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): September 29, 2021

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

On September 29, 2021, Neoleukin Therapeutics, Inc. (the "Company") announced the presentation of data regarding its *de novo* protein decoy, NL-CVX1, in an oral presentation at IDWeek 2021 titled "Antiviral NL-CVX1 efficiently blocks infection of SARS-CoV-2 viral variants of concern (VOC)" (Conference Track A1, Session [O-27]: Novel Microbial Agents). The IDWeek presentation summarizes research performed by the Company and research collaborators at the Instituto de Medicina Molecular João Lobo Antunes in Lisbon and Hong Kong University. A copy of the presentation materials to be used in the IDWeek presentation is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information contained in this Item 7.01, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any other filing by the Company under the Exchange Act or the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events

On September 29, 2021, the Company issued a press release announcing the IDWeek presentation described in Item 7.01 above. The full text of the press release issued by the Company is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Number	Description
99.1	Presentation of Neoleukin Therapeutics, Inc. dated September 29, 2021
99.2	Press Release of Neoleukin Therapeutics, Inc. dated September 29, 2021
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: September 29, 2021

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

Exhi

Antiviral NL-CVX1 efficiently blocks infection by SARS-CoV-2 viral variants of concern (VOC)

Maria Rebelo, PhD

Gonçalo Bernardes Lab

Instituto de Medicina Molecular Lisboa, Portugal

mariarebelo@medicina.ulisboa.pt

Disclosures

Hui-Ling Yen, PhD: received donation from Saiba AG and has performed contract research for Neoleukin Therapeutics, Inc.

Wen Su, PhD: has no conflict of interest to declare.

Gonçalo Bernardes, PhD: consultant and scientific advisor of Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and sto

Maria Rebelo, PhD: has no conflict of interest to declare.

Laurie Tatalick, DVM, PhD, DACVP: Consultant for Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and stock.

Matthew Walker, PhD: employee of Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and stock.

Marianne Riley, BS: employee of Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and stock.

Kevin Yu, BS, MS: employee of Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and stock.

Luis M Blancas-Mejia, PhD: employee of Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and stock

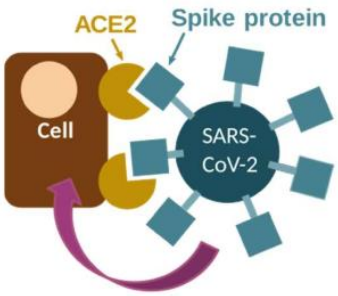
Daniel-Adriano Silva, PhD: scientific advisor of Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and stock.

David Shoultz, PhD, MBA: employee of Neoleukin Therapeutics, Inc. Ownership of Neoleukin options and stock.

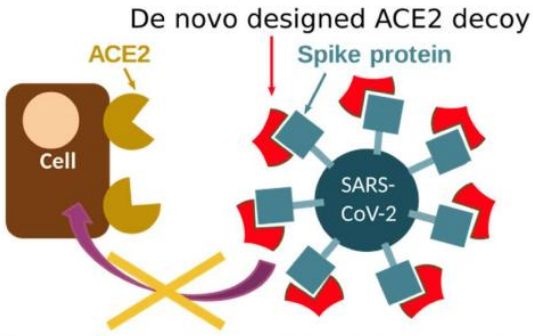
Cong Tang, MD, PhD: has no conflict of interest to declare.

Ana R. Coelho, PhD: has no conflict of interest to declare

NL-CVX1 is a potent de novo protein that blocks SARS-CoV-2



SARS-CoV-2 enter the cell by binding to the ACE2 receptor on the surface of human cells via the spike protein



De novo decoy binds to SARS-CoV-2 spike protein, preventing the virus to bind to ACE2 receptor and thus inhibiting viral entry into cells

neoleukin THERAPEUTICS

NL-CVX1 is a potent de novo protein that blocks SARS-CoV-2

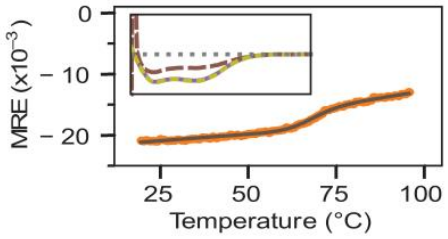
Science

REPORTS

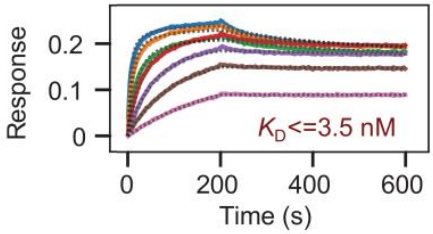
Cite as: T. W. Linsky *et al.*, *Science* 10.1126/science.abe0075 (2020).

