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): January 10, 2022

Neoleukin Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

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

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

o

Item 7.01 Regulation FD Disclosure

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.

The information in this current report on Form 8-K and in Exhibit 99.1 attached hereto is being furnished, but shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended ("Exchange Act"), and is not incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 8.01 Other Items

The Company announced the following updates to its clinical and preclinical programs:

- The Company expects interim data on its Phase 1 clinical trial of NL-201 in patients with solid tumors in 2022, and to initiate a Phase 1 clinical trial of NL-201 in patients with hematologic malignancies.
- The Company currently has three preclinical programs in the discovery phase: (1) Neo-202, which is a next generation IL-2/15 agonist; (2) Neo-5171, which is an IL-2/15 antagonist being developed for the treatment of autoimmune and inflammatory conditions, and (3) Neo-TRA, which is a T-reg agonist being developed for the treatment of autoimmune and inflammatory conditions.
- The Company expects to begin its evaluation of NL-201 and KEYTRUDA (pembrolizumab) in a Phase 1 clinical trial.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Number	Description
99.1	Presentation of Neoleukin Therapeutics, Inc. dated January 2022
104	Cover Page Interactive Data File (formatted as Inline XBRL)

SIGNATURE

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

Date: January 10, 2022

Neoleukin Therapeutics, Inc.
By: /s/ Robert Ho
Name: Robert Ho
Title: Chief Financial Officer

Exhi

Corporate Presentation

January 2022

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, clinic development of its product candidates, including expectations regarding timing of regulatory submissions and initiation of clini 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 expressior These statements are subject to risks and uncertainties that could cause actual results and events to differ materially from thos 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 Sept. 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 Sept. 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.

Key Company Highlights

De novo Protein Platform

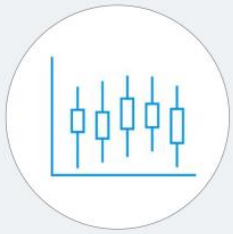
Neoleukin's computational protein design method for creating cytokine mimetics has the potential to overcome biological limitations of natural proteins.

Large Market in I/O Asset

Sales of the top 3 immunotherapy drugs totaled $25M in 2020, which represented compound annual growth of 36% over the prior 3 years.

Proven Mechanism of Action in IL-2

Aldesleukin (rhIL-2) is approved for the treatment of metastatic renal cell carcinoma and melanoma. Neoleukin's NL-201 is designed to stimulate an immunological response with potentially greater selectivity and less toxicity.

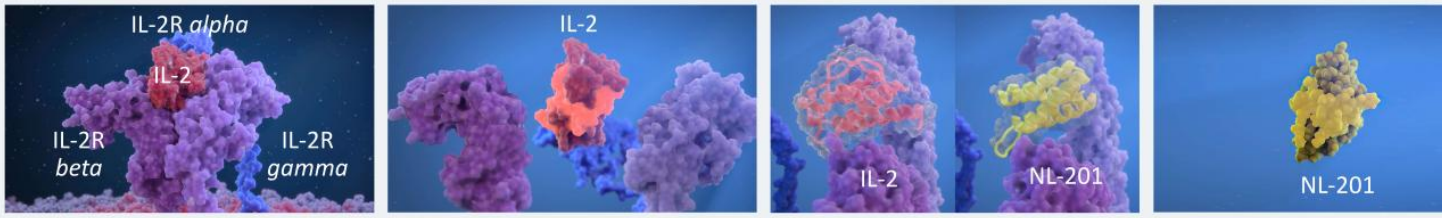


Data in 2022

Initiated phase 1 clinical trial for NL-201 in 2021.

Interim data is expected in 2022.

Building a Neoleukin™ Cytokine Mimetic



1 Develop an accurate structural model of target

2 Identify regions of intermolecular contact

3 Design an idealized topology

4 Assign optimal amin acid sequences

Pipeline

	Program	Mechanism	Discovery	Preclinical Development	Phase 1	Anticipated Milestone / Statu
Oncology	NL-201	IL-2/15 Agonist Solid Tumors				Ph. 1 Interim Data – 2022
		IL-2/15 Agonist Heme Malignancies				Ph. 1 Initiation – 2022
	Neo-202	Next-gen IL-2/15 Agonist				
Inflammation	Neo-5171	IL-2/15 Antagonist Autoimmune / Inflammatory Conditions				Pre-clinical data disclosed Q4 20
	Neo-TRA	T-reg Agonist Autoimmune / Inflammatory Conditions				

NL-201 is believed to be the 1st *de novo* protein in clinic

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

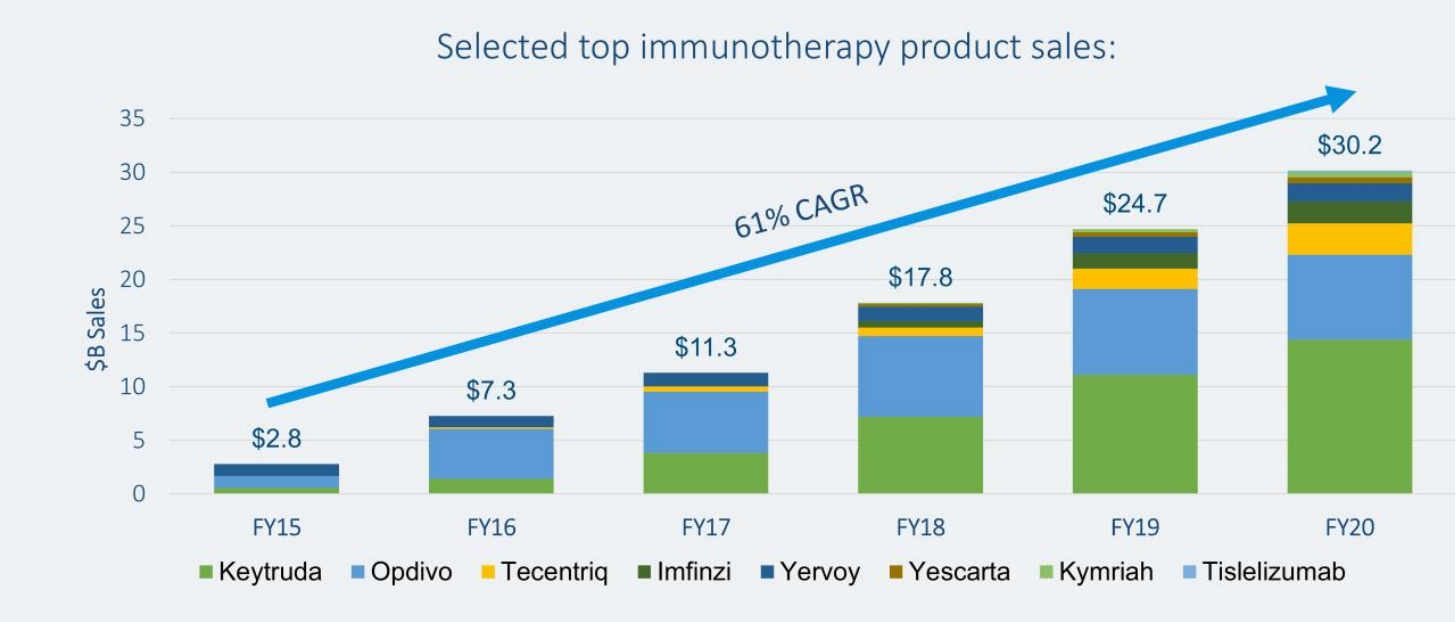
Priti Patel, M.D., M
Chief Medical Officer
PRIOR
AstraZeneca, Acerta Pharma

