UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 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 16, 2021

Neoleukin Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-36327**	**98-0542593**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

188 East Blaine Street, Suite 450
Seattle, Washington 98102
(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: (866) 245-0312

N/A
(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:

☐ 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(s)	Name of each exchange on which registered
Common Stock, $0.000001 par value	**NLTX**	**The Nasdaq Global 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 8.01. Other Events

Neoleukin Therapeutics, Inc. (the "Company") has prepared investor presentation materials with information about the Company, which it intends to use as part of investor presentations. A copy of the investor presentation materials to be used by management for presentations is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL Document)

SIGNATURE

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.

NEOLEUKIN THERAPEUTICS, INC.

Date: November 16, 2021

By: /s/ Robert Ho
Robert Ho
Chief Financial Officer

Exhibit 99.1

neoleukin™
THERAPEUTICS

Corporate Presentation

November 2021

Forward Looking Statements

Certain of the statements made in these slides and the accompanying oral presentation are forward looking, including those relating to Neoleukin's business, strategy, future operations, advancement of its product candidates and product pipeline, clinical development of its product candidates, including expectations regarding timing of regulatory submissions and initiation of clinical trials, regulatory requirements for initiation of clinical trials and registration of product candidates, properties of its product candidates, availability of data, the use and sufficiency of its cash resources and other statements containing the words "anticipate," "believe," "expect," "may," "plan," "project," "potential," "will," "would," "could," "continue," and similar expressions. These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: whether results of early clinical trials or preclinical studies will be indicative of the results of future trials, the adequacy of any clinical models, uncertainties associated with regulatory review of clinical trials; our ability to identify or acquire additional clinical candidates, our ability to obtain and maintain regulatory approval for any product candidates and the potential safety, efficacy or clinical utility of or any product candidates; further impacts of COVID-19 on our operations; and other factors discussed in the "Risk Factors" section of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 as filed with the Securities and Exchange Commission. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. More information about the risks and uncertainties faced by the Company is contained in its Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, Annual Report on Form 10-K for the year ended December 31, 2020, and subsequent reports, filed with the Securities and Exchange Commission. The Company disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Leader in Therapeutic Protein Design

First Program: Cancer Immunotherapy

Platform technology: computational protein design methods for creating *de novo* Neoleukin™ cytokine mimetics

NL-201 program: highly potent, non-alpha, combined IL-2 and IL-15 receptor agonist for cancer immunotherapy

Expanding opportunities: building expertise in *de novo* protein therapeutics for cancer and inflammation

2018 FOUNDED

2019 PUBLIC

2020 NL-201 IND

2021 PHASE 1

2022 BROADEN STRATEGY

SEATTLE WA

NASDAQ: NLTX

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Neoleukin™ Progress in 2021

- Moved into new headquarters in Seattle (~33,000 sq ft)
- Initiated Phase 1 clinical trial in solid tumors for NL-201
- Plan to initiate hematologic malignancy trial in 2022
- Presented preclinical IL-2/IL-15 inhibitor molecule for inflammatory conditions
- Executive leadership: Priti Patel, CMO; Bill Arthur, VP, Head of Research
- Added expertise in CMC and Clinical (~100 FTE)
- Continuing to build our pipeline and technology

Leadership Team

Jonathan Drachman, M.D.
Chief Executive Officer
Prior: CMO, EVP R&D, Seagen

Robert Ho
Chief Financial Officer
Prior: Morgan Stanley & Co., DaVita

Priti Patel, M.D., M.S.
Chief Medical Officer
Prior: AstraZeneca, Acerta Pharma

Bill Arthur, Ph.D.
VP & Head of Research
Prior: Seagen, Merck & Co.

Holly Vance, J.D., Pharm.D.
General Counsel
Prior: Gates Foundation

Carl Walkey, Ph.D.
Senior VP, Corporate Development
Prior: Postdoctoral Fellow, UW-IPD

Samantha Willing
Senior VP, People
Prior: Seagen, Microsoft

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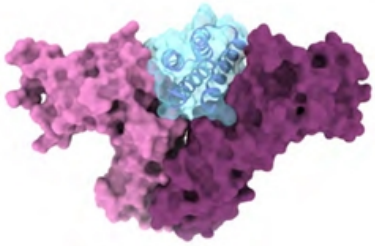
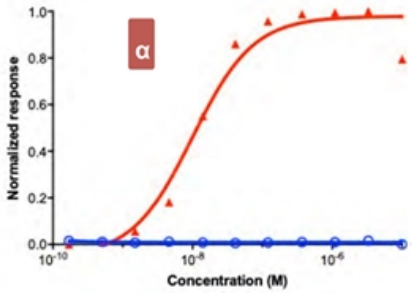
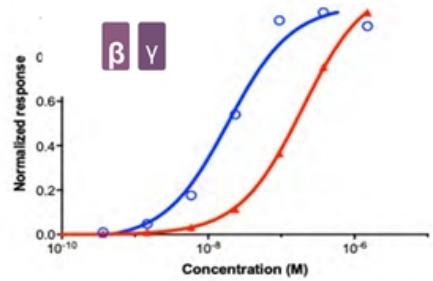
NL-201: *De Novo* IL-2/IL-15 Agonist

Designed to retain benefits of IL-2 without drawbacks

- 100% non-alpha: no residual alpha subunit binding
- No bias toward T-regulatory or endothelial cells
- More potent than IL-2 *and* IL-15
- Activates CD8+ naïve T-cells *and* NK cells
- Hydrophilic, compact, increased thermal stability



