cornea.* 2018;37:633-640

Zhang et al. *Oncol Lett.* 2018;15:8789-8795

Nectin-4 prevalence in cancer



Source: <https://www.proteinatlas.org/ENSG00000143217-NECTIN4/pathology>

Nectin-4 prevalence in cancer

	N	%	Ab used	Ref
Head and Neck Squamous cell ancer	159	13.8% negative 53.5% weak 32.7% medium-high	Abcam clone EPR15613-68	Oncotarget. 2022; 13:1166-1173
Esophageal cancer	92	66% H score \geq 70	AF2659	<i>Cancer Cell Int.</i> 2019; 19:106
Luminal B Her2 Negative Breast cancer	147	IRS scores: 23.8% negative 18.3% low 40.1% moderate 17.7% high	clone N4.61 (MERCK, DAB150)	<i>Pathol Res Pract.</i> 2017; 213:1102-1108
Breast cancer	140	64.3% positive 35.7% negative	AF2659	<i>Folia Histo Cyto</i> 2011; 49:26–33
Non-small cell lung cancer	422	58% strong positive 28% weak Positive 14% absent	clone 19–33	<i>Cancer Res.</i> 2009. 15; 69: 6694-703

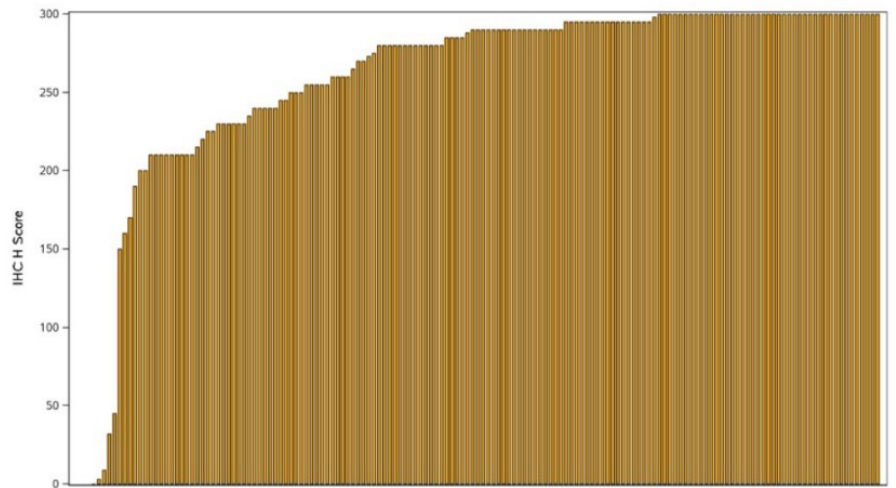
Nectin-4 staining* in urothelial cancer

Required in EV-101 (phase I study of EV in urothelial and other Nectin-4 positive cancers)

Urothelial cancer:
Median H-score, 290; range, 0-300;
4th percentile H-score, 150

EV-201: median H-score 275

EV 101: *J Clin Oncol* 2020 38 1041-1049
EV 201: *J Clin Oncol* 2021 39 6_suppl 394



*M22-321b41.1 (developed by Agensys, not commercially available)

Nectin-4: role in cancer

- Nectin-4 knockdown reduces migration, spheroid formation, cell proliferation
- Plays a role in epithelial-mesenchymal transition
- Upon association with Afadin, Nectin-4 induces PI3K/AKT activation, and cellular proliferation via PI3K/AKT pathway
- Nectin-4 interacts with ERBB2 and trastuzumab resistant splice variants, and leads to activation of PI3K/AKT signaling
- Implicated in stemness, angiogenesis, and metastasis

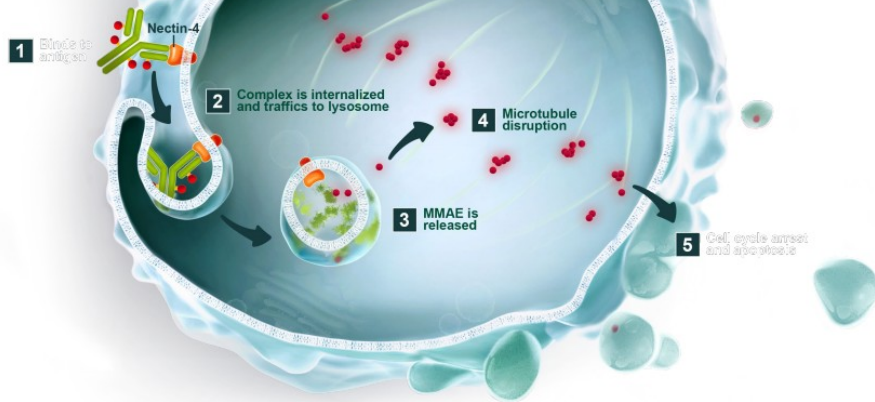
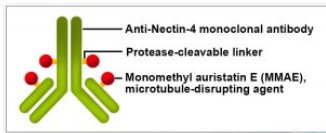
Boylan, et al. *Oncotarget*. 2017; 8:9717-9738

Siddarth et al. *Int J Biochem Cell Biol*. 2017; 89:985-94

Zhang, et al. *Hum Pathol*. 2018;72:107-116

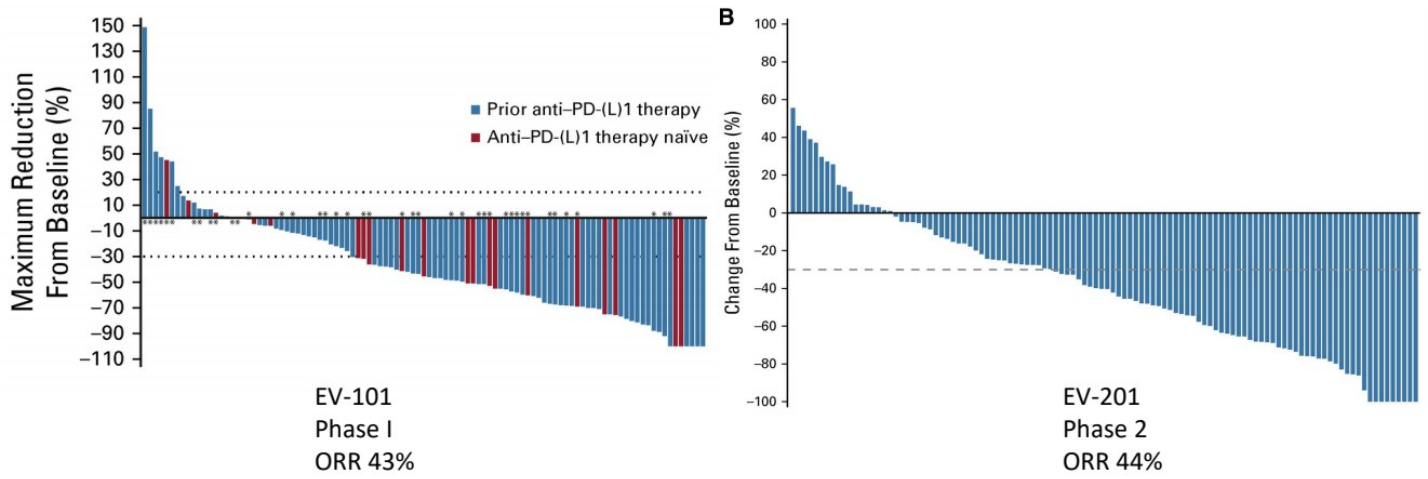
Kedashiro et al. *Sci Rep*. 2019;9:18997

Enfortumab Vedotin: Nectin-4 Targeted Therapy



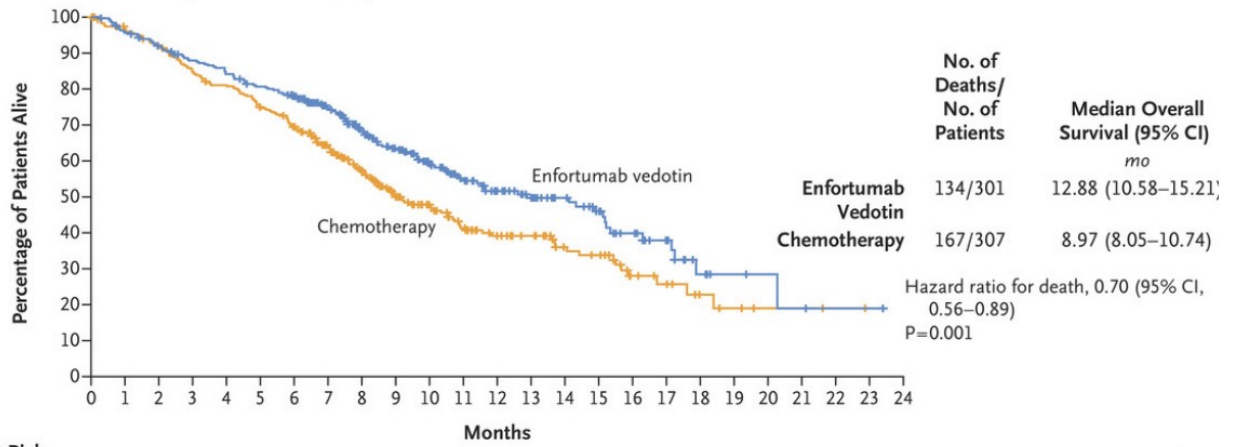
Enfortumab vedotin (EV-202) is an investigational agent, and its safety and efficacy have not been established. Enfortumab vedotin is being developed in collaboration with AstraZeneca. © 2017 Seattle Genetics, Inc. All rights reserved.