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

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

Samantha Willing
Senior VP, People
PRIOR
Seagen, Microsoft

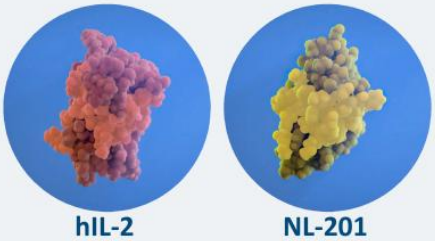
Large Market Opportunity in Immunotherapy



NL-201: *De Novo* is What's New

NL-201 is computationally designed for optimal biological activity:

- Only 14% conserved sequence vs. native IL-2
- No potential/residual alpha subunit (CD25) binding
- Activates both IL-2 and IL-15 pathways
- More potent than native IL-2 on NK- and naïve CD8 T-cells
- Smaller and more thermodynamically stable than IL-2



hIL-2 **NL-201**

Current opportunities

- Infrequent systemic dosing
- Local administration

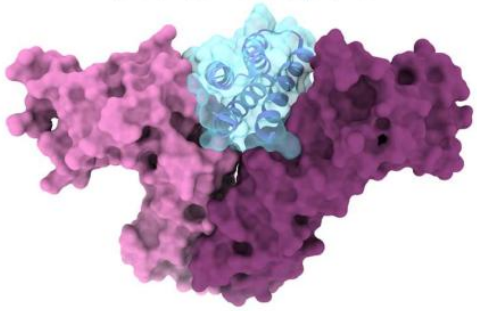
Modifiable for improved biodistribution (future)

- Targeting to tumor microenvironment
- Conditional activation

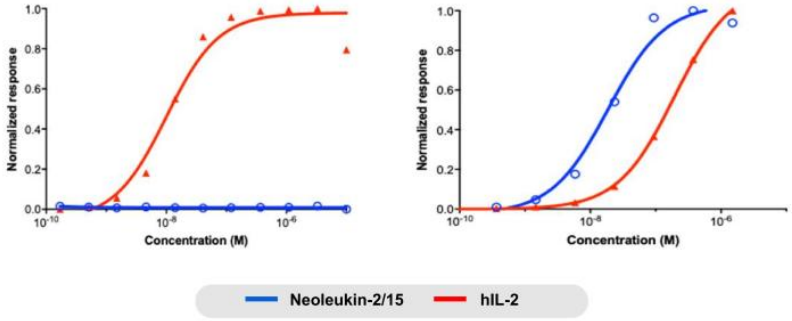
Why NL-201?

More potent IL-2/IL-15 agonist, no bias toward Tregs or endothelial cells

14% Conserved sequence



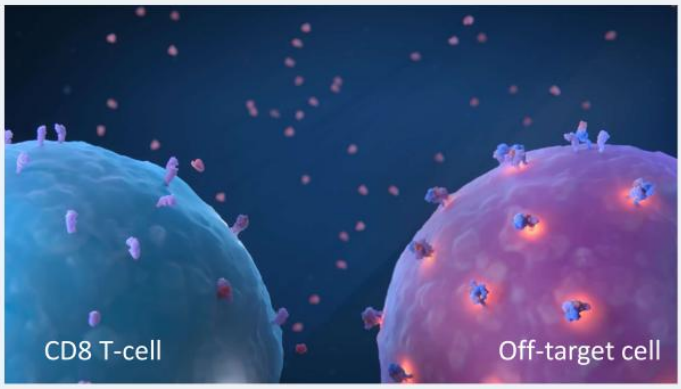
Source: Silva et al. *Nature*, 565, 186-191 (2019)



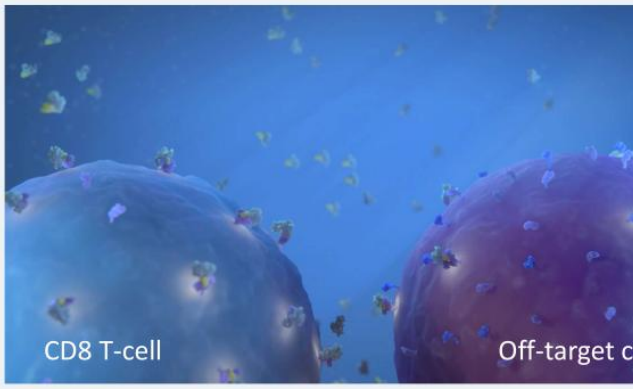
NL-201 is a de novo protein designed with no alpha subunit interaction and increased beta/gamma binding