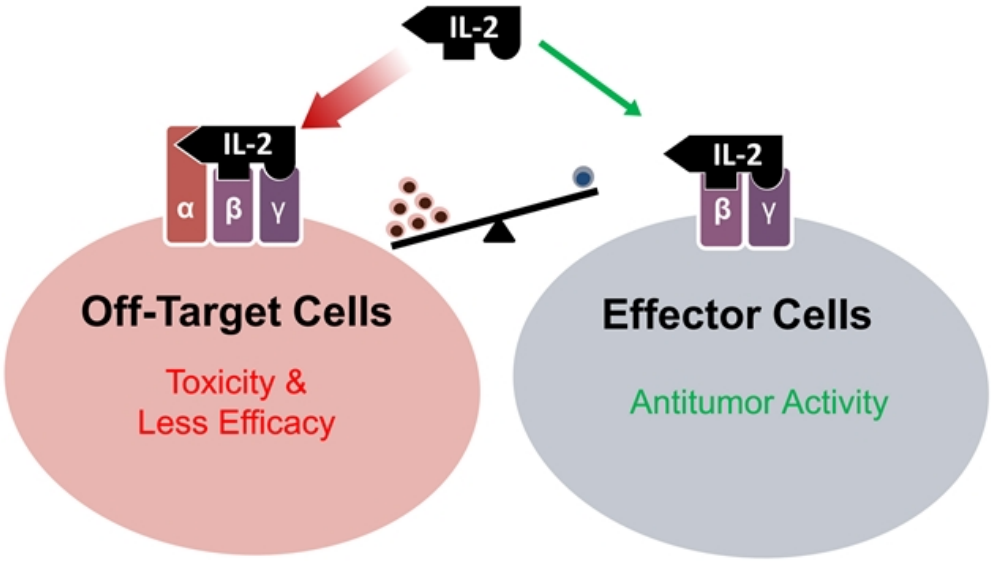




Neoleukin-2/15 hIL-2

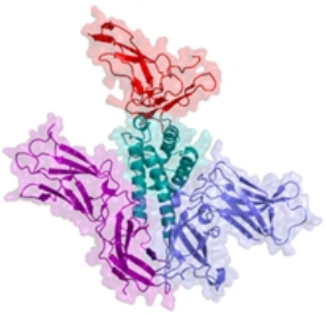
Source: Silva et al. *Nature*, 565, 186-191 (2019)

IL-2 Binds Strongly to Non-Target Cells, Causing Toxicity and Limiting Efficacy

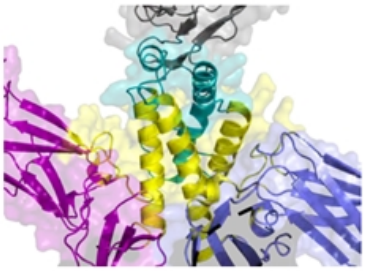


Building a Neoleukin™ Cytokine Mimetic in 4 Steps

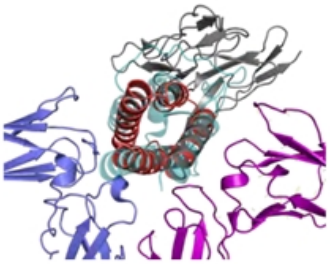
1. Develop an accurate structural model of the target



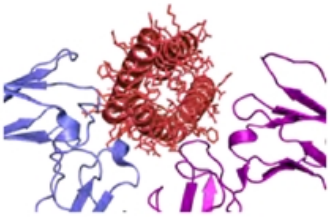
2. Identify regions of intermolecular contact



3. Design an idealized topology



4. Assign optimal amino acid sequence



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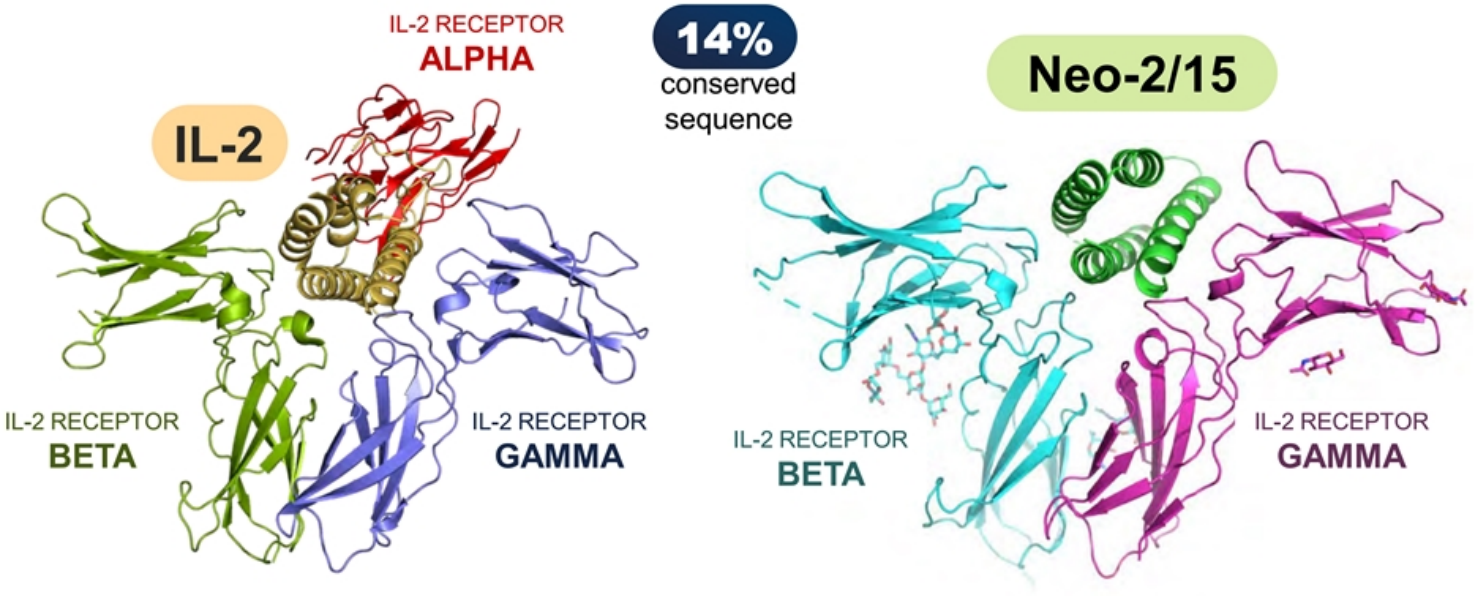
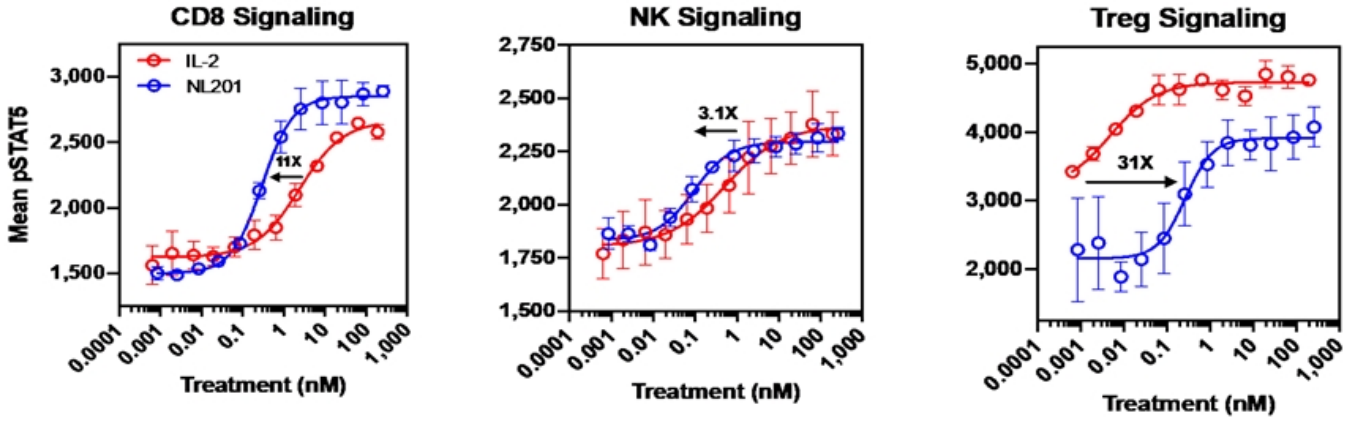
Crystal Structure Shows Neo-2/15 Binding Beta/Gamma as Predicted