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

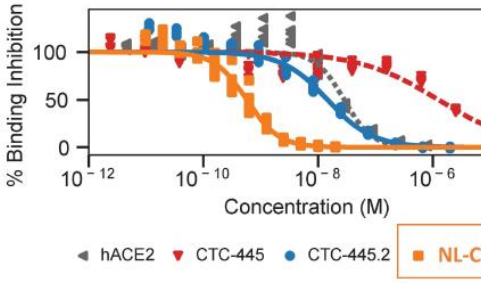
High thermodynamic stability



Low nanomolar affinity for the RBD of SARS-CoV-2



Outcompetes binding of SARS-CoV-2 RBD to hACE2



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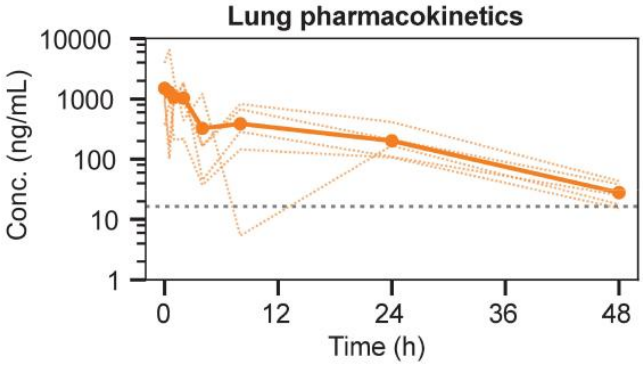
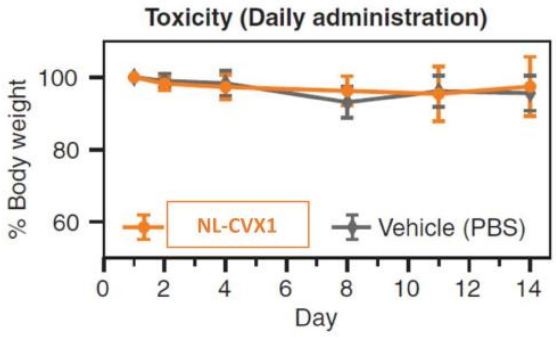
NL-CVX1 demonstrates promising lung PK following a single dose and is well-tolerated with daily administration