Enfortumab vedotin anti-tumor activity



EV-301: EV improves survival compared to standard chemotherapy

A Overall Survival According to Treatment Group



No. at Risk

Enfortumab vedotin	301	286	272	257	246	234	222	190	158	130	105	85	63	52	42	33	23	15	7	4	3	2	1	1	0
Chemotherapy	307	288	274	250	238	219	198	163	131	101	84	66	51	44	32	29	16	11	6	4	2	2	1	0	0

EV ORR 40.6%

PFS 5.55 vs. 3.71 months; hazard ratio for progression or death, 0.62; 95% CI, 0.51 to 0.75; P<0.001)

Common enfortumab vedotin toxicities include fatigue, rash, neuropathy; hyperglycemia occurs and may be severe

Table 2. Treatment-Related Adverse Events (Safety Population).*

Adverse Event	Enfortumab Vedotin Group (N = 296)		Chemotherapy Group (N = 291)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	<i>number of patients (percent)</i>			
Any adverse event	278 (93.9)	152 (51.4)	267 (91.8)	145 (49.8)
Alopecia	134 (45.3)	0	106 (36.4)	0
Peripheral sensory neuropathy†	100 (33.8)	9 (3.0)	62 (21.3)	6 (2.1)
Pruritus	95 (32.1)	4 (1.4)	13 (4.5)	0
Fatigue	92 (31.1)	19 (6.4)	66 (22.7)	13 (4.5)
Decreased appetite	91 (30.7)	9 (3.0)	68 (23.4)	5 (1.7)
Diarrhea	72 (24.3)	10 (3.4)	48 (16.5)	5 (1.7)
Dysgeusia	72 (24.3)	0	21 (7.2)	0
Nausea	67 (22.6)	3 (1.0)	63 (21.6)	4 (1.4)
Maculopapular rash	48 (16.2)	22 (7.4)	5 (1.7)	0
Anemia	34 (11.5)	8 (2.7)	59 (20.3)	22 (7.6)
Decreased neutrophil count	30 (10.1)	18 (6.1)	49 (16.8)	39 (13.4)
Neutropenia	20 (6.8)	14 (4.7)	24 (8.2)	18 (6.2)
Decreased white-cell count	16 (5.4)	4 (1.4)	31 (10.7)	20 (6.9)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

Powles and Rosenberg, et al. *NEJM* 2021

MMAE Payload-related side effects

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Powles and Rosenberg, et al. *NEJM* 2021

Nectin-4 on-target side effects

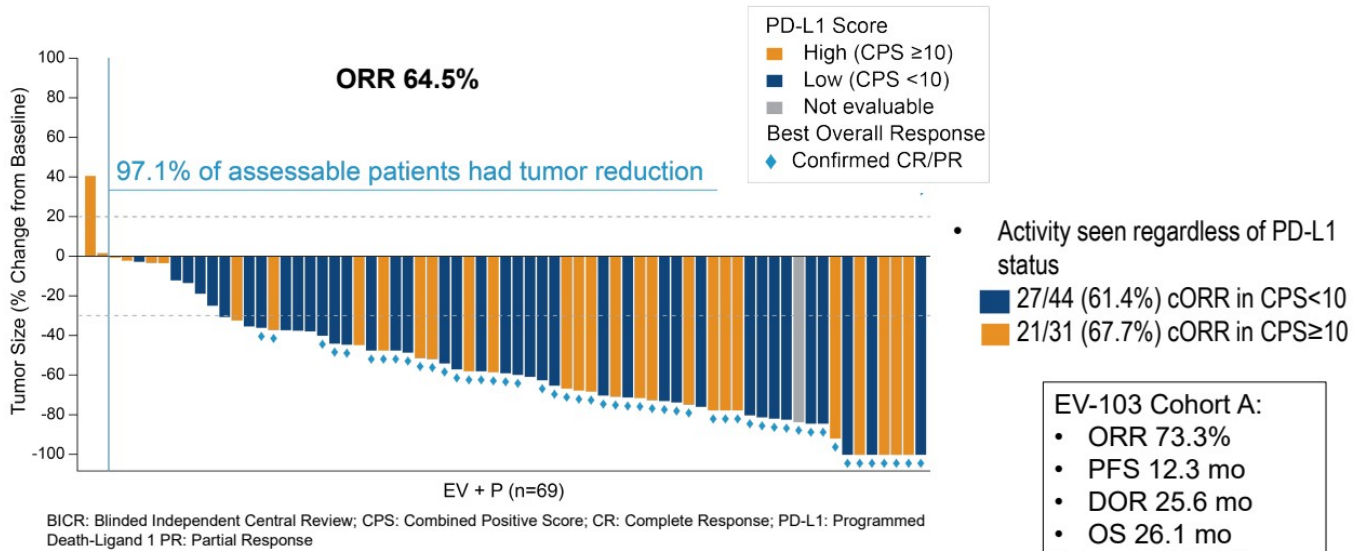
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Overlapping?

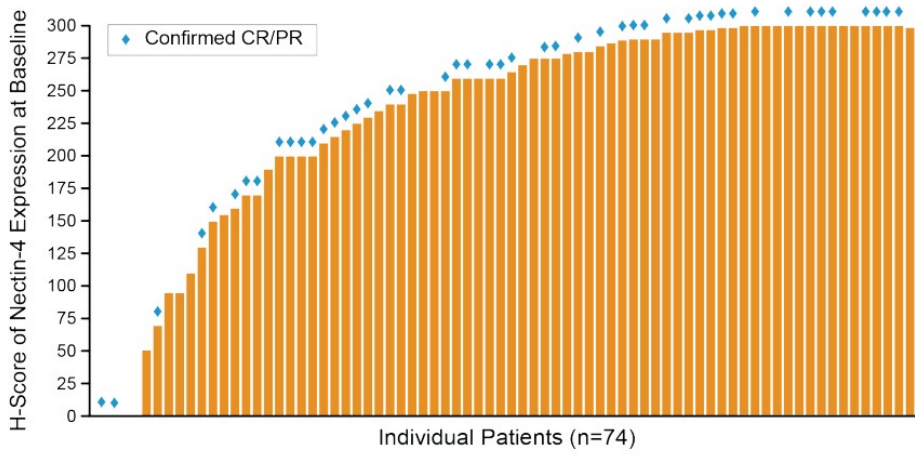
Powles and Rosenberg, et al. *NEJM* 2021

EV-103 Cohort K: Enfortumab vedotin + pembrolizumab leads to deep and durable responses in newly diagnosed cisplatin-ineligible patients with advanced urothelial cancer



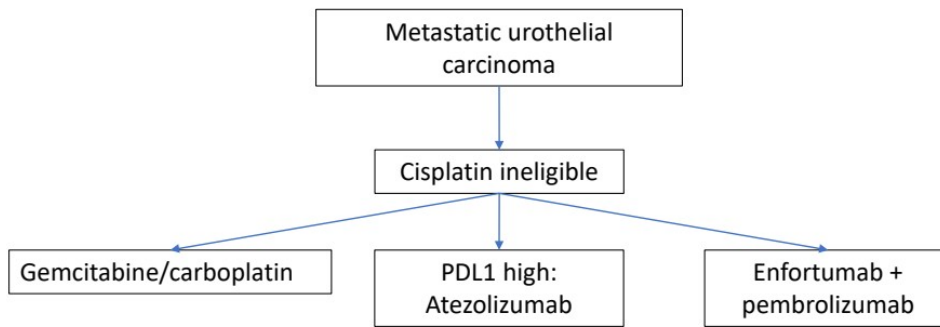
EV+P: Nectin-4 Expression and Best Overall Response

Activity seen regardless of Nectin-4 expression level



- Nectin-4 was detected in tumor tissue from 94.6% of patients who had adequate tissue for testing

Enfortumab moves to first line:
Anticipated accelerated approval with EV-103 Cohort K



Full approval pending results of EV-302 comparing gemcitabine and platinum to enfortumab/pembrolizumab. NCT04223856

Potential mechanisms of resistance to Enfortumab vedotin

- Luminal urothelial cancers may have higher Nectin-4 levels

Clin Cancer Res. 2021 Sep 15;27(18):5123-5130.