NL-201 Is Designed to Have No Bias for Off-Target Cells

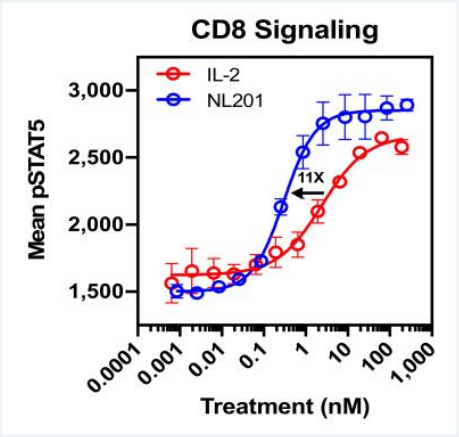
IL-2

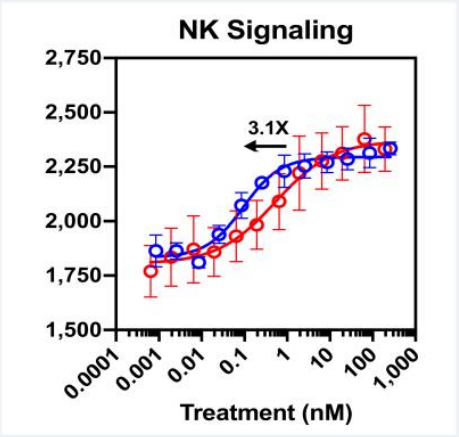


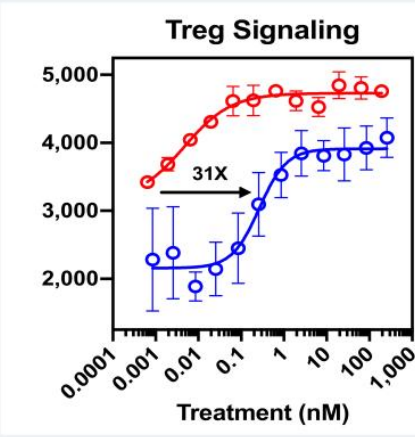
NL-201



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





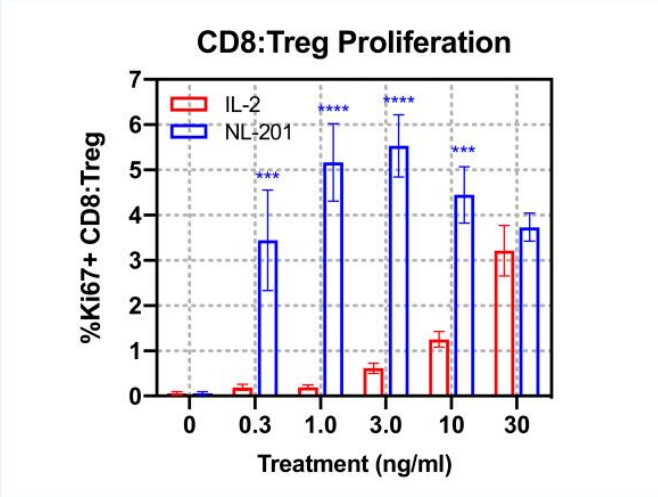


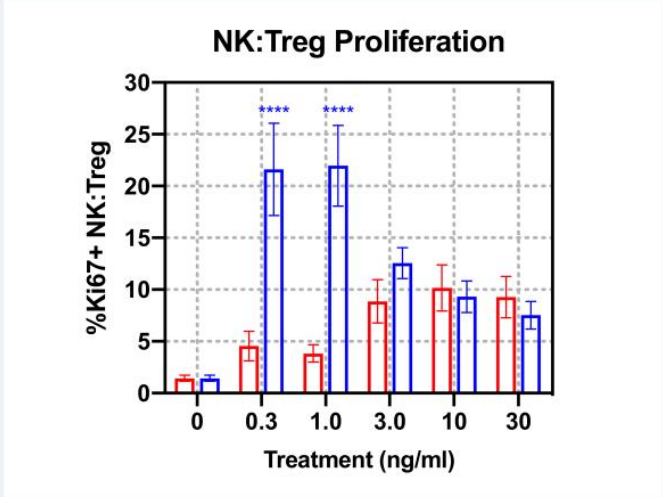
NL-201 is ~330-fold and ~90-fold more selective for CD8+ T and NK cells (vs. Tregs) than IL-2, respectivel

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.

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

NL-201: High CD8:Treg and NK:Treg Ratios at Low Concentration



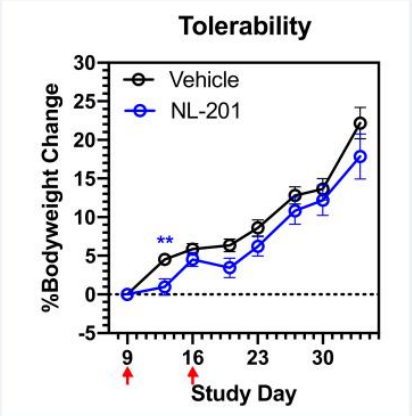


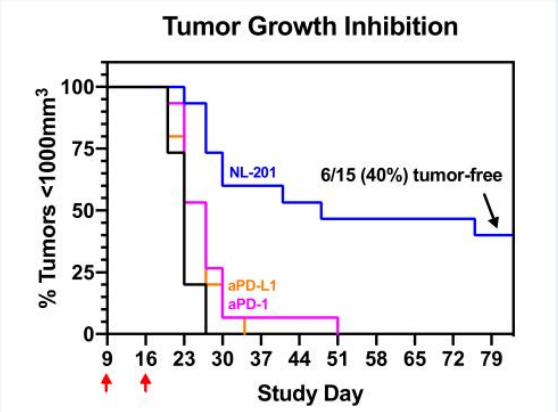
NL-201 vs IL-2: * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001

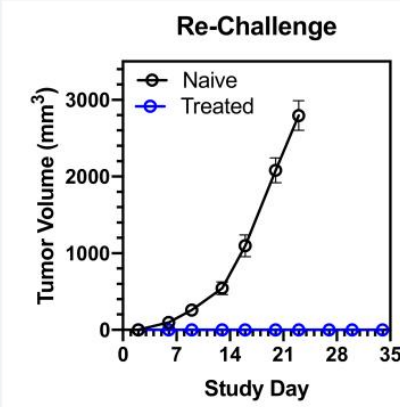
Walkey et. al, AACR Virtual Annual Meeting II, Abstract #4518, June 2020

NL-201: Durable Antitumor Activity at Well-tolerated Doses

CT26 syngeneic murine colon cancer model



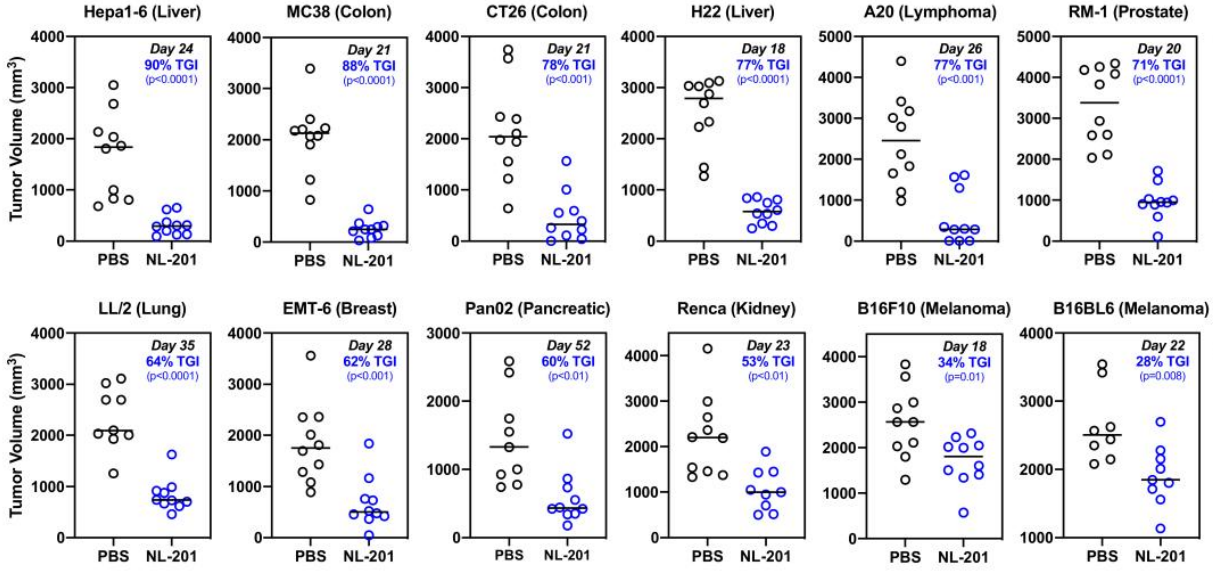




- NL-201 is well-tolerated at therapeutic doses
- Single-agent activity observed
- Tumor-free mice reject CT26 upon re-challenge