In vivo results

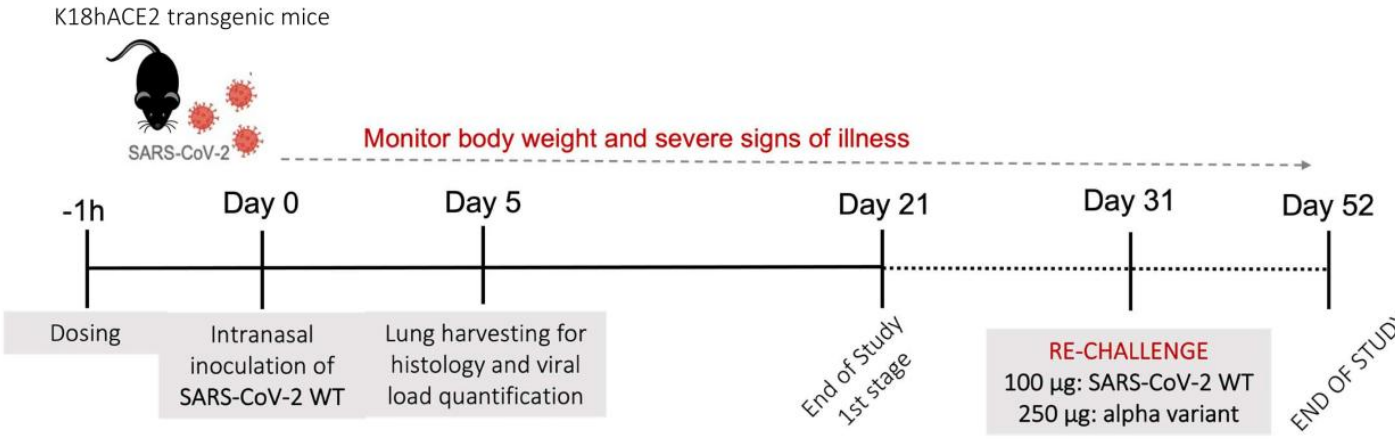




- NL-CVX1 was present for >24 hours in the lungs and respiratory tract of mice.
- NL-CVX1 was well-tolerated by mice with daily intranasal administration

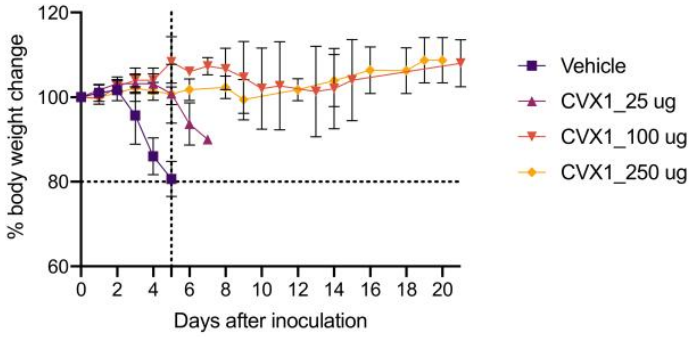
Linsky TW, et al. *Science*. 2020;370(6521):12(

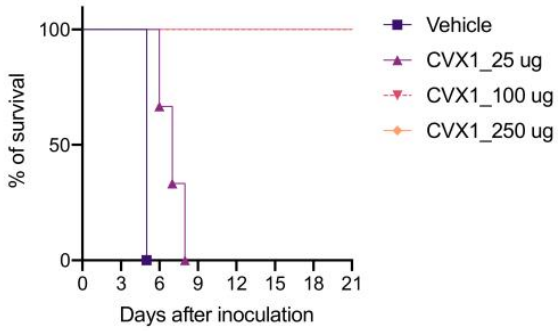
Our K18hACE2 mouse model of SARS-CoV-2 infection



A single dose of NL-CVX1 protects mice from lethal SARS-CoV-2 infection

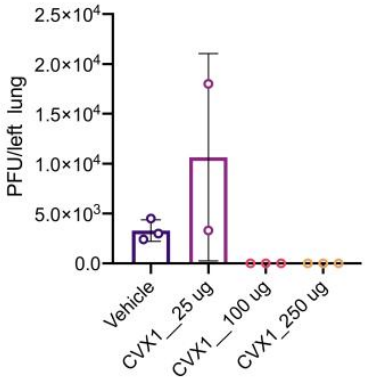
Clinical observations *in vivo*



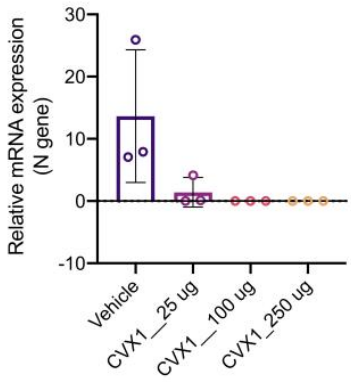


A single dose of NL-CVX1 prevents detectable viral load in the lungs of mice

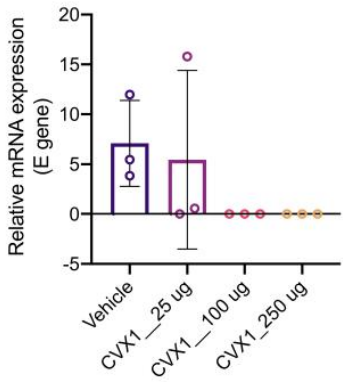
Lung viral load from *in vivo* experiments