- MDR-1/P-glycoprotein overexpression likely leads to MMAE export from cancer cell

Mol Cancer Ther. (2022) 21 (7): 1227–1235.

- Downregulation of Nectin-4 expression on cell surface

• *Eur Urol Oncol.* 2022 Feb 22;S2588-9311 (Online ahead of print).

• *Clin Cancer Res.* 2021 Sep 15;27(18):5123-5130.

- Clinical data is limited- 3 patients with progression on EV retain Nectin-4 expression in post-treatment biopsies

• *Urol Oncol.* 2021 39(10): 619-22.

Other Nectin-4 targeted therapies: bicyclic compounds in early phase trials

- Constrained bicyclic peptides or “bicycles”
- Linear peptide cyclized around a trivalent scaffold
- Can be used to deliver cytotoxics, or bind to other proteins/immune molecules
- Smaller than ADC's, more able to penetrate tumors



Upadhyaya et al. J Immunother Cancer. 2021;9:e001762

Hurov et al. J Immunother Cancer. 2021;9:e002883

Rigby et al. Mol Cancer Ther. 2022;Epub ahead of print

Future landscape for Nectin-4 directed therapy:

Nectin-4 directed therapy moves earlier in the urothelial cancer disease course

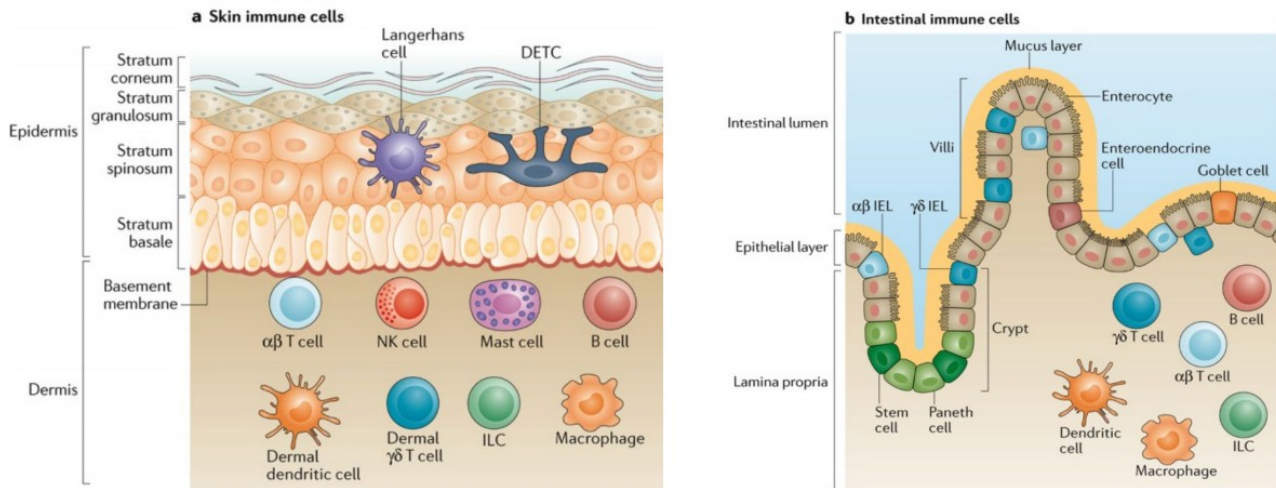
- EV-103 cohort K and EV-302 seek to move EV to first-line therapy
 - KN-B15, KN-905 (EV/pembrolizumab) and VOLGA (EV/durva/treme) testing EV in muscle invasive localized disease
 - Nectin-4 expression may be preserved in EV refractory tumors
 - Subsequent opportunities include late-line disease states
 - Accelerated approval still possible in areas of unmet need (multiply refractory patients)
 - EV-202 (NCT04225117) is testing enfortumab in multiple diseases:
 - Breast cancer, lung cancer, gastric/GE junction, esophageal cohorts
-



Rationale for iPSC-derived $\gamma\delta$ CAR-T cells
Hy Levitsky, MD | President, R&D



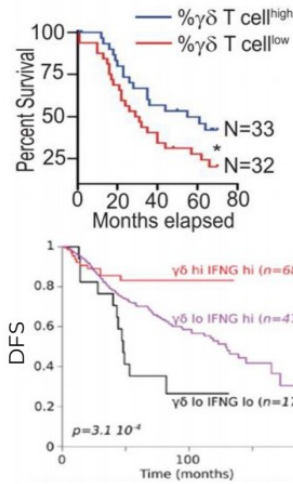
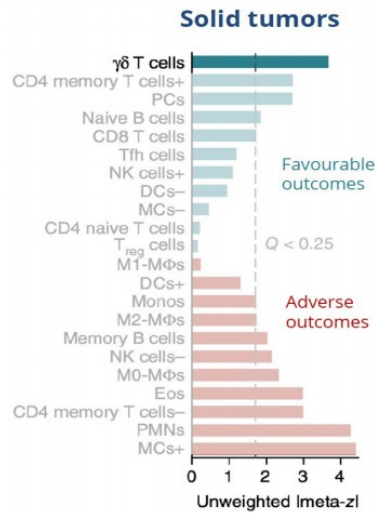
$\gamma\delta$ T cells in Homeostasis and Host Defense of Epithelial Barrier Tissues



$\gamma\delta$ T cells make up between 1-20% of peripheral blood T cells, but comprise the majority of T cells that reside in tissues

Abundance of $\gamma\delta$ T cell in TIL Associated with Favorable Prognosis

18,000 human tumor samples across 39 malignancies

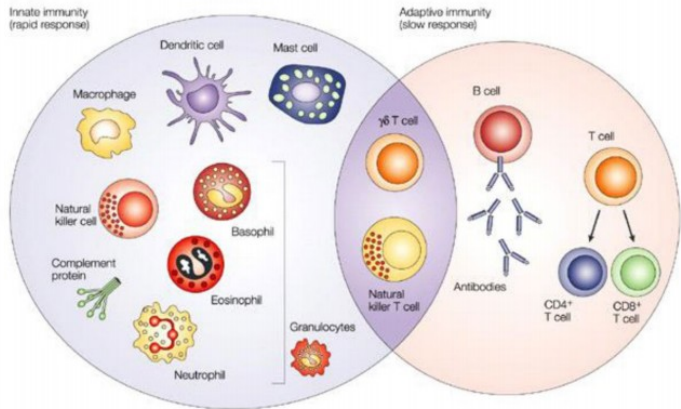


Ovarian Cancer

Colorectal Cancer

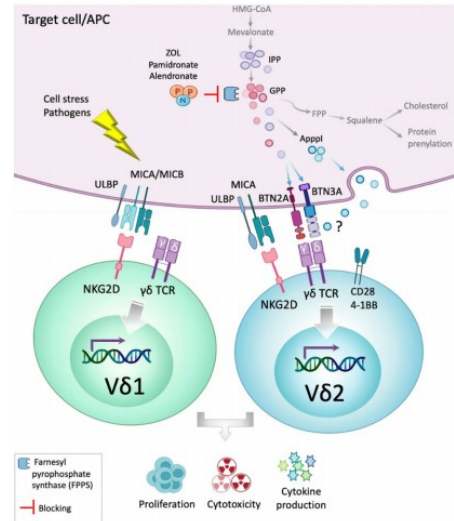
Gentles et al Nature Med. 2015; Payne et al Science 2020; Meraviglia et al Oncoimmunology 2017