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

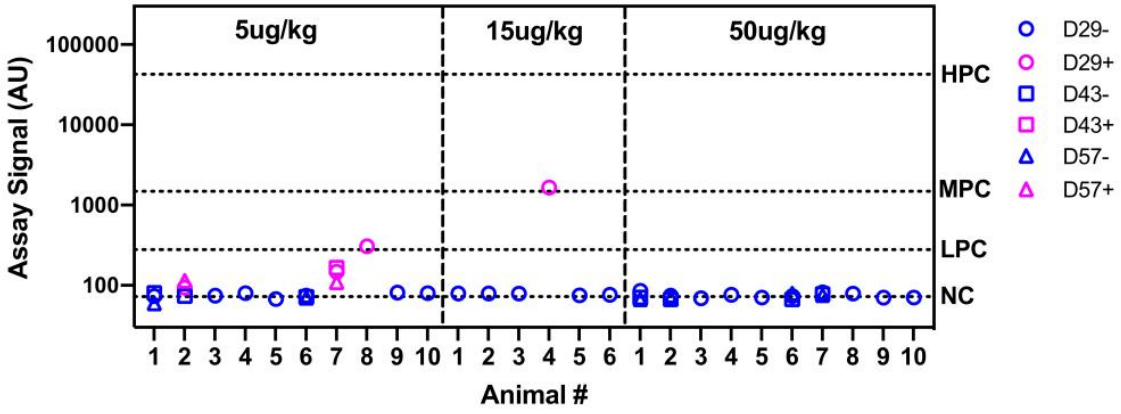
NL-201 Demonstrates Robust Single-Agent Activity in Multiple Tumor Models



- NL-201 was administered QW when tumors rea ~100mm3
- Tumor growth inhibition (TGI) is reported in each vs. control.
- NL-201 significan inhibited tumor growth in all mo including those t are refractory to checkpoint inhib

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

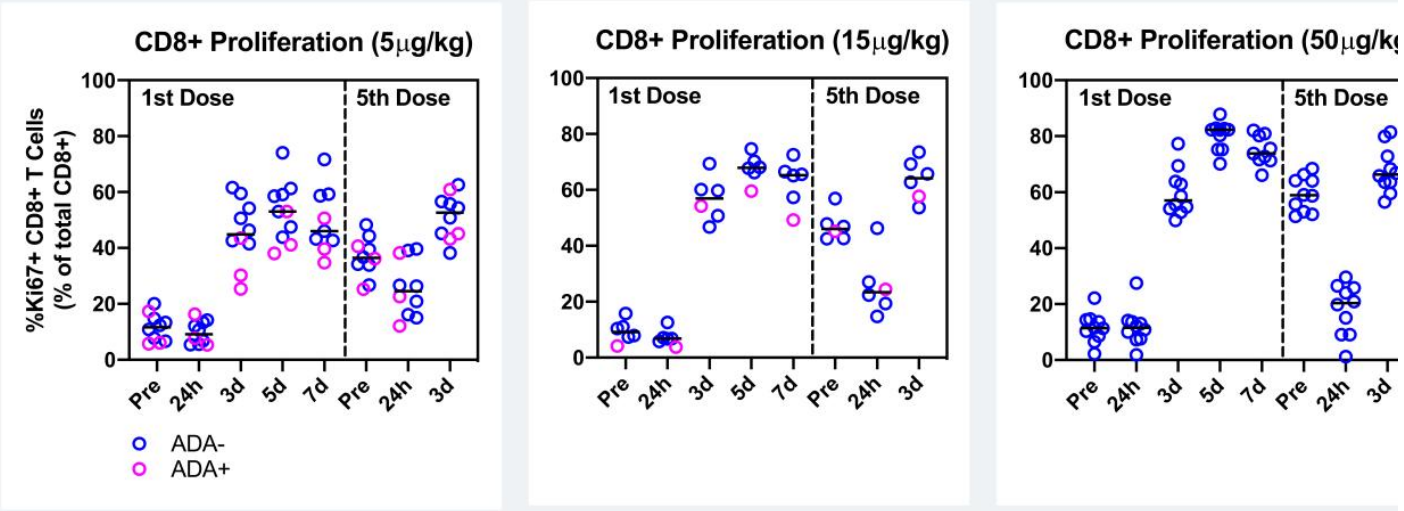
NL-201: Low ADA Detected After Repeated Systemic Administration in NHPs



- ADAs 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 ≤ low positive control (LPC) level

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

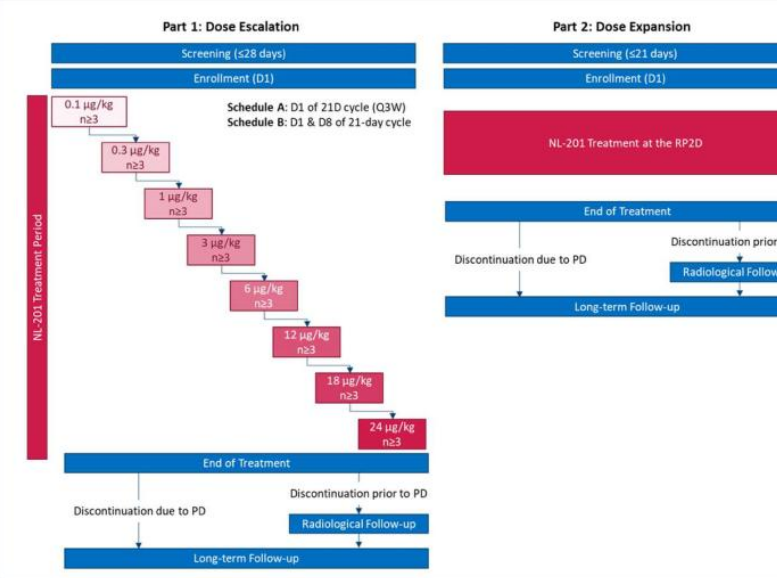
Similar Pharmacodynamic Response in ADA+ vs ADA- NH