Source: Silva et al. *Nature*, 565, 186-191 (2019)

NL-201 Stimulates CD8 Effector T and NK Cells More Selectively Than IL-2

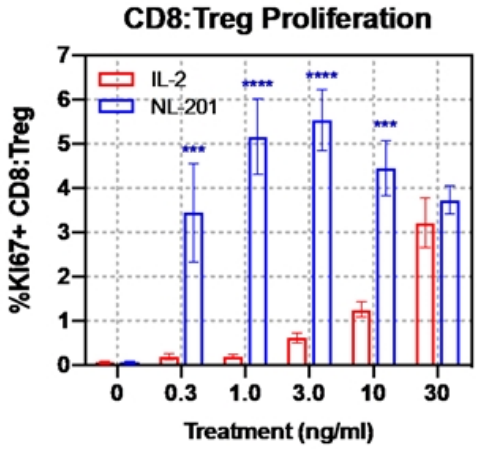


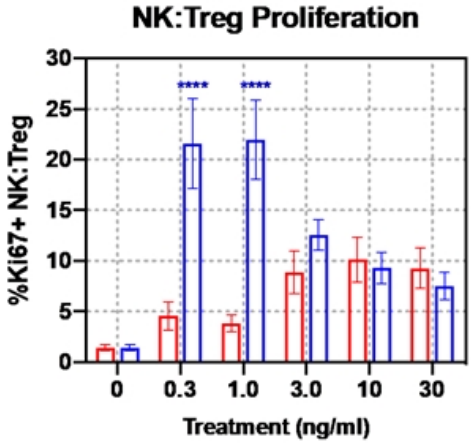
- NL-201 is ~330-fold and ~90-fold more selective for CD8+ T and NK cells (vs. Tregs) than IL-2, respectively

Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

1) STAT5 phosphorylation in CD8+ T cells, NK cells, and Tregs was measured by flow cytometry using PBMCs from 10 healthy human donors. Proliferation was evaluated using Ki67.

NL-201 Stimulates Dose-Dependent CD8:Treg and NK:Treg Proliferation More Potently Than IL-2





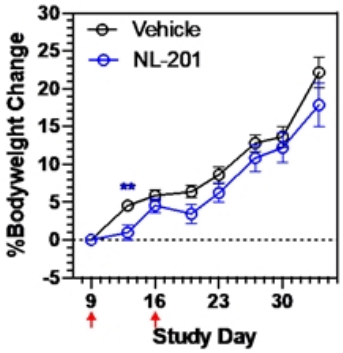
Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

1) NL-201 vs IL-2: * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001

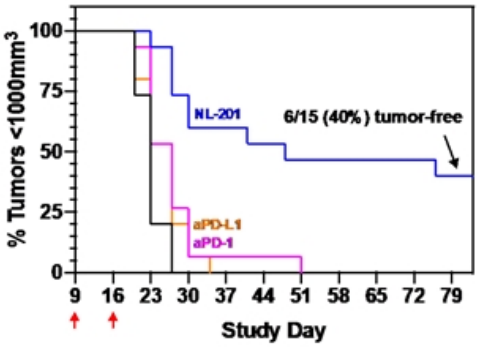
NL-201: is Well Tolerated and Promotes Durable Antitumor Activity

CT26: syngeneic colon cancer model

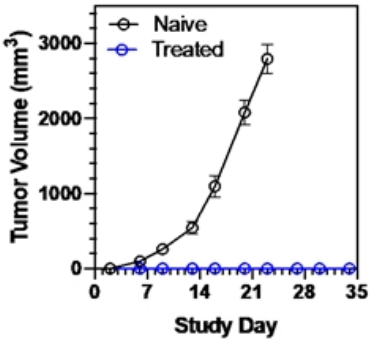
Tolerability



Tumor Growth Inhibition



Re-Challenge



- NL-201 is well-tolerated at therapeutic doses
- NL-201 treatment exhibits single-agent activity
- NL-201 promotes durable anti-tumor immunity

Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

1) Study in a checkpoint inhibitor-resistant CT26 colon cancer murine model.

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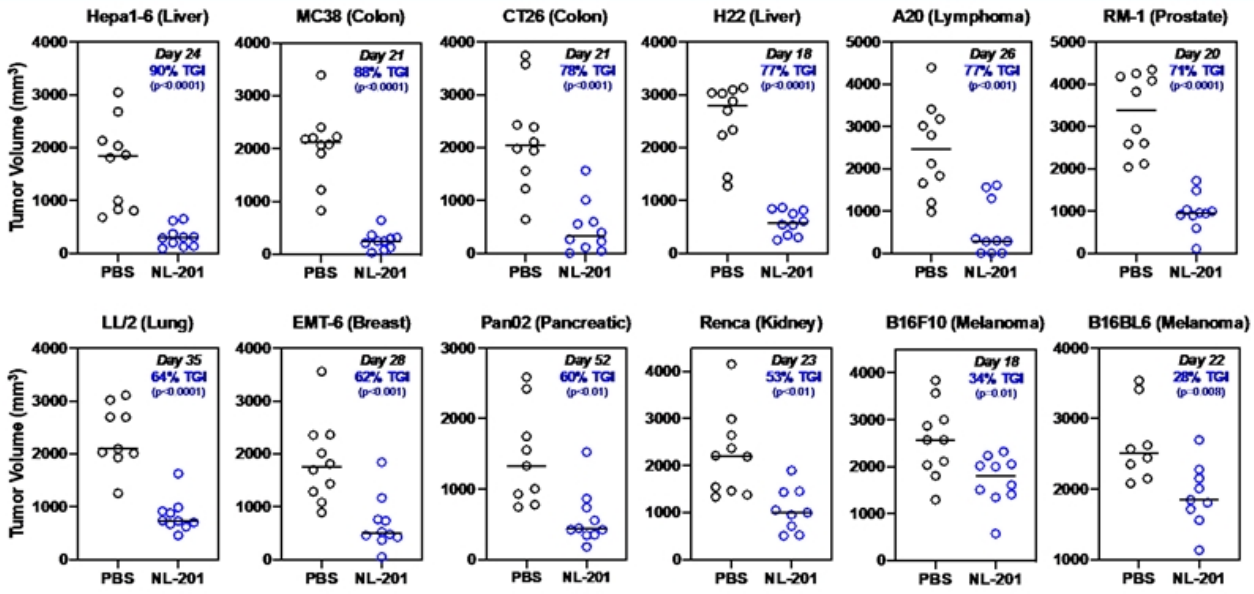
NL-201 Demonstrates Robust Single-Agent Activity in Multiple Tumor Models



1) NL-201 was administered QWx2 when tumors reached ~100mm3. Tumor growth inhibition (TGI) is reported in each graph vs. control.
2) NL-201 treatment inhibited tumor growth in all models: NL-201 significantly inhibited tumor growth in models that are typically refractory to anti-PD-1 checkpoint inhibitors.

Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

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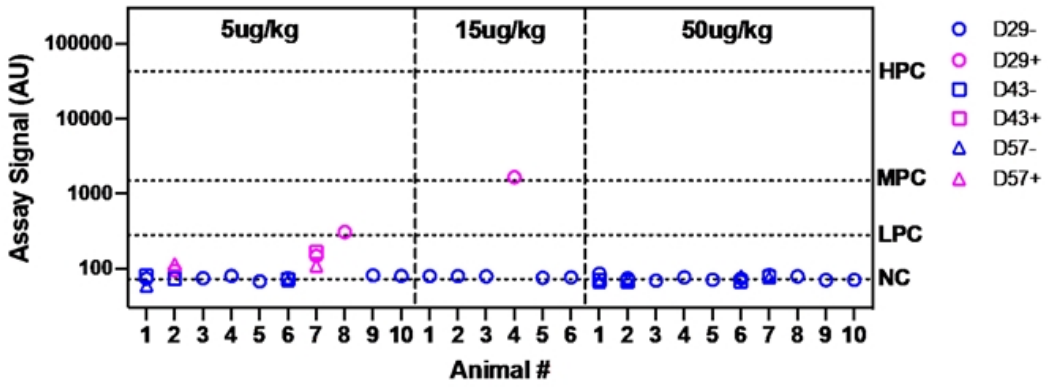
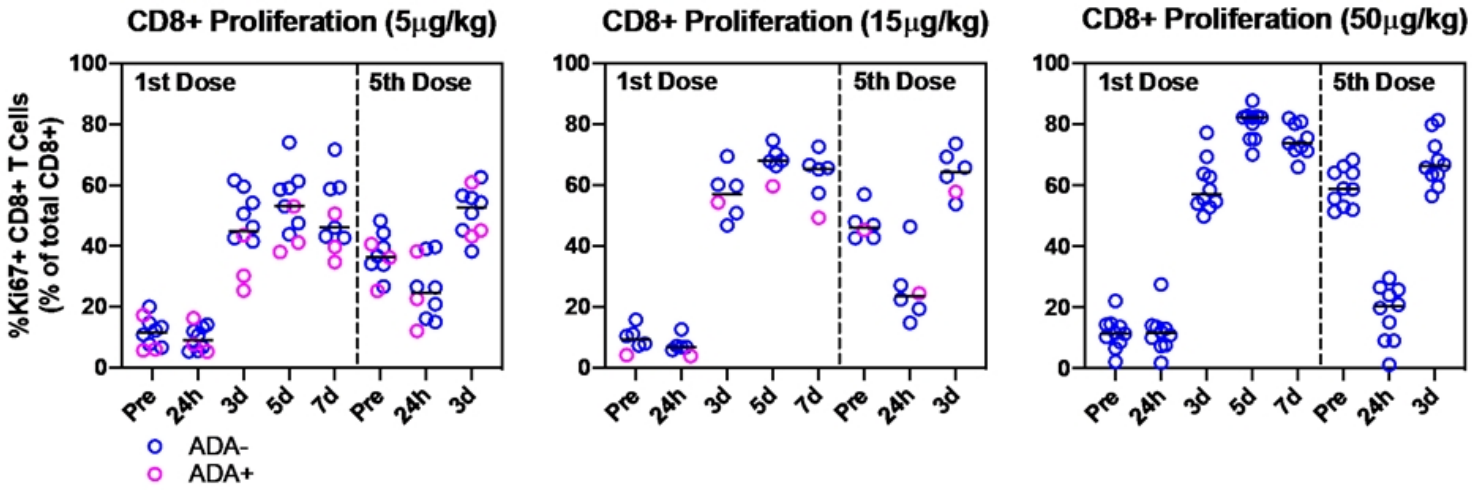
NL-201 Shows Minimal Immunogenicity in NHPs



- ADAs were detectable in: 3/10 NHPs at 5µg/kg; 1/6 NHPs at 15µg/kg; 0/10 NHPs at 50µg/kg NL-201
- 3 of 4 ADA+ NHPs were at or below the low positive control (LPC) level

Abstract #4518, Walkey et. al, AACR Virtual Annual Meeting II, June 2020

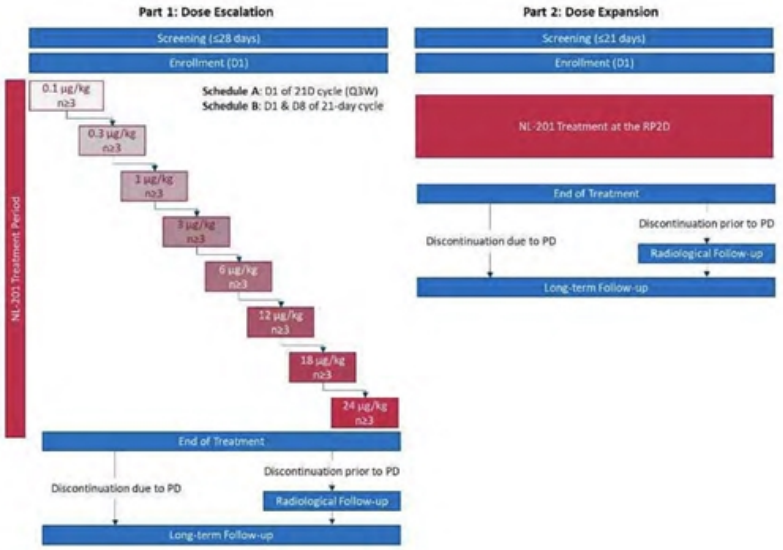
Similar Pharmacodynamics and Tolerability Observed in ADA+ vs ADA- NHPs



Adapted from Abstract #4518, Walkey et. al, AACR Virtual Annual Meeting II, June 2020

NL-201 Phase 1 Clinical Trial in Solid Tumors

- IV, monotherapy in patients with relapsed or refractory solid tumors
- Part 1: Identify optimal dose and schedule; assess safety, PK, PD, and antitumor activity
- Part 2: Indication-specific expansion cohorts, including renal cell carcinoma and melanoma
- Clinical sites in Australia, U.S. and Canada
- Enrollment up to 120 patients
- Interim data expected in 2022