$\gamma\delta$ T cells: At the Interface of Innate and Adaptive Immunity



Dranoff, *Nature Reviews Cancer*, 4, 11-22, 2004

Nature Reviews | Cancer



Yazdanifar et al *Cells* 2020, 9(5), 1305

$\gamma\delta$ TCRs Do Not Recognize Classical HLA And Are Not Alloreactive

Clinical Evidence

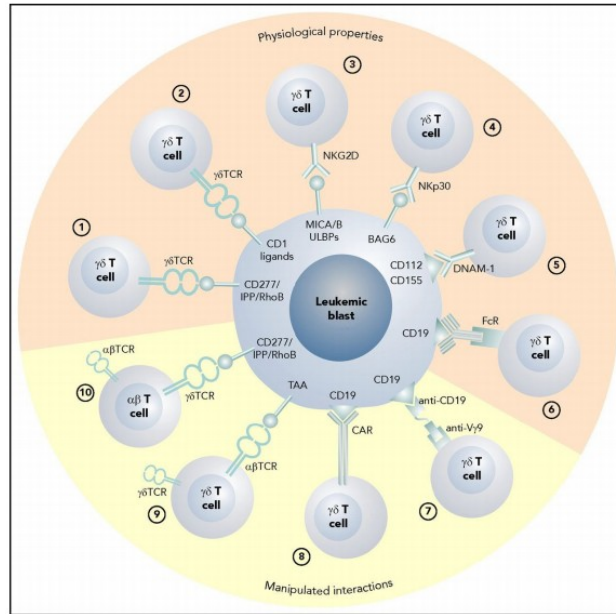
- Partial HLA-mismatched allo-HCT with $\alpha\beta$ T cell depleted grafts showed improved DFS as a function of the number of $\gamma\delta$ T cells (median $11 \times 10^6/\text{kg}$) infused *with no increase in GVHD*¹⁻⁴
- $\gamma\delta$ T cell enriched donor lymphocyte infusion post allo-HST (up to $83 \times 10^6/\text{kg}$), *no GVHD*⁵
- Recent or ongoing studies of adoptive transfer of allogeneic ex vivo expanded $\gamma\delta$ T cells (with or without genetic engineering)^{6,7,8}

¹Lamb et al. *Cytotherapy*. 1999;1(1):7-19, ²Codder et al. *Bone Marrow Transplant*. 2007;39(12):751-757, ³Otto et al. *J Immunother*. 2005;28(1):73-78, ⁴Lang et al. *Bone Marrow Transplant*. 2015;50(Suppl 2):S6-S10, ⁵Radestad et al. *J Immunol Res*. 2014;578741

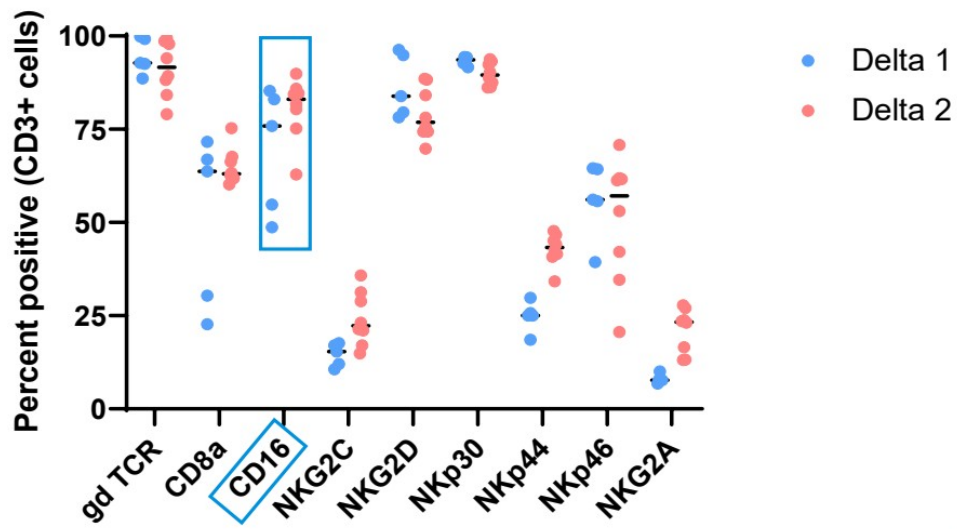
⁶Lin et al., *Signal Transduction Targeted Ther* (2020) 5(1):215, ⁷Xu et al, *Cell Mol Immunol* (2021) 18(2):427-39

⁸ Neelapu, et al. *J Clin Oncol* 40, 2022 (suppl 16; abstr 7509), Nabors, et al. *J Clin Oncol* 40, 2022 (suppl 16; abstr 2044), Xu, et al. *Cell Mol Immunol* 2021 Feb;18(2):427-439

Multiple Potential Mechanisms for Tumor Recognition Both Intrinsic and Synthetic

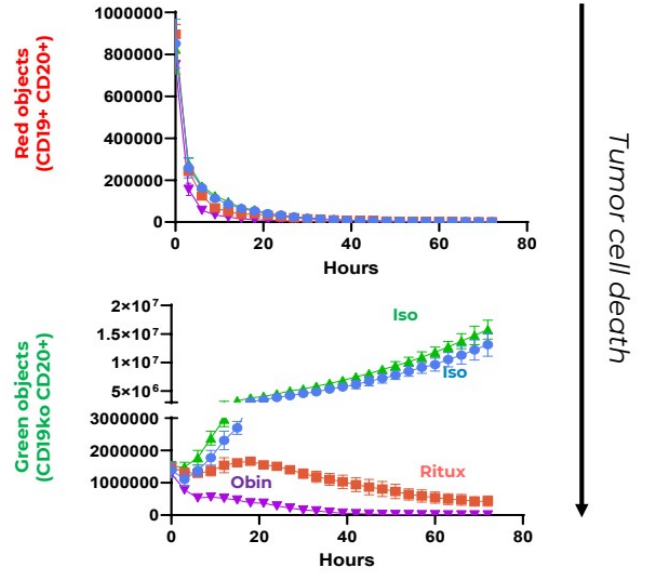
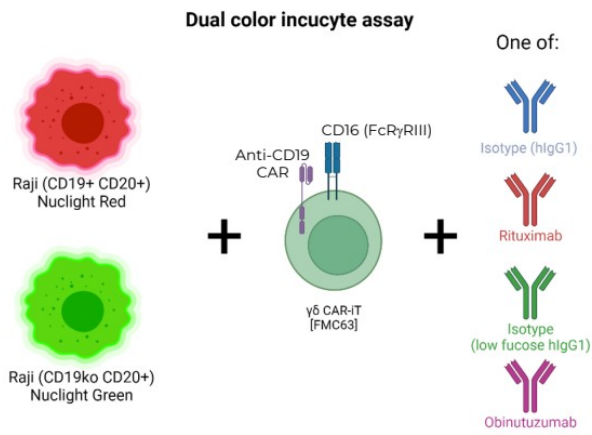


Diverse Innate Mechanisms for Tumor Targeting



N=13 clinical grade TiPSC lines at T cell stage (post differentiation); All lines are Vy9

$\gamma\delta$ CAR-iT cells mediate ADCC



Key Takeaways

The biological properties of $\gamma\delta$ T cells make them an ideal platform for genetically modified cell therapy of cancers

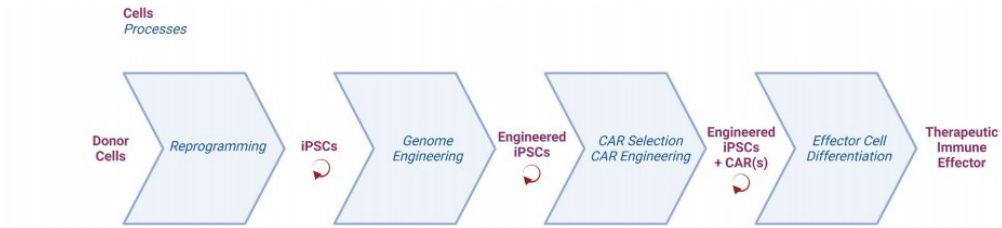
- Innate receptors provide multiple orthogonal mechanisms for tumor recognition
- Functional Fc receptors enable combination therapies with monoclonal antibodies
- Tissue tropism and long-lived persistence favor prolonged tumor surveillance
- Expansion capacity in response to antigen and cytokines mirror $\alpha\beta$ T cells (and is > than NK cells)
- Allogeneic sources can be utilized with little risk of GVHD
- Differentiation from iPSCs yields highly potent immune effectors