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

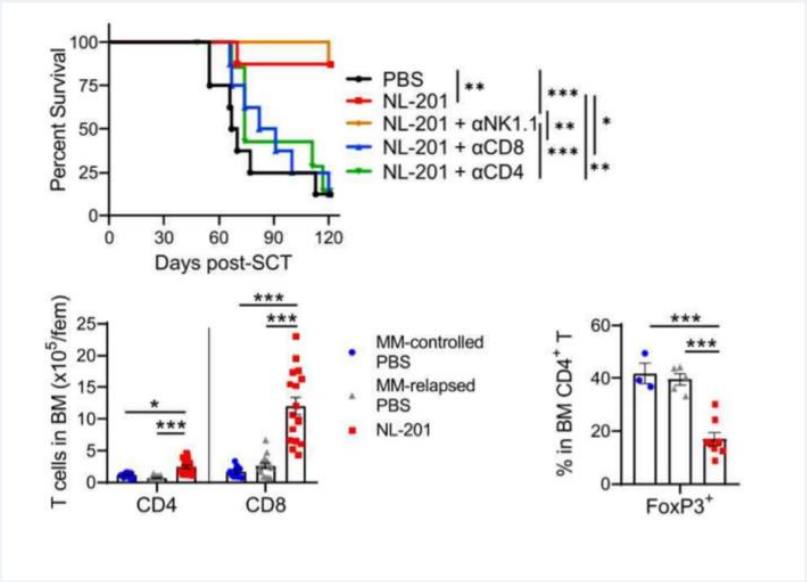
NL-201 Phase 1 Clinical Trial in Solid Tumors

- 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 in Hematologic Malignancies: Preclinical Data



- NL-201 delays relapse in murine myeloma model following autologous stem cell transplant
- NL-201 induces expansion of cytotoxic CD T-cells and a decrease in T-regulatory CD4 cells in the bone marrow
- NL-201 treated mice had an increase in bone marrow T-cells expressing granzyme and a decrease in the T-cell exhaustion phenotype
- Phase 1 trial for NL-201 in patients with hematologic malignancies anticipated to begin in 2022

Minnie et al, American Society of Hematology 63rd Annual Meeting. Abstract 1609. December 2021

NL-201: Broad Opportunity in Cancer

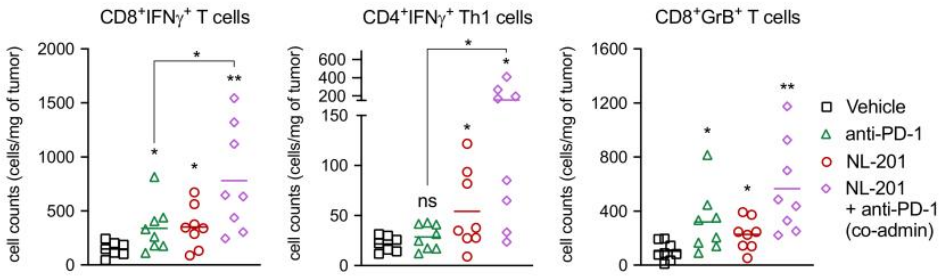
- Solid tumor monotherapy trial ongoing
- Plan to initiate monotherapy trial for patients with heme malignancies in 20
- Future opportunities to combine with checkpoint inhibitors, monoclonal antibodies, cellular therapies, and other standard-of-care agents
- Potential advantages of NL-201 local administration presented at SITC 2021

NL-201 Turns 'Cold' Tumors 'Hot'

Augments inflammatory milieu in preclinical B16 melanoma model

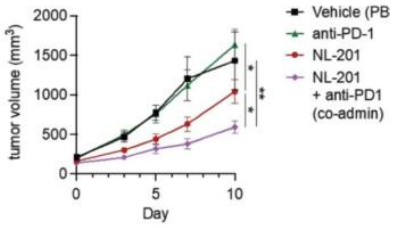
TCRβ Sequencing Summary

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 th tumor microenvironment
- augments IFNγ and granzyme expression in T-cells
- synergizes with anti-PD1 to inhibit tumor growth

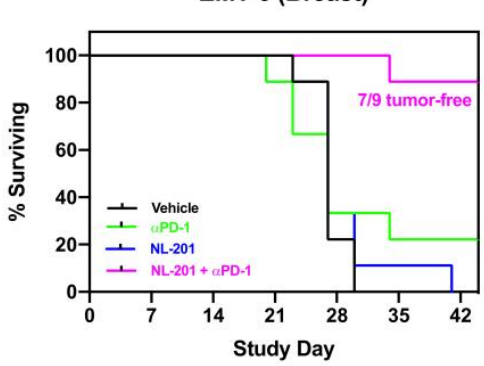


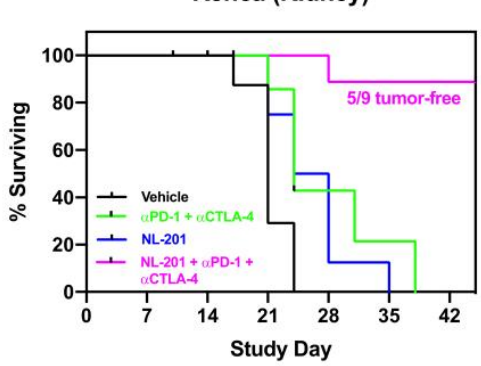
Mortales et. al, SITC 2021, Abstract #716, Nov 2021

neoleu THERAPEUTICS

NL-201 Enhances Activity of Checkpoint Inhibitors in Preclinical Models

Combination with NL-201 in CPI-resistant syngeneic tumors





NL-201: 90µg/kg QWx2
αPD-1: 10mg/kg BiWx6
αCTLA-4: 10gm/kg BiWx6

Treatment began when tumors reached ~90mm³

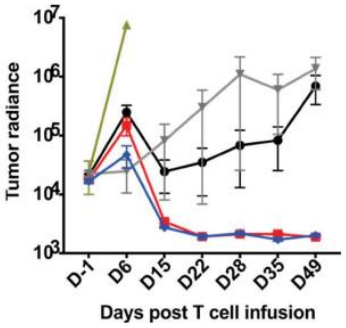
p=0.0029: αPD-1 vs NL-201 + αPD-1
p<0.0001: NL-201 vs NL-201 + αPD-1

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

Promising NL-201 Preclinical Combinations In Vivo

Enhanced antitumor activity with CAR-T cells and antibodies

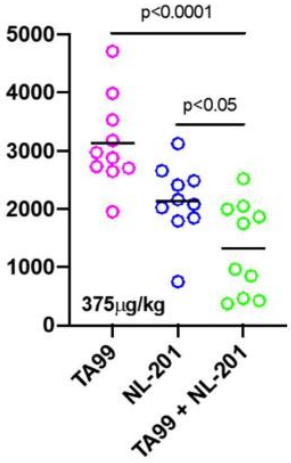
RAJI Lymphoma Model



- NL-201 combined with a subcurative dose of CAR-T cells 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