Naing et al, SITC Nov 2021

NL-201: Broad Clinical Opportunity

- Plan to initiate a trial for patients with heme malignancies in 2022
  - IL-2 and IL-15 have activity in multiple B-cell lineage preclinical models
  - Abstract to be presented at ASH 2021 (Atlanta, GA) on antitumor activity of NL-201 in multiple myeloma
- Future opportunities to combine with checkpoint inhibitors, monoclonal antibodies, cellular therapies, and other standard-of-care agents
- Potential advantages of NL-201 local administration presented at SITC 2021

NL-201 Turns 'Cold' Tumor 'Hot'

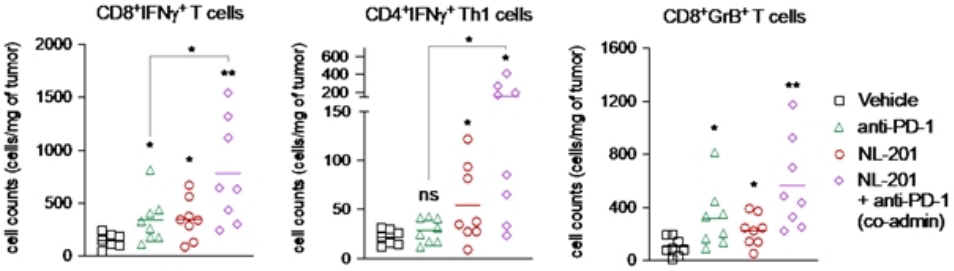
Augments inflammatory milieu in preclinical B16 melanoma model

TCRβ Sequencing Summary

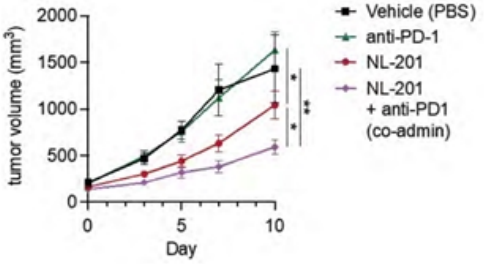
Mean (range)	Total T cells	Unique T cells	Simpson Clonality
Vehicle (n=5)	1,406 (358-2,708)	445 (196-807)	0.194 (0.106-0.411)
anti-PD-1 (n=5)	2,456 (987-4,713)	464 (314-775)	0.34 (0.138-0.57)
NL-201 (n=5)	2,664 (1,578-3,816)	869 (611-1,064)	0.206 (0.11-0.292)
NL-201 plus anti-PD-1 (co-admin) (n=5)	2,865 (1,504-3,456)	1,042 (536-1,486)	0.128 (0.073-0.165)

NL-201:

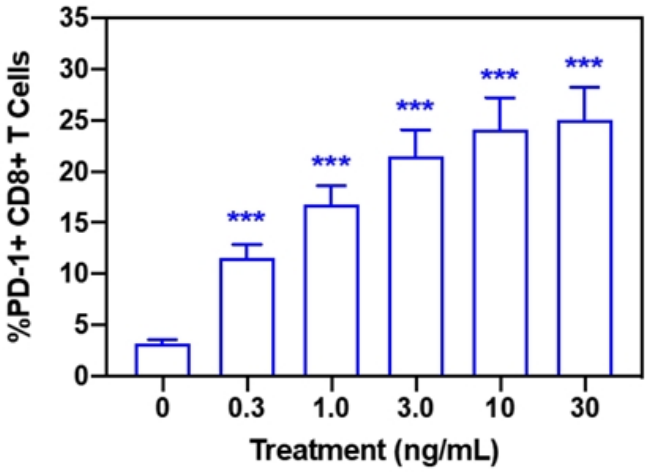
- increases T-cell diversity in the tumor microenvironment
- augments IFNγ and granzyme B expression in T-cells
- synergizes with anti-PD1 to inhibit tumor growth



Mortales et. Al, SITC 2021, Abstract #716, Nov 2021



NL-201 Upregulates PD-1 Expression by CD8+ T Cells



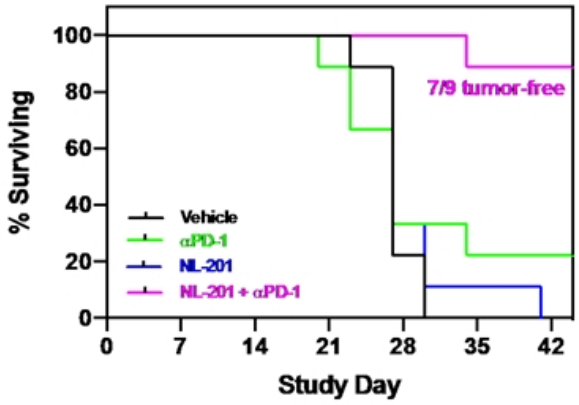
- NL-201 induces concentration-dependent PD-1 expression by CD8+ T cells
- Combining NL-201 with a checkpoint inhibitor may overcome PD-L1 mediated T cell inhibition

Walkey et. Al, SITC 2020, Abstract #576, November 2020

NL-201 Enhances Activity of Checkpoint Inhibitors in Preclinical Models

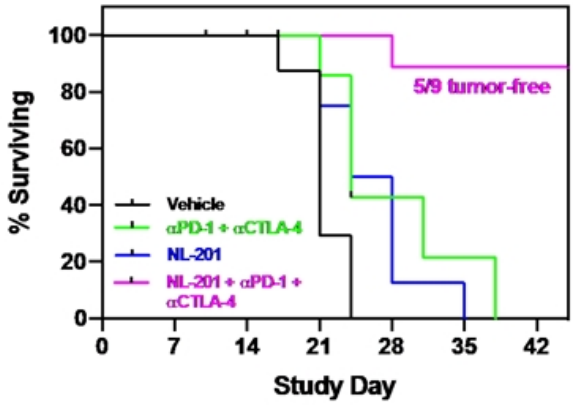
- NL-201 enhances activity of CPIs in breast and kidney cancer models
- Combination with NL-201 beneficial in CPI-resistant syngeneic tumors

EMT-6 (Breast)



p=0.0029: αPD-1 vs NL-201 + αPD-1
p<0.0001: NL-201 vs NL-201 + αPD-1

Renca (Kidney)



p=0.0001: αPD-1 + αCTLA-4 vs NL-201 + αPD-1 + αCTLA-4
p=0.0006: NL-201 vs NL-201 + αPD-1 + αCTLA-4

NL-201: 90µg/kg QWx2
αPD-1: 10mg/kg BiWx6
αCTLA-4: 10gm/kg BiWx6
Treatment began when tumors reached ~90mm³