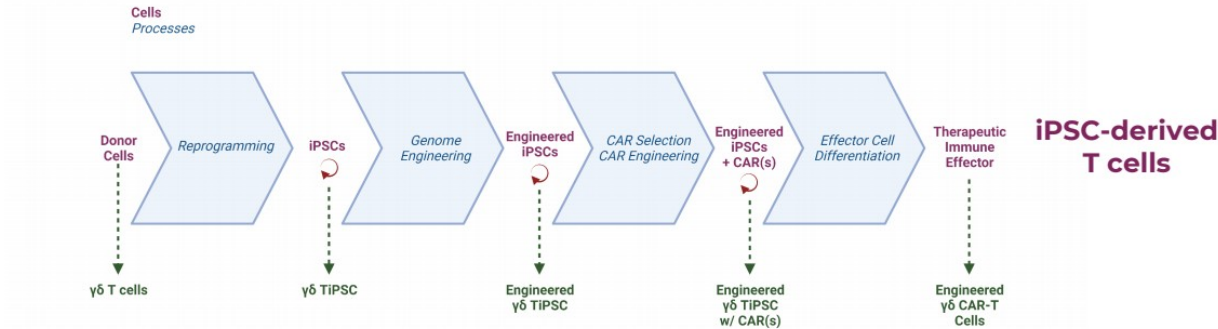
$\gamma\delta$ T Cell Platform

Mark Wallet, PhD | VP Immuno-Oncology

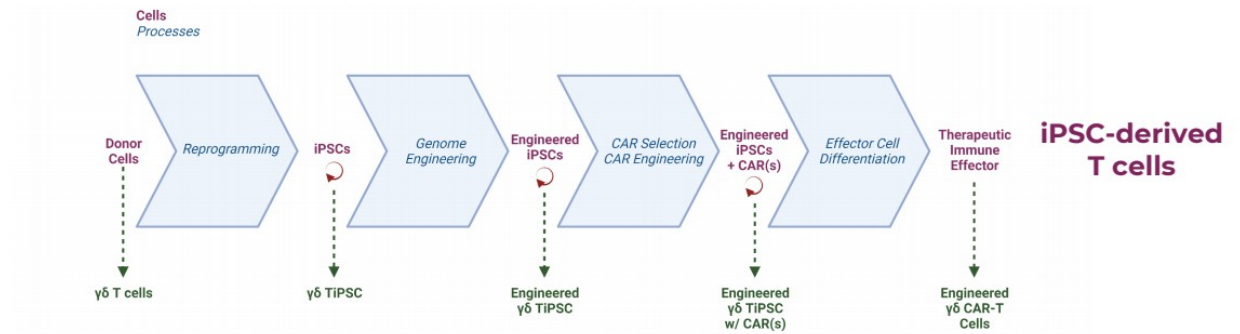
iPSC-derived Therapeutics are Developed from Unique Cells and Processes



iPSC-derived Therapeutics are Developed from Unique Cells and Processes



iPSC-derived Therapeutics are Developed from Unique Cells and Processes



Today's update on T cell platform:

1. Reprogramming
γδ T cells into TiPSC

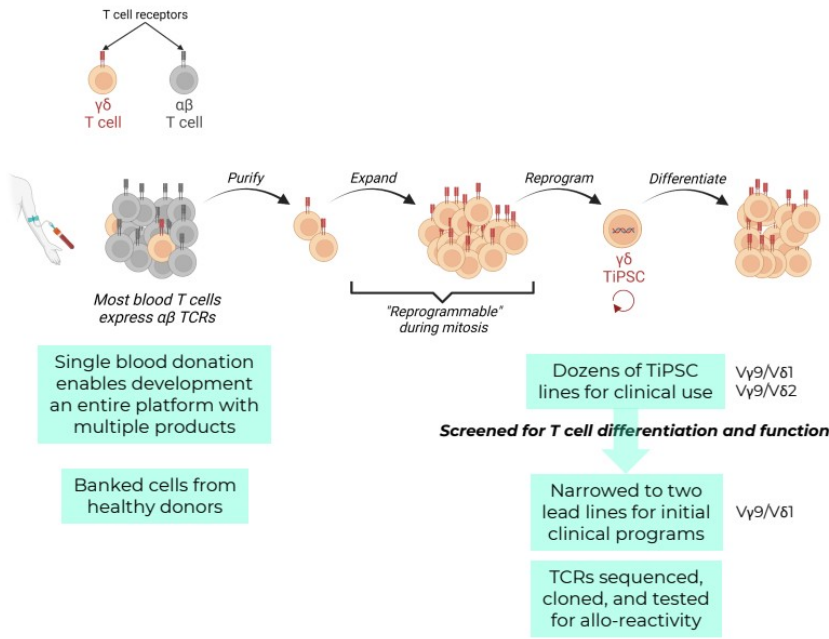
2. Engineering TiPSC
for enhanced fitness

3. Differentiation
of TiPSC into high-yield, high-purity
γδ CAR-T cells

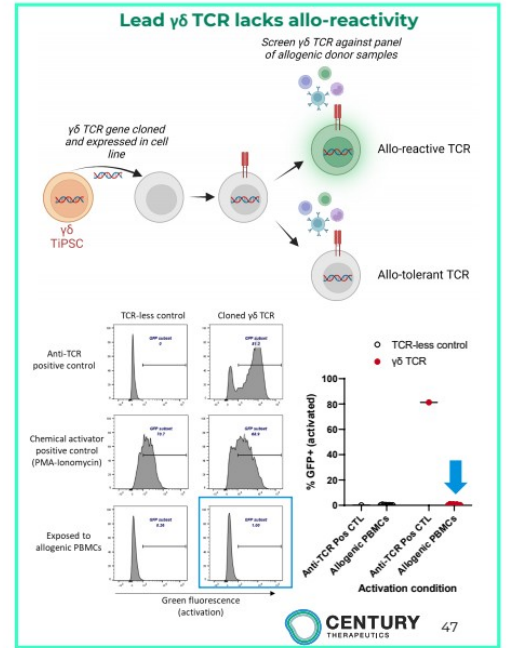
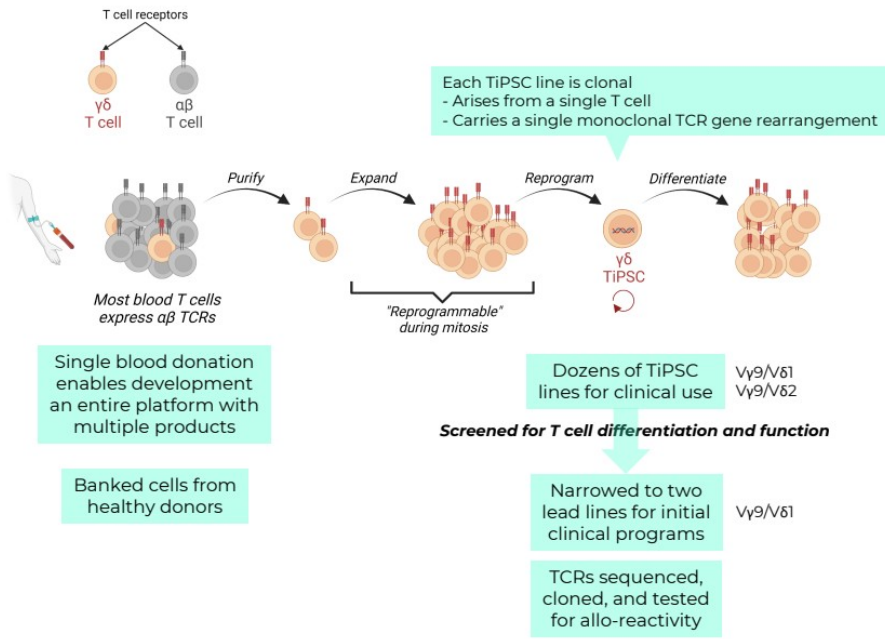
4. Pre-clinical
studies exhibiting
potent activity of
γδ CAR-T cells
against solid tumors

5. Leveraging Century's
T cell platform for CNTY-107
[Luis Borges, CSO]

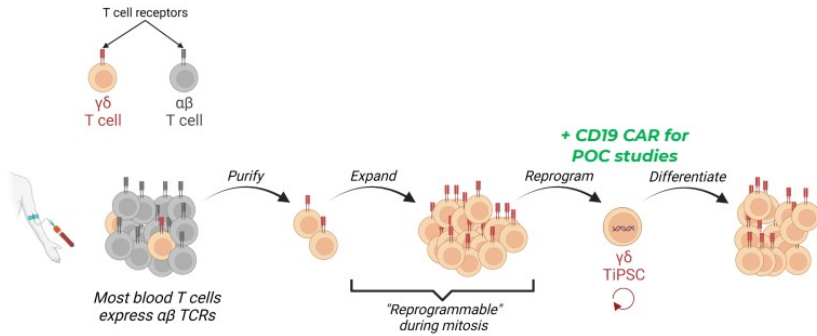
1. Reprogramming $\gamma\delta$ T cells into TiPSC



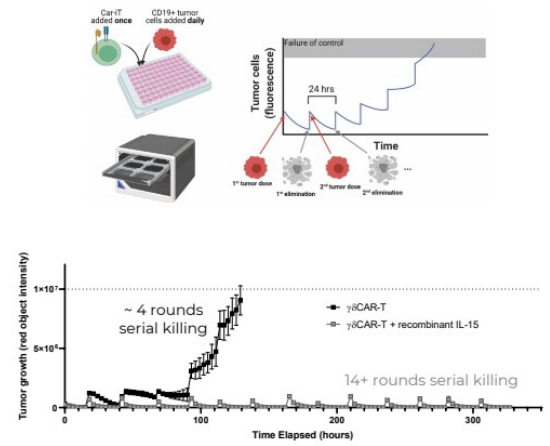
1. Reprogramming $\gamma\delta$ T cells into TiPSC