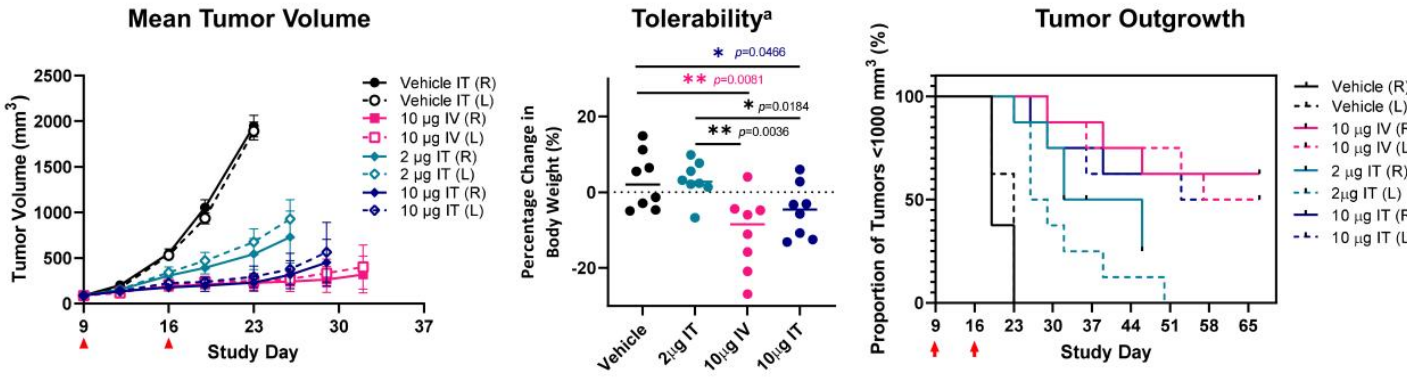
B16 Melanoma Model



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

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

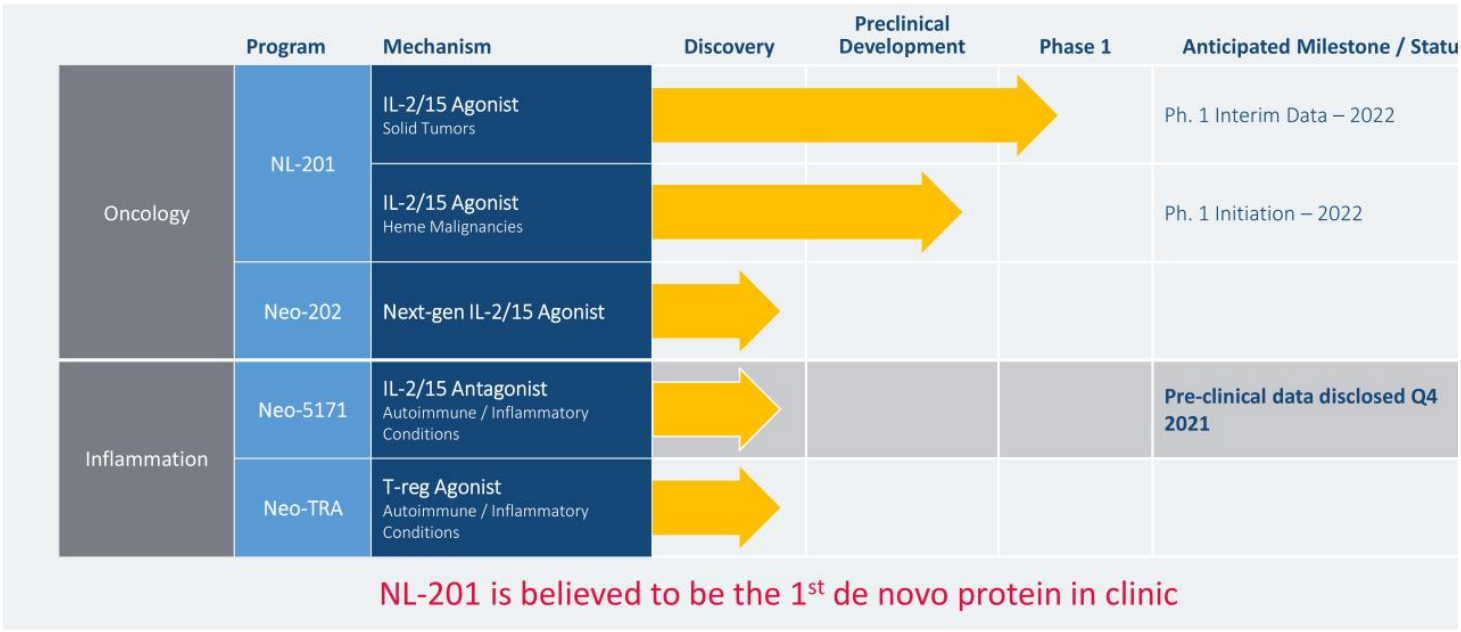
Intratumoral NL-201: Local and Distant Antitumor Control with Improved Tolerability



- CT26 syngeneic tumor model with bilateral tumor implants
- IT (R only) or IV NL-201 administered qWx2
- 10 mcg IV exceeded 20% weight loss in some mice

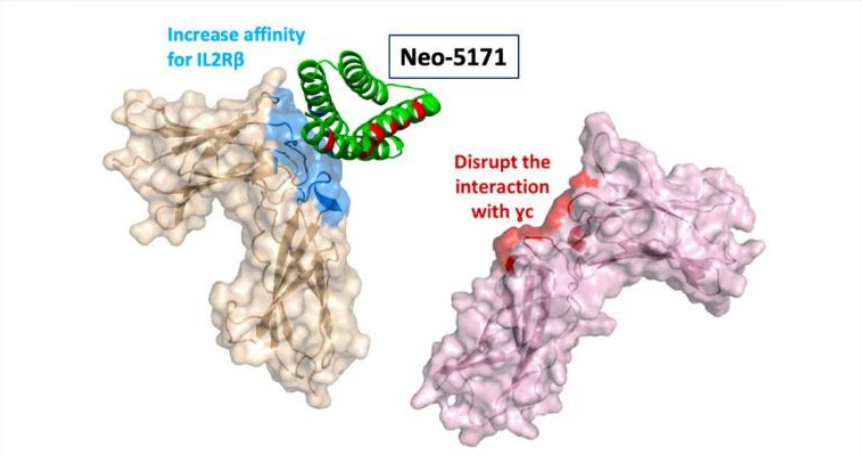
Tatalick et al, SITC 2021, Abstract #898, November 2021