- No plaque forming units observed in either the 100 ug or 250 ug dose groups

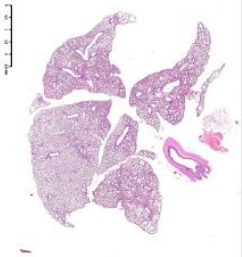
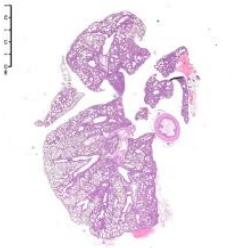
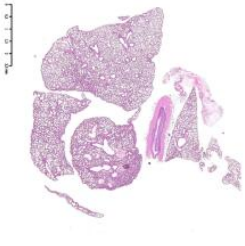
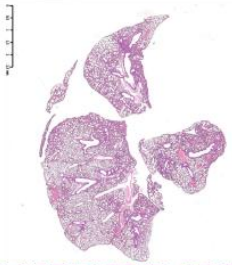
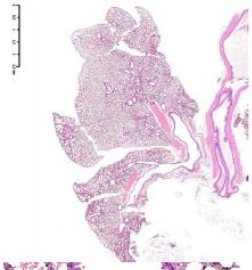
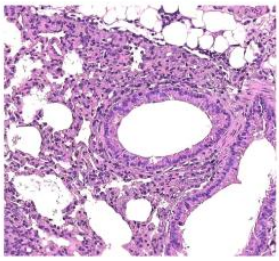
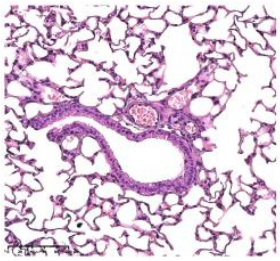
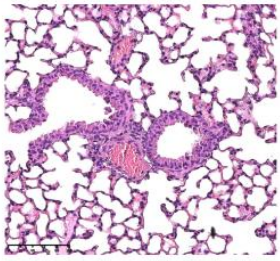
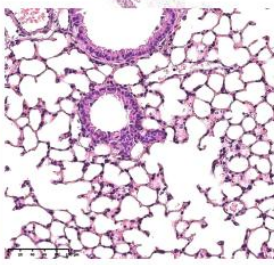


- No detection of the nucleocapsid (N) gene in either the 100 ug or 250 ug dose groups



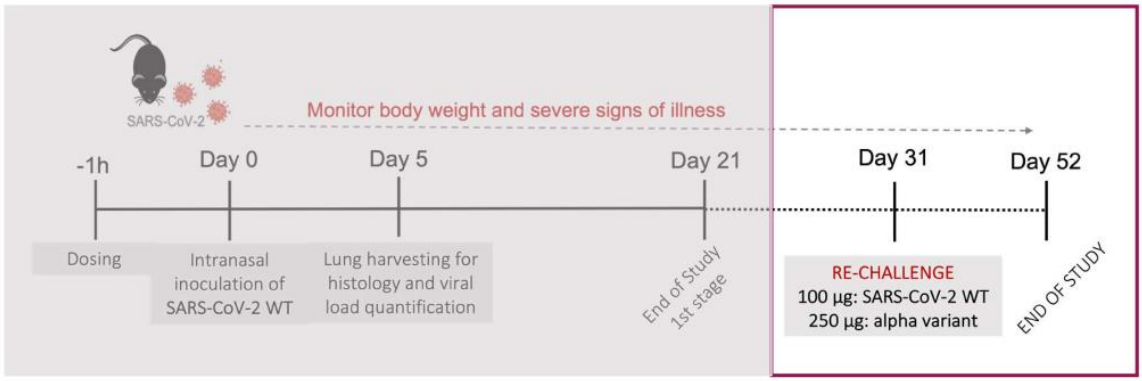
- No detection of the envelope (E) gene in either the 100 ug or 250 dose groups

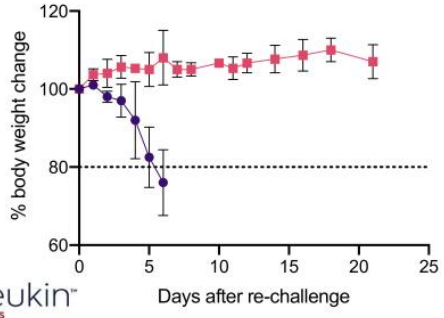
A single dose of NL-CVX1 protects mice from lethal SARS-CoV-2 infection