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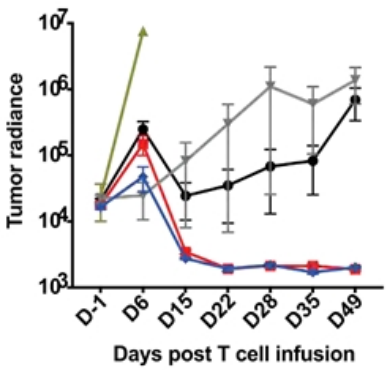
Promising NL-201 Preclinical Combinations In Vivo

Enhanced antitumor activity with CAR-T cells and antibodies

RAJI Lymphoma Model

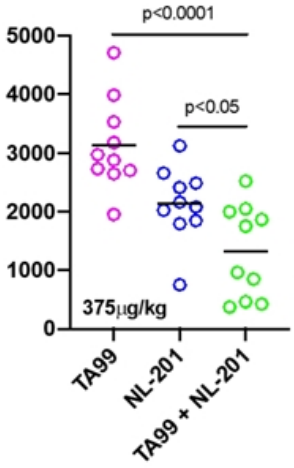


Subcurative doses of CAR-T cells combined with NL-201 achieve deep tumor control and 100% survival

NL-201 enhances intratumoral CD8:Treg ratios (~1000x vs. ~50x for IL-2)

Leung et. al, AACR Annual Meeting II, Abstract #2222, June 2020

B16 Melanoma Model



NL-201 + TA99 (mAb) significantly improved tumor growth inhibition when combined

Walkey et. Al, SITC 2020, Abstract #576, November 2020

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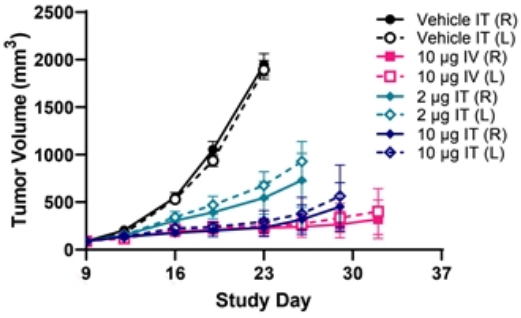
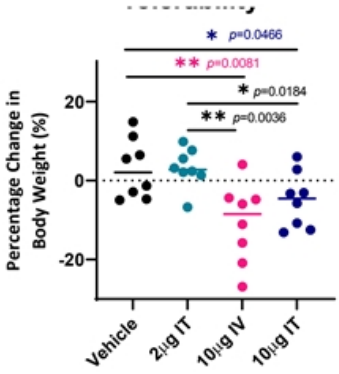
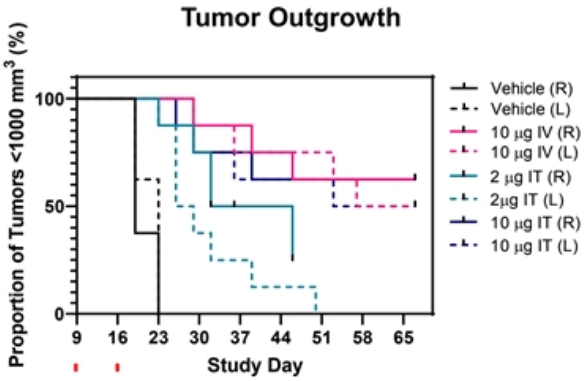
Intratumoral NL-201: Local and Distant Antitumor Activity with Improved Tolerability







- CT26 syngeneic tumor model with bilateral tumor implants
- IT (R only) or IV NL-201 administered q7dx2
- 10 mcg IV exceeded 20% weight loss in some mice

Tatalick et al, SITC 2021, Abstract #898, November 2021

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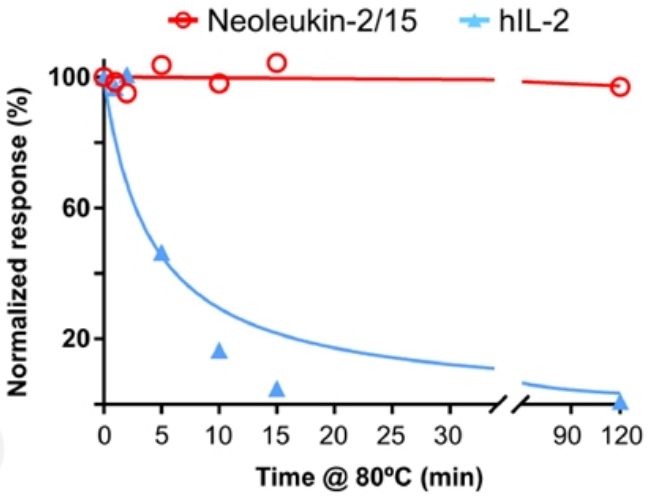
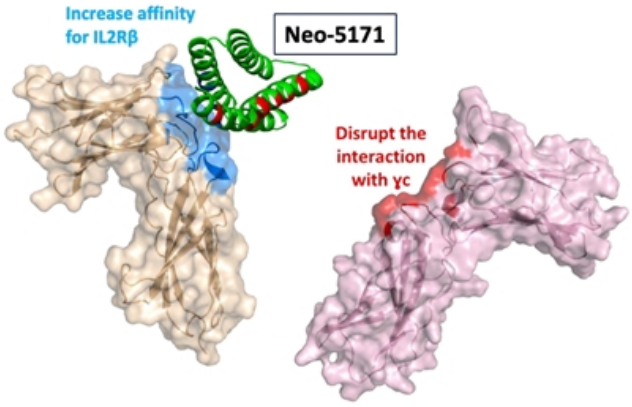
Neoleukin™ Cytokine Mimetics are Hyperstable and Easily Modified

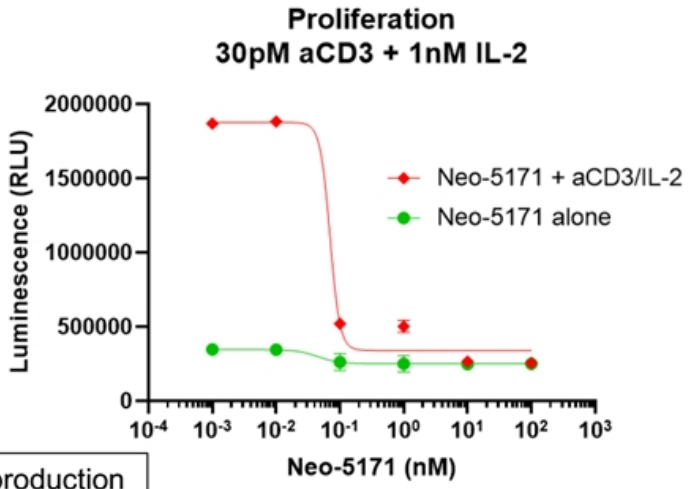
- Able to withstand extreme conditions
- Able to adjust half-life or tune affinity
- Can use with targeting domain to improve biodistribution
- Can be conditionally activated in the tumor microenvironment
- Can be modified to make cytokine antagonists for inflammatory and autoimmune diseases