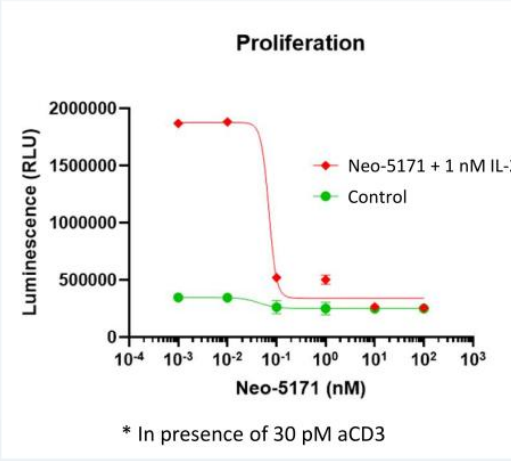
Pipeline



NL-201 is believed to be the 1st de novo protein in clinic

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



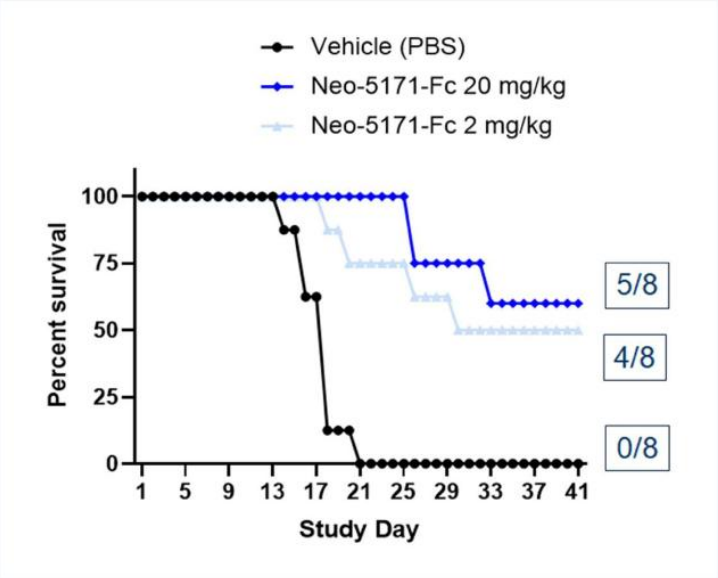


* In presence of 30 pM aCD3

- Potent inhibitor of CD8 T-cell proliferation and IFN-g 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

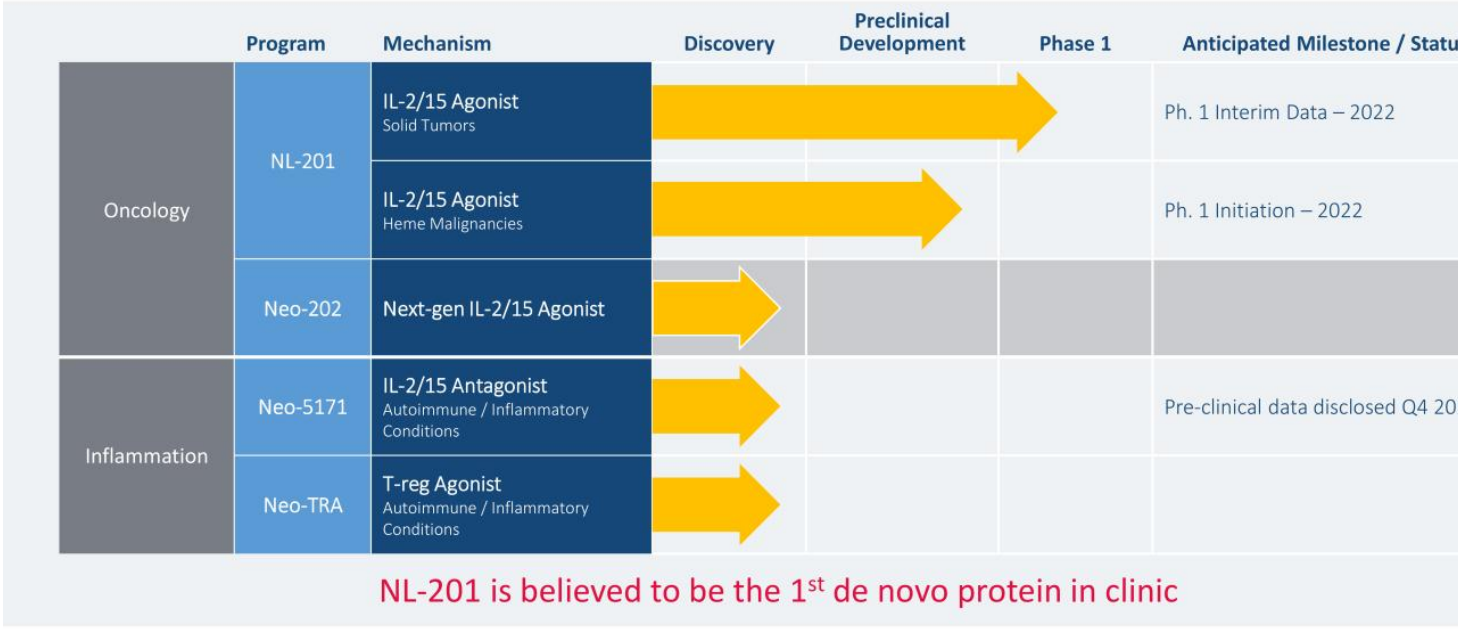
Neo-5171-Fc prolongs survival in a preclinical model o graft-vs-host disease (GVHD)



- Immunodeficient NSG mice were irradia received 10^7 human PBMC on Day -1
- Intraperitoneal dosing with Neo-5171-F q3d, beginning Day 0
- Mice were euthanized when experienci >20% body weight loss
- At high dose 62.5% of mice survived at study end (Day 42)

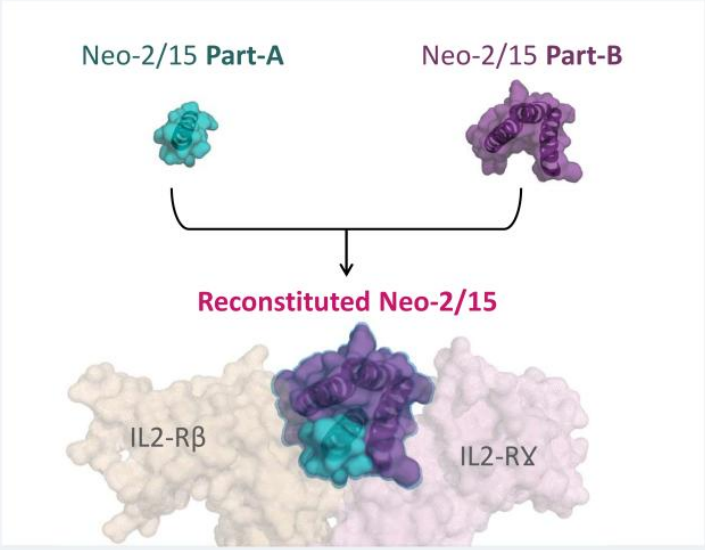
R. Swanson et. al. Am. Coll Rheum. (ACR) 2021; Abstract 1438, Nov 2021