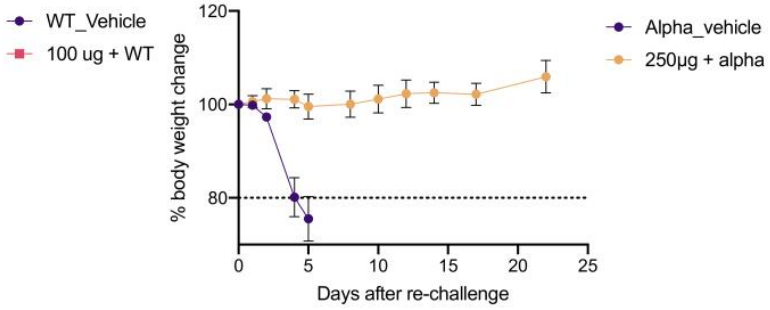
Non-infected	Vehicle	25 µg	100 µg	250 µg
				
				
	• Proliferative epithelium • Pulmonary edema • Mononuclear inflammatory cell and neutrophil infiltration, with occasional necrotic and dying cells.	• Mild pulmonary edema and mononuclear cell infiltrates observed	• Mild pulmonary edema	• No changes

Source: Pedro Ruivo, iM

Primary prophylaxis with NL-CVX1 protects against a second SARS-CoV-2 infection 30 days later