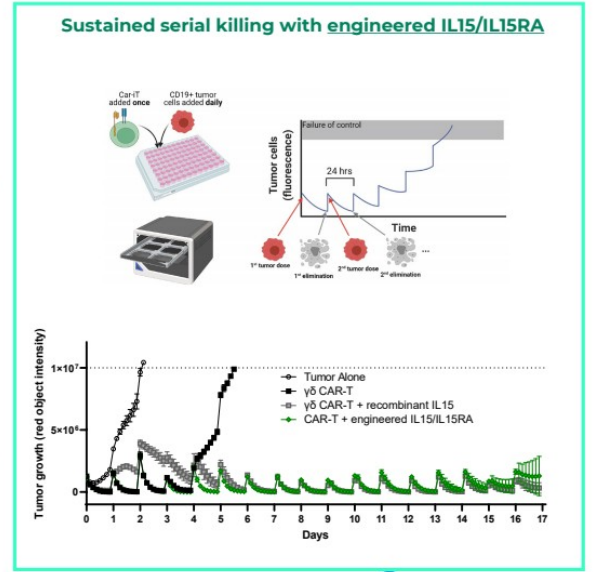
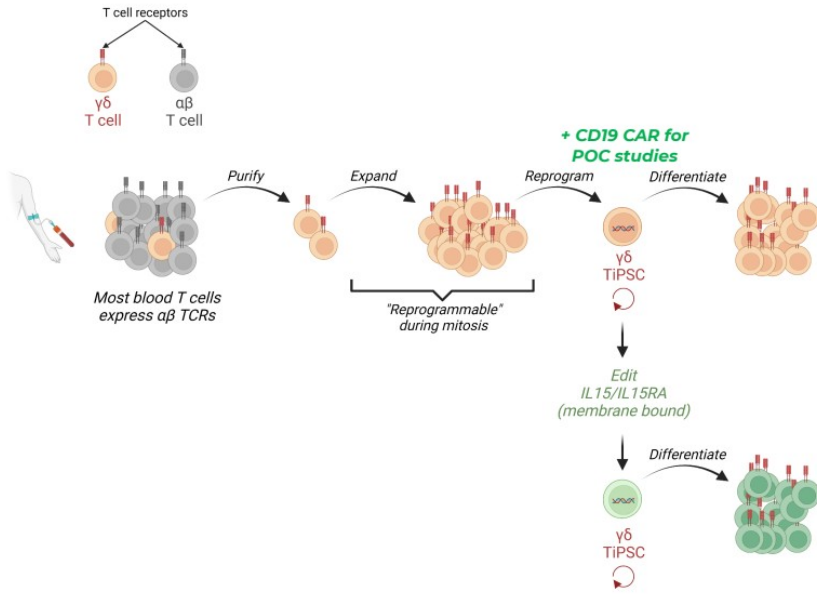
2. Engineering TiPSC for Enhanced Fitness



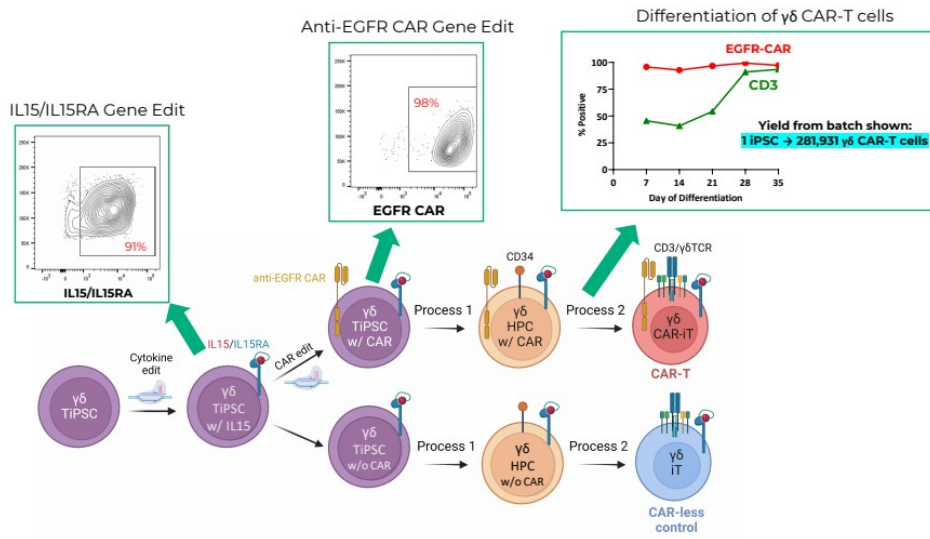
Sustained serial killing in presence of recombinant IL-15



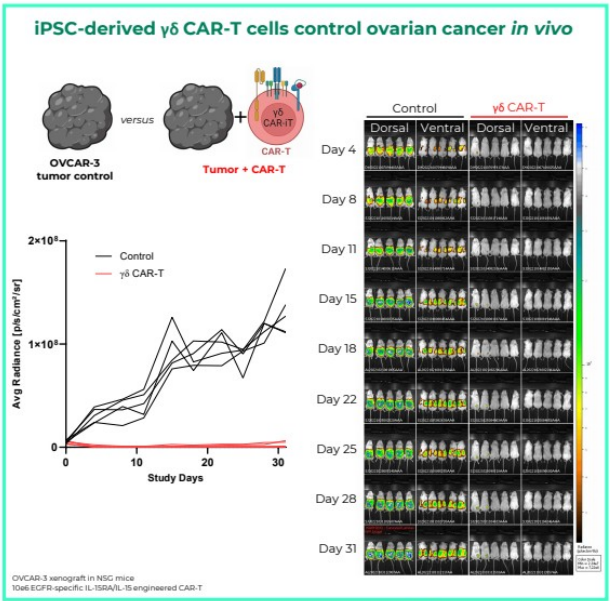
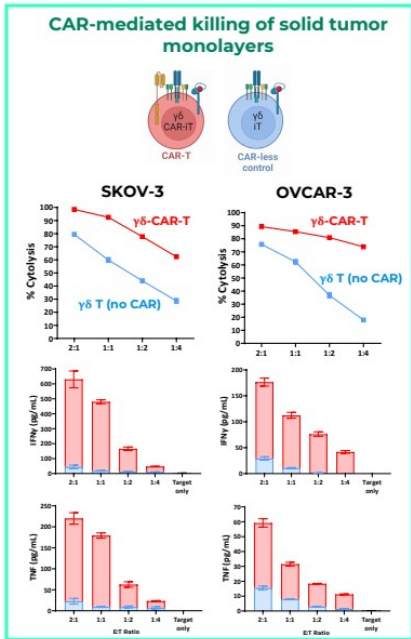
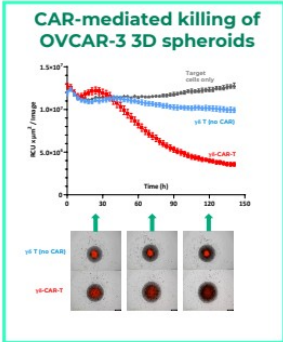
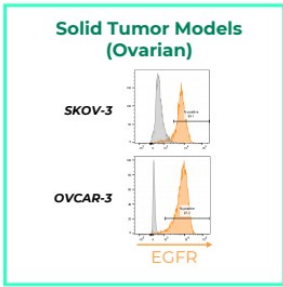
2. Engineering TiPSC for Enhanced Fitness



3. Differentiation of TiPSC into High-yield / High-purity T cells



4. Preclinical Studies Exhibiting Potent Activity of $\gamma\delta$ CAR-T Cells Against Solid Tumors



Summary

- Century has developed a fully in-house iPSC-derived $\gamma\delta$ T cell platform
- Technical advances have enabled successful proof of concept for pre-clinical utility of $\gamma\delta$ CAR-T cells for solid tumors
- The team is well-positioned to develop a solid tumor program for the clinic

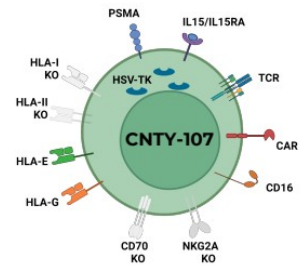


CNTY-107, our $\gamma\delta$ iT Product Candidate for the Treatment of Solid Tumors Expressing Nectin-4