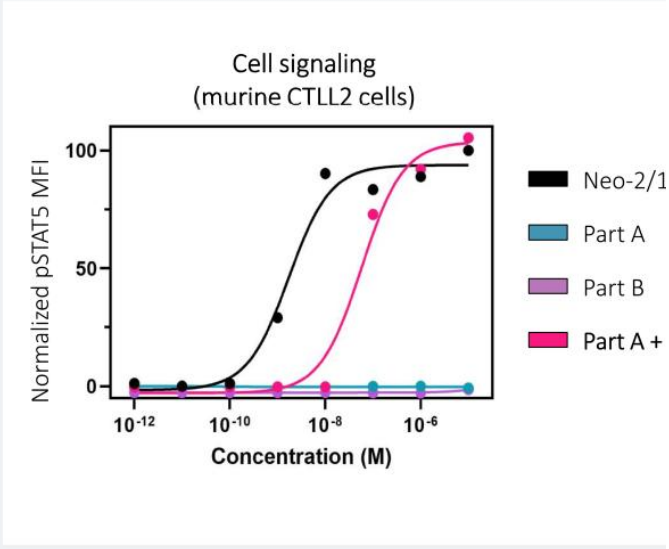
Pipeline



NL-201 is believed to be the 1st de novo protein in clinic

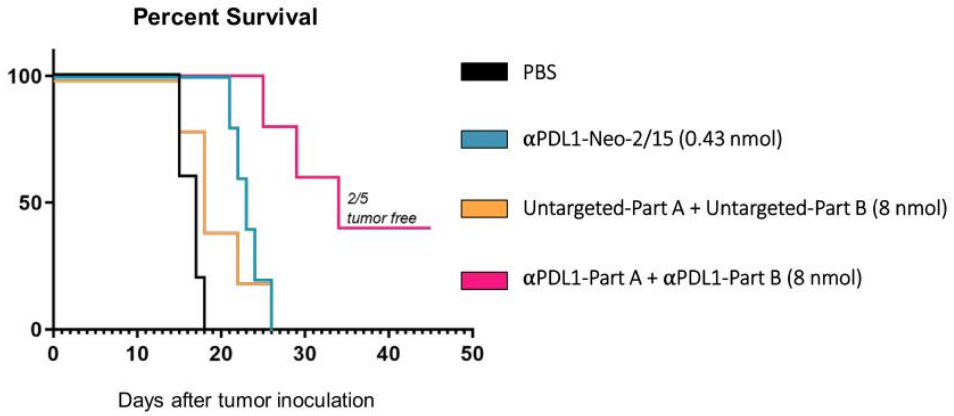
De Novo Split Technology: Conditionally Active IL-2 Mimetic

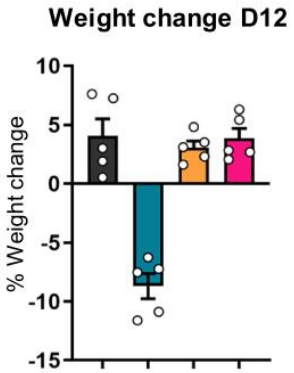




Quijano-Rubio et. al., AACR Virtual Annual Meeting II, Abstract #1075, Jun 2020

Targeted Split Neo-2/15 Increases Therapeutic Windo



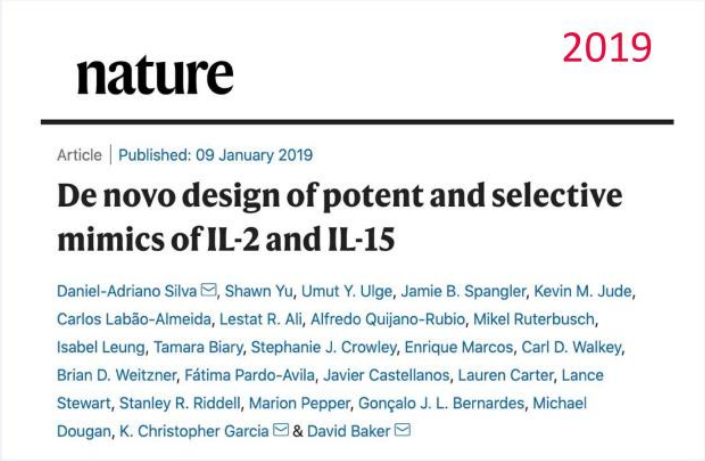


- C57BL/6J mice bearing B16 PDL1Hi melanoma cells in flank
- All groups were co-treated biweekly with Ta99 mAb (150µg/mice)
- Targeted Neo-2/15 variants and Part-A fusions administered i.p.; Part-B fusions administered s.c. opposite flank of tumor

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

Functional De Novo Proteins

Better Therapies by Design



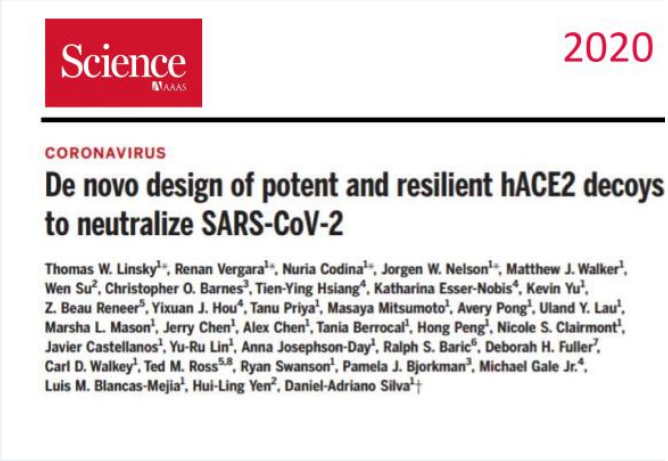
nature

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

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

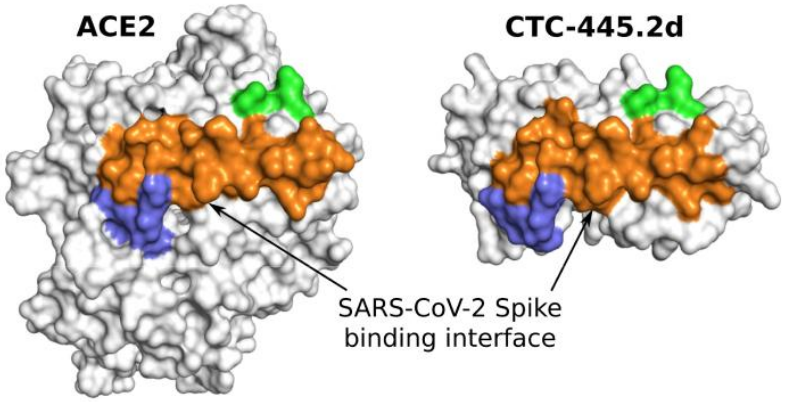
Thomas W. Linsky, Renan Vergara, Nuria Codina, Jorgen W. Nelson, Matthew J. Walker, Wen Su, Christopher O. Barnes, Tien-Ying Hsiang, Katharina Esser-Nobis, Kevin Yu, Z. Beau Reneer, Yixuan J. Hou, Tanu Priya, Masaya Mitsumoto, Avery Pong, Uland Y. Lau, Marsha L. Mason, Jerry Chen, Alex Chen, Tania Berrocal,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

- 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

neoleu THERAPEUTICS

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
- Plan to evaluate NL-201 + KEYTRUDA (pembrolizumab) in phase 1 trial

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

Improving on nature.
Designing for life.