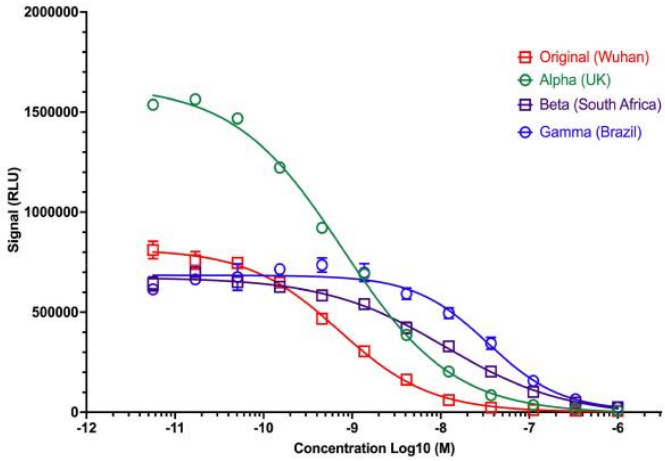






NL-CVX1 outcompetes hACE2 and efficiently binds to RBD of SARS-CoV-2 VOC

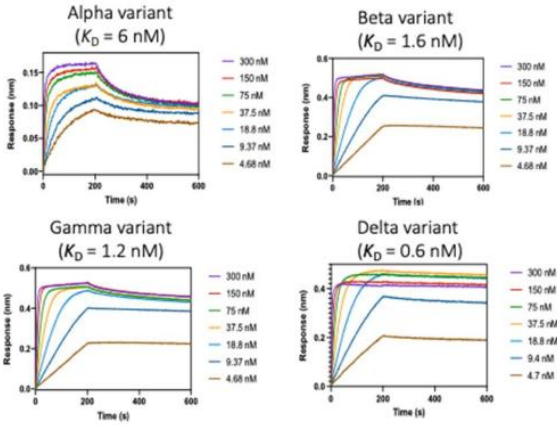
ELISA competition assay



- NL-CVX1 outcompetes binding of SARS-CoV-2 RBD to hACE2

Biolayer interferometry (OCTET) binding assays

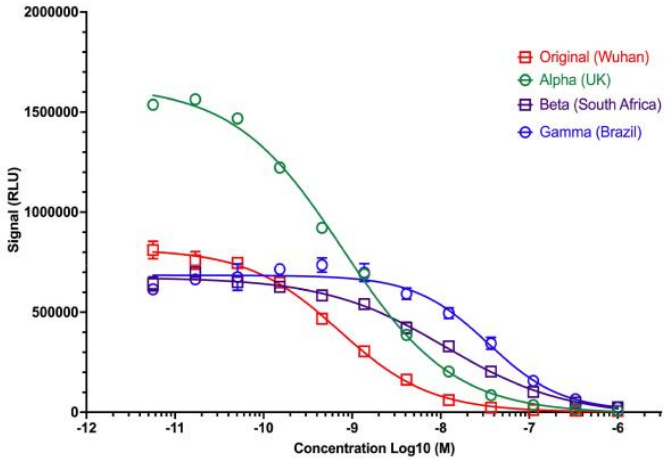
- Original Wuhan virus (K_D = 0.5 nM)



- NL-CVX1 binds at high picomolar to low nanomo concentrations to RBD of **SARS-CoV-2 VOC**

NL-CVX1 efficiently binds the Delta VOC with a low dissociation rate

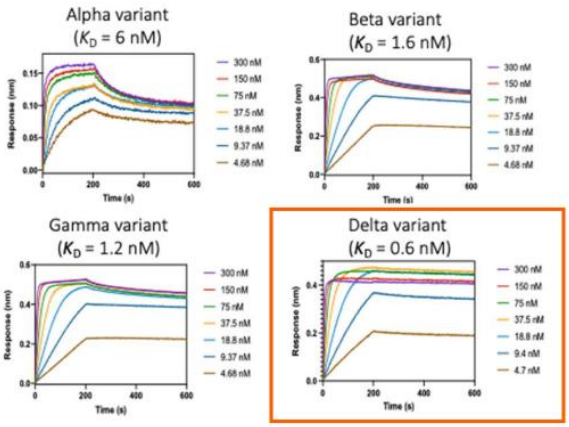
ELISA competition assay



- NL-CVX1 outcompetes binding of SARS-CoV-2 RBD to hACE2

Biolayer interferometry (OCTET) binding assays

- Original Wuhan virus (K_D = 0.5 nM)



- NL-CVX1 binds at high picomolar to low nanomo concentrations to RBD of **SARS-CoV-2 VOC**

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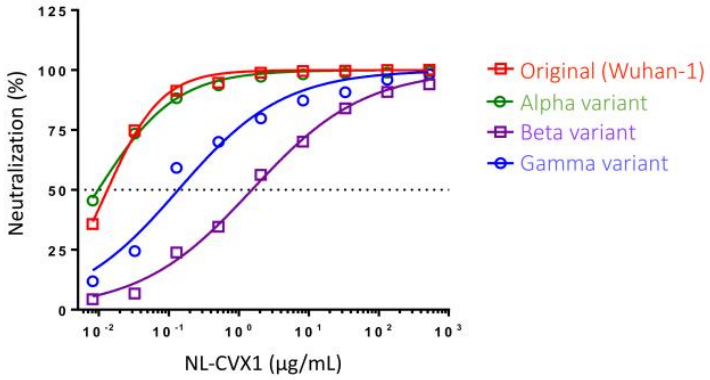
NL-CVX1 neutralizes pseudoviruses with SARS-CoV-2 VOC spike proteins

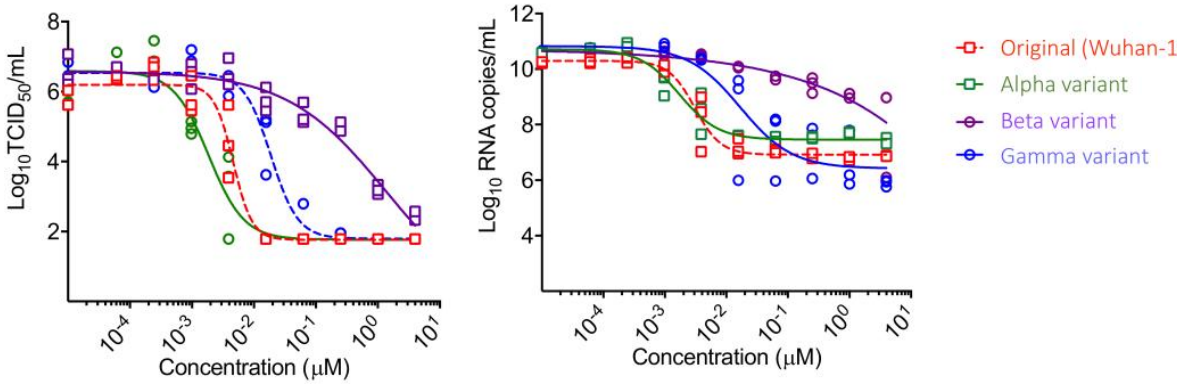
	Original (Wuhan-1)	Alpha variant (B.1.1.7)	Beta variant (B.1.351)	Gamma variant (P.1)
IC50 (ng/mL)	13.2	9.7	1500	136