Source: Silva et al. *Nature*, 565, 186-191 (2019)

Neo-5171: A computationally designed de novo protein inhibitor of IL-2 and IL-15 signaling





- Potent inhibitor of CD8 T-cell proliferation and IFN-γ production
- Resistant to proteases and low pH
- Less impact on T-regulatory cells

R. Swanson et. al. Am. Coll Rheum. (ACR) 2021; Abstract 1438, Nov 2021

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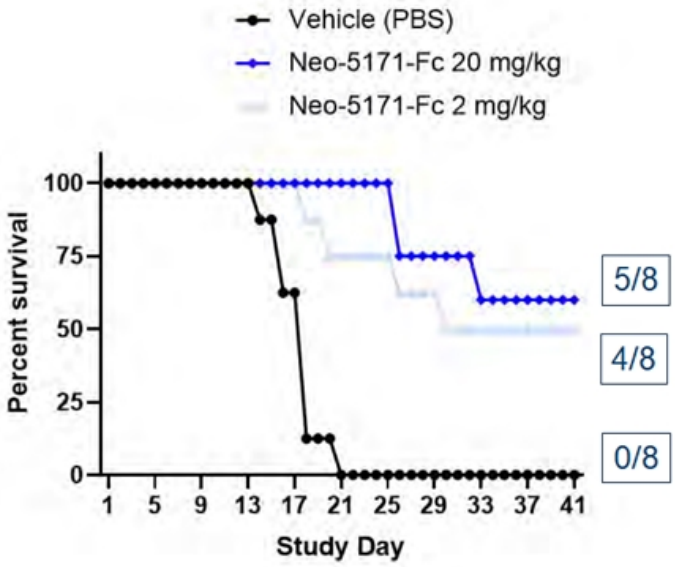
Neo-5171-Fc prolongs survival in a preclinical model of graft-vs-host disease (GVHD)



- Immunodeficient NSG mice were irradiated and received 10 million human PBMC, Day -1
- Intraperitoneal dosing with Neo-5171-Fc q3d, beginning on Day 0
- Mice were euthanized when experiencing >20% body weight loss
- 62.5% of mice survived at study end (Day 42)

R. Swanson et. al. Amer Coll Rheum (ACR) 2021; Abstract 1438, Nov 2021

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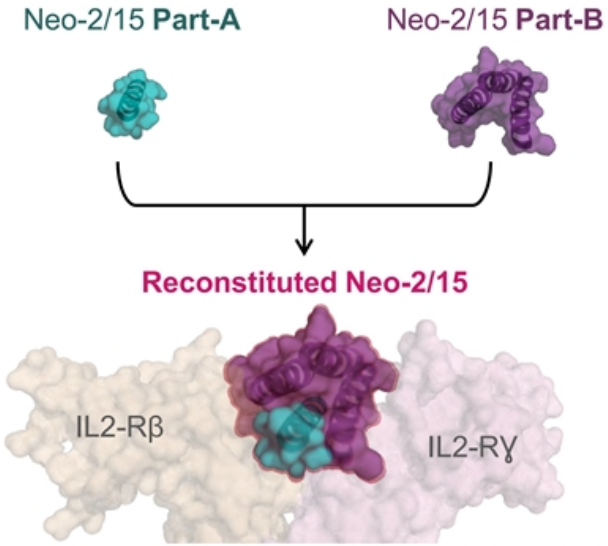
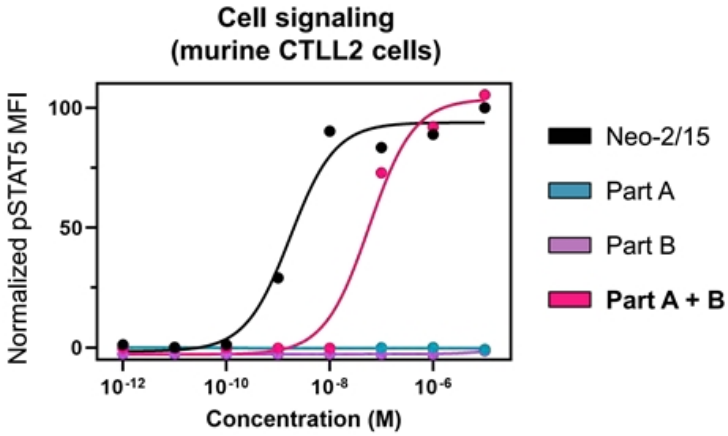
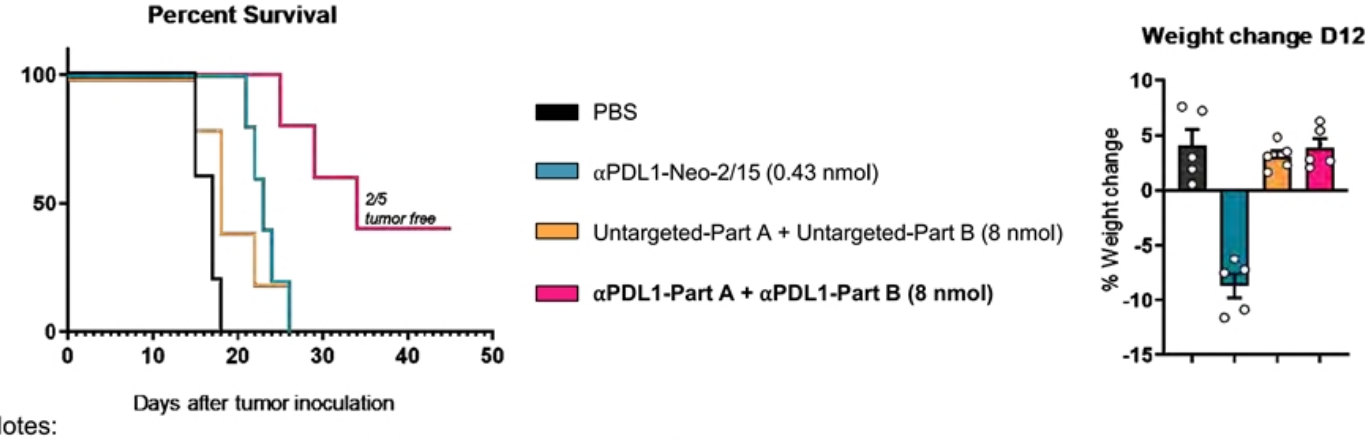
De Novo Split Technology - Conditionally Active IL-2 Mimetic





