NEWS RELEASE

A Milestone Clinical Study Reveals that Elevating Nicotinamide Adenine Dinucleotide (NAD+) with Nicotinamide Riboside (NR) Supplementation Effectively Reduces Inflammation in Both Healthy Subjects and Immune Cells Derived from Psoriasis Patients

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Celebrating a significant achievement in NAD + research, these findings contribute to the mounting evidence indicating that NR may serve as a proactive safeguard against inflammatory cytokines in healthy adults and those with inflammation-related disorders

LOS ANGELES--(BUSINESS WIRE)-- **ChromaDex Corp.** (NASDAQ:CDXC), a global authority on Nicotinamide Adenine Dinucleotide (NAD+) research and healthy aging, shares results from a newly published clinical study, as reported in the peer-reviewed journal **Cell Reports**, demonstrating that supplementation with nicotinamide riboside (NR), one of the most efficient and superior NAD+ precursors, reduced inflammation in both healthy subjects and in cells derived from psoriasis patients. The clinical trial was part of the **ChromaDex External Research Program** (CERP™), which donated ChromaDex's patented nicotinamide riboside (NR) ingredient, Niagen, for the advancement of this research.

"We express our gratitude to Dr. Michael Sack, Senior Investigator of Mitochondrial Biology and Metabolism at the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), for his exceptional contributions with this research. This is Dr. Sack's fourth published study on NR, and the seventh clinical study overall, that demonstrates NR's effectiveness in reducing inflammation, an important indicator of how the body is aging," remarked Rob Fried, CEO of ChromaDex. "In addition to a balanced diet and regular exercise, elevating

NAD+ levels with Tru Niagen remains the safest, most effective, legally protected, and extensively researched NAD+ dietary supplement that helps us age better. This research is a testament to why ChromaDex continues to be the gold standard in the rapidly expanding NAD+ space."

An evolution in NAD+ research, this study builds on a growing body of evidence suggesting that NR defends against inflammation not only in individuals who are elderly or have inflammation-related disease, as they are associated with lower levels of NAD+ and higher inflammation markers, but may also provide anti-inflammatory benefits for healthy individuals. This is the third published human clinical study demonstrating that NR supplementation has a protective effect in healthy individuals and lays the foundation for future clinical research (**Elhassan et al. 2019**, **Remie et al. 2020**).

The connection between NAD+ and inflammation

Underlying chronic inflammation, also known as metaflammation or inflammaging, appears to be a consistent factor in ailing populations, in illness associated with age-related decline, and even in relatively healthy individuals, and has been linked to the development of autoimmune disorders, such as psoriasis and lupus, and chronic diseases, such as diabetes, cardiovascular disease, Alzheimer's disease, Parkinson's disease, among others. Research has demonstrated environmental and lifestyle factors such as smoking, poor diet, lack of exercise, and sleep deprivation can contribute to states of chronic underlying inflammation.

NAD+ is a critical coenzyme for all living cells and maintaining intracellular NAD+ pools is critical in supporting cellular and metabolic processes, including adenosine triphosphate (ATP) production (the source of cellular energy) and DNA repair. Research suggests a depletion of NAD+ is associated with impaired inflammatory responses and innate immune dysfunction, indicating NAD+ levels may have a critical impact on the function of immune cells.

Research supporting anti-inflammatory effects of NR, the most efficient NAD+ precursor

NR is one of the most efficient and superior NAD+ precursors, clinically proven to increase NAD+ safely and effectively. There is an ever-growing body of clinical evidence demonstrating the anti-inflammatory effects of NR supplementation (either alone or in combination with other ingredients) for healthy, older adults, or those with inflammation-related disorders, with potential for more robust effects among the elderly and diseased populations as they tend to have compromised NAD+ and a higher inflammatory status. These studies are outlined in table 1.

TABLE 1. Summary of peer-reviewed, published NR studies demonstrating an anti-inflammatory effect in humans.