- NL-CVX1 retains neutralizing activity against all VOC tested.
- When compared to the original strain, the Alpha VOC displayed the highest sensitivity to NL-CVX1

NL-CVX1 is efficacious *in vitro* against SARS-CoV-2 VOC

	Original (Wuhan-1)	Alpha variant (B.1.1.7)	Beta variant (B.1.351)	Gamma variant (P.1)
TCID50 EC50 (nM)	4.6	1.9	1384	18.8
PCR EC50 (nM)	3.1	1.7	> 4000	16.8



- NL-CVX1 showed **comparable efficacy against the Alpha and Gamma VOC.**
- Higher concentrations of NL-CVX1 were required for neutralization of the Beta VOC.

Source: Su Wen and Hui-Ling Yen, HK

Summary and conclusions

- NL-CVX1 is a *de novo* human ACE2 decoy protein that neutralizes SARS-CoV-2 *in vitro* and in animal models.
- NL-CVX1 is effective against VOC tested *in vitro* at different concentrations.
- Binding to the Delta variant spike protein and low dissociation rate is encouraging.
- Single intranasal dose not only protects mice from to SARS-CoV-2 but also protects from a second experimental infection a month later.

Future directions

- Investigate **in vivo efficacy of NL-CVX1 against new VOC** in K18hACE2 mice.
- Characterize the **underlying immune response** that protects mice from secondary SARS-CoV-2 exposure.
- **Evaluate the nature of antibodies developed** by mice following primary prophylactic exposure to NL-CVX1 and SARS-CoV-2 infection

Acknowledgments

Daniel Adriano Silva
Thomas W. Linsky
Jonathan Drachman
Laurie Tatalick
Matthew Walker
Marianne Riley
Kevin Yu
Luis M. Blancas-Mejia
David Shoultz

Gonçalo Bernardes
Cong Tang
Ana R Coelho
Marta Miranda
Pedro Ruivo
Iolanda Moreira
Pedro Simas

Hui-Ling Yen
Su Wen
Sin Fun Sia
Ka Tim Choy
Prathanporn Kaewpreedee

Juan Lama
Isabel Cisneros

Neoleukin Therapeutics Announces Oral Presentation at IDWeek 2021 of Data Demonstrating that NL-CVX1, a Computationally Designed *De Novo* Protein, Can Block Infection by SARS-CoV-2 Viral Variants of Concern

– Single intranasal dose of NL-CVX1 in mice prevents infection by multiple variants of SARS-CoV-2 –

– Transgenic mice that are protected from disease by NL-CVX1 remain resistant to rechallenge after one month –

SEATTLE, Washington, September 29, 2021 – Neoleukin Therapeutics, Inc., “Neoleukin” (NASDAQ:NLTX), a biopharmaceutical company utilizing sophisticated computational methods to design de novo protein therapeutics, today announced new data highlighting the ability of its *de novo* protein decoy, NL-CVX1, to block SARS-CoV-2 infection in certain viral variants. Data were presented in an oral presentation at IDWeek 2021 titled “Antiviral NL-CVX1 efficiently blocks infection by SARS-CoV-2 viral variants of concern (VOC)” (Conference Track A1, Session [O-27]: Novel Microbial Agents).*