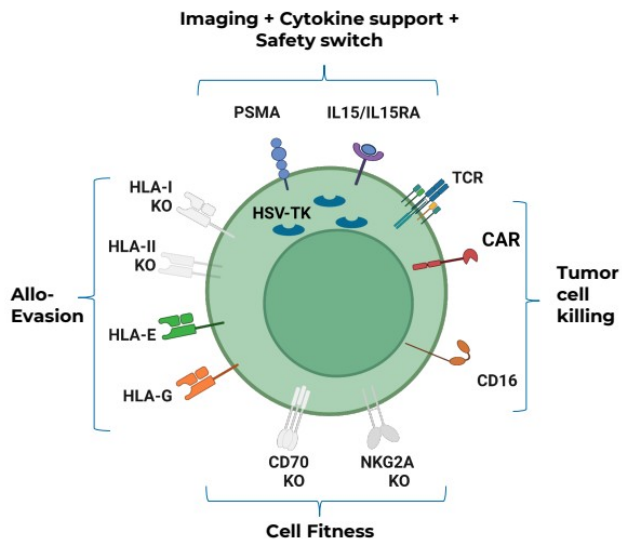
Luis Borges, PhD | CSO

CNTY-107, Next-Generation Product Candidate For The Treatment Of Nectin-4 Expressing Cancers

Challenges	Century's Solution	CNTY-107
Trafficking and infiltration	$\gamma\delta$ iT cells - tissue homing	$\gamma\delta_1$ iT cells, subset of $\gamma\delta$ T cells that preferentially home to tissues
Sufficient homeostatic cytokine support for enhanced persistence	Novel conditioning regimens Engineering	Cells engineered with homeostatic cytokine IL15/IL15R α and Allo-Evasion™
Tumor heterogeneity	Engage innate, endogenous immunity Multi tumor targeting pathways	Three major pathways for tumor targeting: Nectin-4 CAR, CD16, and innate receptors
TME / Immunosuppressive environment	Future engineering strategies	CD16 helps maximize combinations with antibodies that modulate TME

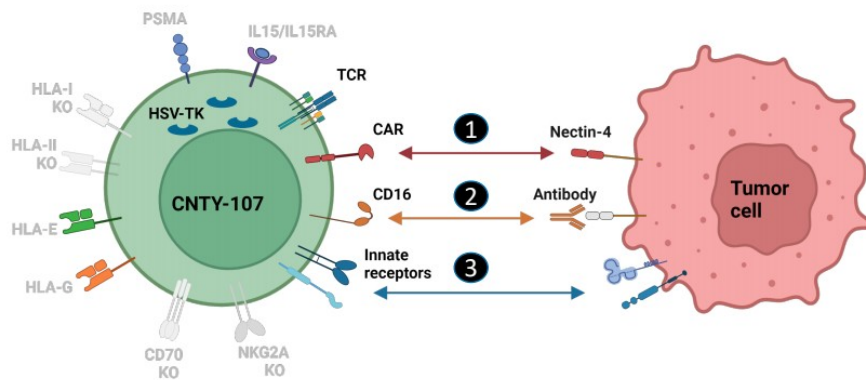


Engineering Profile of CNTY-107



ENGINEERING PROFILE			
Step	Gene Edit		Rationale
1	KO	β 2M	Allo-Evasion
	KI	HLA-E-2A-HLA-G	Allo-Evasion
2	KO	NKG2A	KO landing pad, potential to block inhibitory signal
	KI	IL15/IL15R α	Homeostatic cytokine support
3	KO	CD70	KO landing pad, potential to increase cell fitness
	KI	CD16	Tumor killing through ADCC
4	SHL	CLYBL	Safe harbor locus (SHL)
	KI	PSMA+HSV-TK	PSMA for cell tracing, HSV-TK as a safety switch
5	SHL	AAVS1	Safe harbor site
	KI	Nectin-4-CAR	Tumor targeting
6	KO	CIITA	Allo-Evasion

CNTY-107 Has Multiple Built-In Mechanisms for Tumor Killing



PATHWAYS FOR TUMOR KILLING

1. CAR-mediated killing
2. ADCC (Antibody-dependent cellular cytotoxicity)
3. Innate receptors (NCRs, others) mediated killing through recognition of stress ligands

Nectins

Nectins are cell adhesion molecules (CAMs) involved in Ca^{2+} -independent cell-cell interactions

The Nectin family includes four Nectins

- Nectins 1-3 are enriched in normal adult tissues
- Nectin-4 is mostly expressed during fetal development and its expression declines in adult tissues (low expression levels in skin, bladder, placenta, oral mucosa, and tonsils)

Nectins interact with other cell surface molecules including cadherins, integrins and growth factor receptors

- These interactions help modulate cell adhesion, migration, and proliferation

Nectin-4 dimers bind to Nectin-1 or Nectin-4 on adjacent cells

Nectin-4 also binds TIGIT on immune cells and this interaction leads to inhibition of NK cells

Interactions of Nectins and Cadherins Interact to Form Adherens Junctions and Promote Cell Adhesion

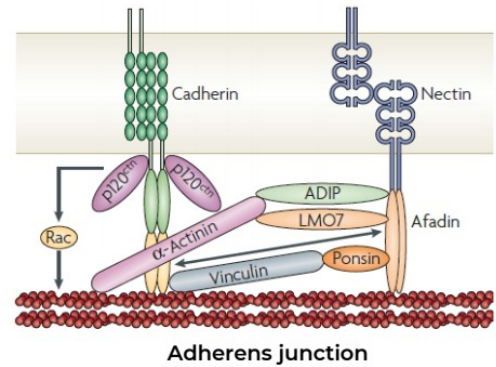


Figure adapted from Takai et al, Nat Rev Mol Cell Biol, 2008

Nectin-4 Expression in Cancer

- Nectin-4 is expressed in high frequency in bladder, breast, lung, pancreatic, ovarian, head & neck, and esophageal cancers
- The highest levels of expression of Nectin-4 are seen in bladder, breast, lung and pancreatic cancers
- Clinical validation of Nectin-4 as a tumor target has been demonstrated by the approval Enfortumab vedotin for the treatment of urothelial cancer

IHC Analysis of the Expression of Nectin-4 in a Panel of 2,394 Human Tumor Specimens

Cancer type	Intensity of staining*				Overall positive (%)
	Strong # (%)	Moderate # (%)	Low # (%)	Negative # (%)	
Bladder (N = 524)	362 (31)	84 (29)	18 (2)	90 (7)	83
Transitional (N = 467)	(34)	(30)	(2)	(16)	
Metastasis (N = 25)	(1)	(44)	(34)	(19)	
Others (N = 32)	(6)	(16)	(3)	(47)	
Breast (N = 654)	174 (27)	166 (26)	170 (26)	142 (22)	78
Ductal carcinoma (N = 388)	(3)	(25)	(2)	(2)	
Lobular carcinoma (N = 30)	(20)	(27)	(3)	(20)	
Metastasis (N = 205)	(18)	(27)	(3)	(24)	
Others (N = 35)	(3)	(26)	(2)	(20)	
Pancreatic (N = 164)	21 (13)	39 (24)	56 (34)	48 (29)	71
Lung (N = 688)	46 (7)	121 (20)	173 (28)	278 (45)	55
Squamous (N = 235)	(10)	(22)	(30)	(38)	
Adenocarcinoma (N = 212)	(5)	(25)	(34)	(36)	
Small cell carcinoma (N = 50)	(1)	(1)	(2)	(98)	
Metastasis (N = 77)	(2)	(19)	(29)	(40)	
Others (N = 44)	(7)	(3)	(8)	(70)	
Ovarian (N = 180)	0	21 (12)	46 (26)	51 (28)	57
Serous (N = 60)	0	(2)	(45)	(53)	
Mucinous (N = 34)	0	(5)	(7)	(43)	
Metastasis (N = 40)	0	(5)	(4)	(25)	
Others (N = 4)	0	(1)	(0)	(100)	
Head & Neck (N = 135)	3 (2)	22 (16)	54 (40)	56 (41)	59
Esophageal (N = 81)	7 (4)	37 (20)	55 (30)	82 (45)	55
Total (N = 2,394)	413 (17)	962 (24)	672 (28)	747 (31)	69

*Intensity of staining: strong, H-score = 200-300; moderate, H-score = 100-199; low, H-score = 15-99; negative, H-score = 0-14.