Quijano-Rubio et. Al., AACR Virtual Annual Meeting II, Abstract #1075, Jun/2020

Targeted Split Neo-2/15 Increases Therapeutic Window



Notes:

1) C57BL/6J mice bearing B16 PDL1Hi melanoma cells in flank.
2) All groups were co-treated biweekly with Ta99 mAb (150µg/mice)
3) Targeted Neo-2/15 variants and Part-A fusions administered i.p.; Part-B fusions administered s.c. opposite flank of tumor

Quijano-Rubio et. Al., AACR Virtual Annual Meeting II, Abstract #1075, Jun/2020

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Functional De Novo Proteins

Better Therapies by Design

nature 2019

Article | Published: 09 January 2019

De novo design of potent and selective mimics of IL-2 and IL-15

Daniel-Adriano Silva, Shawn Yu, Umut Y. Ulge, Jamie B. Spangler, Kevin M. Jude, Carlos Labão-Almeida, Lestat R. Ali, Alfredo Quijano-Rubio, Mikel Ruterbusch, Isabel Leung, Tamara Biary, Stephanie J. Crowley, Enrique Marcos, Carl D. Walkey, Brian D. Weitzner, Fátima Pardo-Avila, Javier Castellanos, Lauren Carter, Lance Stewart, Stanley R. Riddell, Marion Pepper, Gonçalo J. L. Bernardes, Michael Dougan, K. Christopher Garcia & David Baker

Science 2020

CORONAVIRUS Article | Published: 4 December 2020

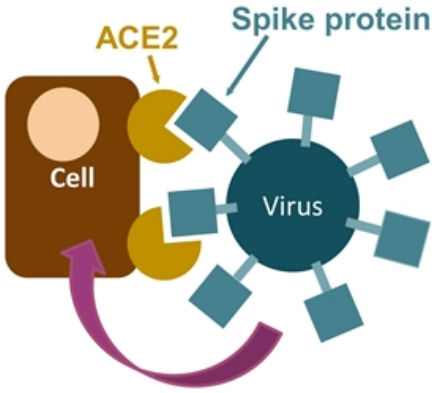
De novo design of potent and resilient hACE2 decoys to neutralize SARS-CoV-2

Thomas W. Linsky[1*], Renan Vergara[1*], Nuria Codina[1*], Jorgen W. Nelson[1*], Matthew J. Walker[1], Wen Su[2], Christopher O. Barnes[3], Tien-Ying Hsiang[4], Katharina Esser-Nobis[4], Kevin Yu[1], Z. Beau Reneer[5], Yixuan J. Hou[4], Tanu Priya[1], Masaya Mitsumoto[1], Avery Pong[1], Uland Y. Lau[1], Marsha L. Mason[1], Jerry Chen[1], Alex Chen[1], Tania Berrocal[1], Hong Peng[1], Nicole S. Clairmont[1], Javier Castellanos[1], Yu-Ru Lin[1], Anna Josephson-Day[1], Ralph S. Baric[6], Deborah H. Fuller[7], Carl D. Walkey[1], Ted M. Ross[5,8], Ryan Swanson[1], Pamela J. Bjorkman[3], Michael Gale Jr.[4], Luis M. Blancas-Mejia[1], Hui-Ling Yen[2], Daniel-Adriano Silva[1]†

- Scientific founders are world leaders in *de novo* protein design
- Technology originated at University of Washington Institute for Protein Design
- Exclusive license obtained for commercialization of NL-201 and other *de novo* protein assets

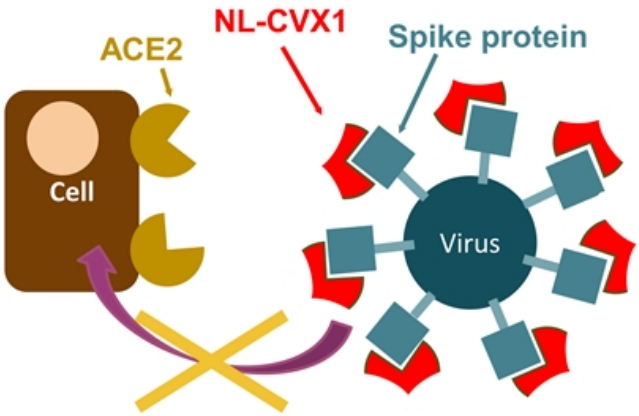
De Novo Platform Potential – COVID-19

SARS-CoV-2 uses **ACE2** as a receptor to gain access to and infect cells



NL-CVX1 - *de novo* ACE2 decoy:

- *Binds to SARS-CoV2 spike protein*
- *Inhibits viral infection in vitro*
- *Designed, tested, optimized in ~10 weeks*



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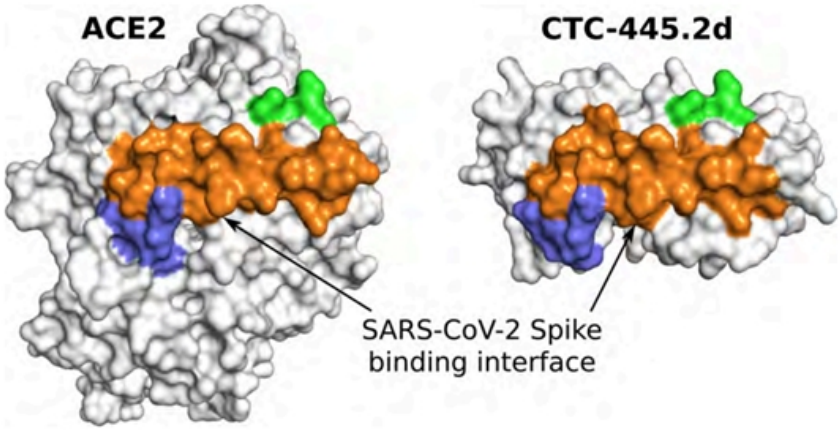
NL-CVX1 – *De Novo* Protein Decoy

De novo design of potent and resilient hACE2 decoys to neutralize SARS-CoV-2



Science AAAS

T. W. Linsky et. al. Science. 10.1126/science.abe0075 (2020)

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Financial Highlights & Upcoming Milestones

Financial

- $154.9 million cash & cash equivalents as of September 30, 2021
- Cash and cash equivalents expected to fund operations into 2H 2023
- 42.4M common shares outstanding and 12.7M pre-funded warrants[1]

Upcoming Milestones

- Expect to release NL-201 interim phase 1 data in 2022
- Plan to initiate phase 1 heme malignancy trial for NL-201

[1] Warrants to purchase common shares 1:1 with an exercise price of $0.000001 as of September 30, 2021.


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Designing for life.