NL-CVX1 is a computationally designed, *de novo* protein that acts as a hACE2 decoy, neutralizing SARS-CoV-2 both *in vitro* and *in vivo* and inhibiting SARS-CoV-2 replication. (T. W. Linsky et. al. Science. 10.1126/science.abe0075 (2020)). New data presented demonstrates that NL-CVX1 protects transgenic hACE2 mice from SARS-CoV-2 infection with a single intranasal dose and that this protection persists following a viral rechallenge one month later. In addition, the data indicates that NL-CVX1 effectively outcompetes binding of the SARS-CoV-2 receptor binding domain to hACE2 in the variants of concern that were tested. Findings also revealed the ability of NL-CVX1 to neutralize pseudoviruses expressing spike proteins of SARS-CoV-2 variants. The IDWeek presentation summarizes research performed by Neoleukin and research collaborators at the Instituto de Medicina Molecular João Lobo Antunes in Lisbon and Hong Kong University.

“These latest findings are encouraging as we now see the resiliency that NL-CVX1 has to protect animals from SARS-CoV-2 variants of concern. We're particularly interested in the protective effect to rechallenge in the mouse model. Our data suggest that while NL-CVX1 protects mice from acute infection, it also enables development of lasting immunity that protected mice from re-challenge with SARS-CoV-2 after one month. That is very exciting to us," said Gonçalo Bernardes, Ph.D., Associate Professor of Chemical Biology, University of Cambridge, U.K, and Group Leader at the Instituto de Medicina Molecular, Portugal, and member of the Neoleukin Scientific Advisory Board.

"The global impact of the SARS-CoV-2 pandemic and emerging variants of concern highlights the urgent need for effective prophylaxis and early treatment of SARS-CoV-2 infection. These data demonstrate that NL-CVX1 is resilient to mutations of the SARS-CoV-2 spike protein and

provide evidence of both the potential value of NL-CVX1 and the broad power and promise of our de novo protein design platform," said Jonathan Drachman, M.D., Chief Executive Officer of Neoleukin. "We are grateful to our outstanding collaborators, including Dr. Maria Rebelo, presenter of these exciting data at IDWeek 2021."

*IDWeek abstracts/presentations will be published in an online supplement to Open Forum Infectious Diseases (OFID), the Open Access Journal from the Infectious Diseases Society of America (IDSA), on or about November 1, 2021.

About Neoleukin Therapeutics, Inc.

Neoleukin is a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation and autoimmunity using de novo protein design technology. Neoleukin uses sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins. Neoleukin's lead product candidate, NL-201, is a combined IL-2 and IL-15 agonist designed to improve tolerability and activity by eliminating the alpha receptor binding interface. For more information, please visit the Neoleukin website: www.neoleukin.com.

About NL-CVX1

NL-CVX1 is a computationally designed, *de novo* protein that binds to the spike protein of SARS-CoV-2. In preclinical studies, NL-CVX1 has been shown to neutralize SARS-CoV-2 both *in vitro* and *in vivo* and to inhibit SARS-CoV-2 replication. NL-CVX-1 has progressed through preclinical development, including toxicology and process development, which could potentially enable future low-cost scale up and manufacturing for intranasal administration. Neoleukin is considering opportunities to license NL-CVX1. Inquiries should be directed to partnering@neoleukin.com.

Safe Harbor / Forward-Looking Statements

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the therapeutic properties and potential of the company's *de novo* protein design technology, the ability to develop or identify a partner for the NL-CVX1 program, and planned clinical and development activities and timelines. Forward-looking statements can be identified by words such as: "anticipate," "intend," "plan," "goal," "seek," "believe," "project," "estimate," "expect," "strategy," "future," "likely," "may," "should," "will" and similar references to future periods. These statements are subject to numerous risks and uncertainties, including risks and uncertainties related to the company's cash forecasts, the company's ability to advance its product candidates, the receipt and timing of potential regulatory submissions, designations, approvals and commercialization of product candidates, the timing and results of preclinical and clinical trials, the timing of announcements and updates relating to the company's clinical trials and related data market conditions and further impacts of COVID-19, that could cause actual results to differ materially from what Neoleukin expects. Further information on potential risk factors that could affect Neoleukin's business and its financial results are detailed under the heading "Risk Factors" in documents the company files from time to time with the Securities and Exchange Commission (SEC), and other reports as filed with the SEC. Neoleukin undertakes no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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