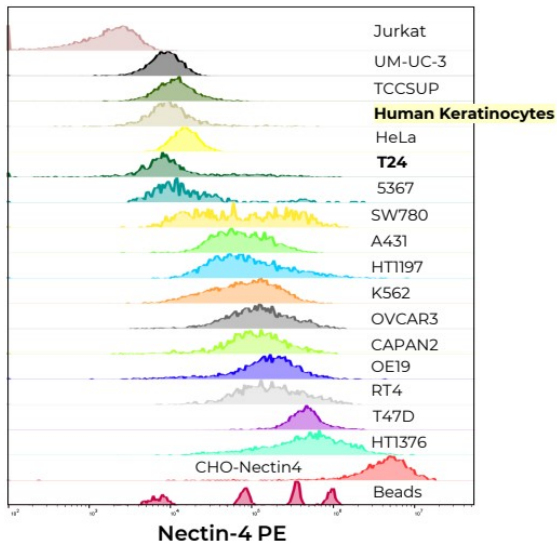
From Challita-Eid et al., Cancer Research, 2016

Tumors With the Highest Expression of Nectin-4

Tumor Histology	Moderate to High Expression
Bladder	60%
Breast	53%
Pancreatic	37%
Lung	27%

Nectin-4 Expression Levels On Human Skin Keratinocytes Is Lower Than In Most Tumor Cell Lines

Nectin-4 Expression in Multiple Cells

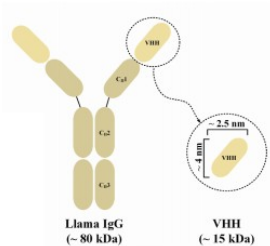


Ranking Of Tumor Cells Based On Nectin-4 Expression Level

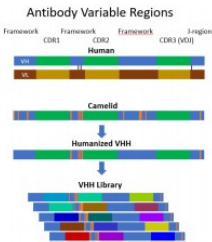
Cell Line	Origin	Ranking
UM-UC-3	Bladder cancer	Negative
TCCSUP	Bladder cancer	
JURKAT	T cell	
HeLa	Cervical cancer	Low (50-250)
T24	Bladder cancer	
Human keratinocytes	Normal skin	Medium (3,000 - 10,000)
S637	Bladder cancer	
HT1197	Bladder cancer	
SW780	Bladder cancer	
K562	CML	
A431	Breast cancer	
CAPAN2	Pancreatic cancer	
OVCAR3	Ovarian cancer	
OE19	Esophageal cancer	High (10,000+)
RT4	Bladder cancer	
HT1376	Bladder cancer	
T47D	Breast cancer	
CHO-Nectin4	Chinese Hamster Ovary	

Selection of VHH Binders to Build Nectin-4 CAR

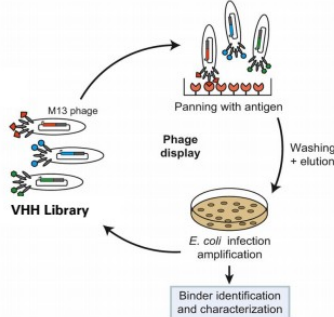
Llama VHH antibodies



Century's Proprietary VHH Libraries



Llama VHH Library Screens



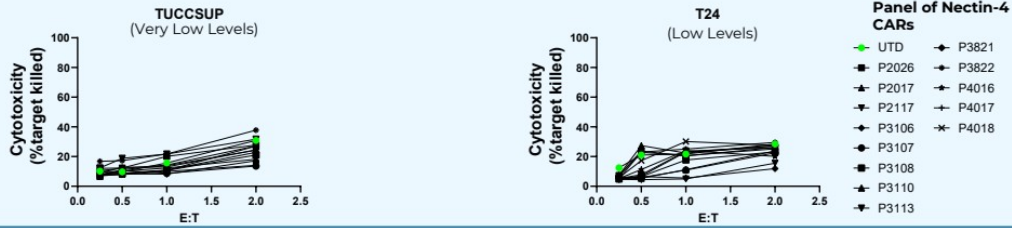
Assay Screening Flow to Select Nectin-4 Binders and CARs



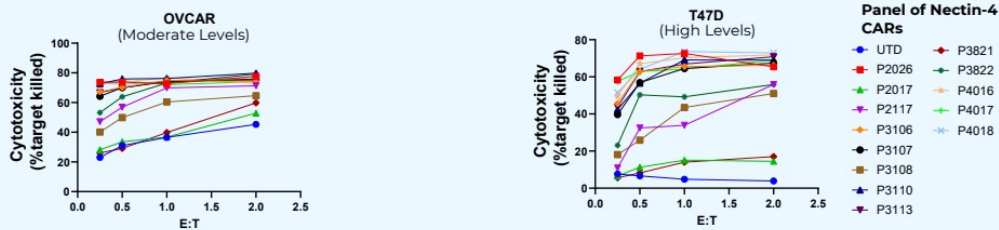
Not for further distribution

Century's Nectin-4 CARs Distinguish Between Cells Expressing Low vs. Moderate to High Levels Of Nectin-4

Century's Nectin-4 CARs Do Not Kill Cells Expressing Low Levels of Nectin-4

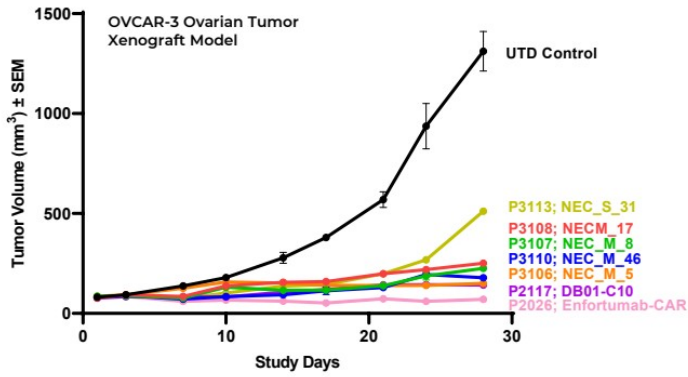


Century's Nectin-4 CARs Kill Cells Expressing Moderate to High Levels of Nectin-4



CNTY-107 Nectin-4 CARs Mediate Robust Anti-Tumor Activity *in Vivo*

In Vivo Evaluation of the Anti-tumor Activity Nectin-4 CARs Using Peripheral Blood CAR-T Cells



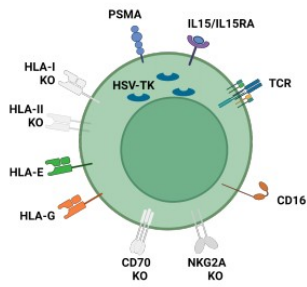
- 5×10^6 OVCAR-3 cells implanted subcutaneously in the right flank
- Mice randomized after tumors reached 75-125 mm³
- Mice treated with 5×10^6 CAR-T cells

All CAR Constructs Mediated Statistically Significant Tumor Growth Inhibition (TGI)

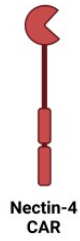
Treatment Group	Day 28 % TGI	Day 28 P-Value
P3108 - NECM_17	80.8	0.0003
P3107 - NEC_M_8	82.8	0.0002
P3110 - NEC_M_46	86.4	0.0001
P3106 - NEC_M_5	88.5	0.0001
P2117 - DB01-C10	89.2	0.0007
P3113 - NEC_S_31	61.1	0.0116
P2026 - Enfortumab-CAR	94.7	<0.0001

CNTY-107 Next Steps and Milestones

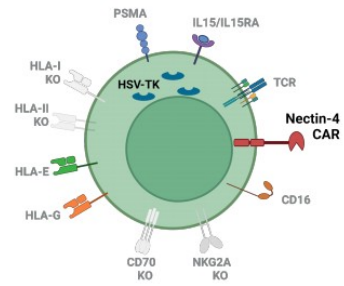
Complete Engineering of the $\gamma\delta$ iT Common Progenitor



Select Nectin-4 CAR



Add CAR to $\gamma\delta$ iT CP to Generate CNTY-107



Major CNTY-107 Product Candidate Milestones

Completion of CNTY-107 Engineering	Clinical Candidate Selection	IND Filing
1H23	2H23	2025

CNTY-107 Preliminary Clinical Strategy

- **Initial Phase I clinical study is planned to be run as a basket trial that will include multiple Nectin-4 positive cancers**
 - Cancers under consideration include bladder, breast, pancreatic, non-small cell lung cancer, esophageal, head and neck, and/or ovarian cancers
- **Dose-escalation will be done in the basket trial**
- **The clinical trial will be designed to expand in any indication with acceptable tox and clinical responses**
- **To enrich for potential responders among selected indications, we are developing an IHC-based Nectin-4 screening assay to potentially help select patients**
 - We will develop our own fit-for-trial IHC assay
- **Ability to evaluate combination therapies**
 - Combination therapy cohorts could be indication-specific (e.g., HER-2 antibody for breast cancer) or "generic", addressing modulation of the TME (e.g., PD-L1 antibody, Avelumab)



Thank you



Q&A