NICOTINAMIDE RIBOSIDE ONLY			
Publication	Dose/Duration	Study Population	Key Results
Elhassan et al., 2019	1,000 mg/day for 21 days	Marginally overweight, but otherwise healthy older adult men	NR reduced levels of circulating inflammatory cytokines IL-6, IL-5, IL-2, and TNF-α
Zhou et al., 2020	1,000 mg/day for 5-9 days	Hospitalized patients with stage D heart failure undergoing advanced heart failure therapy evaluations	NR reduced gene expression of NLRP3 and inflammatory cytokines (IL-1B, IL-6, and IL-18)
Remie et al., 2020	1,000 mg/day for 6 weeks	Healthy overweight and obese men and postmenopausal women	NR resulted in a significant trend toward a reduction in plasma IL-1α levels
Wu et al., 2022	1,000 mg/day for one week	Young healthy subjects and patients with systemic lupus erythematosus (SLE)	NR reduced relative mRNA expressions of inflammatory cytokines IFN-β and CXCL10
Brakedal et al., 2022	1,000 mg/day for 4 weeks	Newly diagnosed dopaminergic therapy-naïve Parkinson's disease patients	NR reduced levels of inflammatory cytokines in the serum: VEGF and GDF15, as well as in cerebrospinal fluid: G-CSF, IL-7, IL-1RA, CCL4
Wang et al., 2022	2,000 mg/day for 12 weeks	Stage C heart failure with reduced ejection fraction patients and age-matched healthy subjects	NR reduced expression of NLRP3 and resulted in directionally similar, though nonsignificant, changes in expression of other inflammatory markers (IL-1B, IL-6, IL-18, and TNF-α) **[AH1]**
Han et al., 2023	1,000 mg/day for 1 week	Young, healthy subjects	NR blunted TH1 and TH17 immune cell responsiveness and depressed the secretion of IFNγ and IL-17 in CD4+ T cells
NICOTINAMIDE RIBOSIDE IN COMBINATION WITH OTHER INGREDIENTS			
Zeybel et al., 2022	CMA*	Nonalcoholic fatty liver disease (NAFLD) patients	CMA decreased levels of inflammatory cytokines CD-8A, CCL23, FGF-21, and oncostatin-M (OSM)
Altay et al., 2021	CMA*	Ambulatory COVID-19 patients	CMA decreased levels of inflammatory cytokines CSF-1, IL-15RA, IL-18, MCP-1, and TNF-α

About the study

The first part of this clinical study analyzed the effects of ex-vivo (outside of the living organism) NR supplementation on adaptive immunity in CD4+ T cells, which play a vital role in regulating effective immune response to pathogens. CD4+ T cells were extracted from patients with mild-moderate psoriasis and age and gender-matched healthy controls (average age of 48). The second part of the study analyzed the effects of oral NR supplementation on primary CD4+ T cell function using samples obtained from a prior pilot, randomized, double-blinded, placebo-controlled study in which 25 healthy subjects (average age of 24 and average BMI of 23) were supplemented with 1000mg NR or placebo daily for 7 days (**Wu et al., 2022**).

Study highlights

- Ex vivo NR supplementation in CD4+ T cells in both healthy volunteers and patients with mild-moderate psoriasis reduced TH1 and TH17 immune responsiveness, characteristic features in psoriasis, and depressed the secretion of IFNγ and IL-17 (pro-inflammatory factors observed in autoimmune disorders that contribute to overactive CD4+ T cells).
    - Genes related to antioxidant defense pathways were upregulated in CD4+ T cells in response to NR treatment.
    - NR decreased the production and activity of harmful reactive oxygen species (which causes damage to the building blocks of the cell including DNA), and reduced lipid peroxidation (a process by which oxidants attack healthy lipids, resulting in cell death) in CD4+ T cells.
    - Psoriatic T cells demonstrated both a reduction of NAD+ and upregulation of NAD+ consuming enzymes, as compared to the cells extracted from healthy individuals. These data suggest that psoriasis amplifies NAD+ consumption and that boosting NAD+ levels is necessary to blunt TH17 immune cell responsiveness.

- In the in-vivo analysis, oral NR supplementation in healthy participants reflected the immune-modulating effects of ex-vivo NR supplementation. More specifically, oral NR reduced inflammatory biomarkers and enhanced antioxidant gene expression in immune cells.

Relevance

Due to the success of data collected from both studies led by Dr. Sack, **Han et al., 2023** and **Wu et al., 2022**, the effects of NR supplementation in mild-moderate psoriasis patients are currently being explored by the investigators in an **in vivo placebo-controlled clinical trial**. The findings from this study builds on a growing body of evidence suggesting that increasing NAD+ levels with NR supplementation not only defends against inflammation for healthy individuals, but also suggests a potential therapeutic application for individuals with autoimmune disorders, such as psoriasis, pending further research confirmation.

For additional information on ChromaDex, visit **www.chromadex.com**.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Research reported in this press release was supported by the Mitochondrial Biology and Metabolism, National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health under award number ZIA-HL005102.

About ChromaDex:

ChromaDex Corp. is a global bioscience company dedicated to healthy aging. The ChromaDex team, which includes world-renowned scientists, is pioneering research on nicotinamide adenine dinucleotide (NAD+), levels of which decline with age. ChromaDex is the innovator behind NAD+ precursor nicotinamide riboside (NR), commercialized as the flagship ingredient Niagen®. Nicotinamide riboside and other NAD+ precursors are protected by ChromaDex's patent portfolio. ChromaDex maintains a website at **www.chromadex.com** to which ChromaDex regularly posts copies of its press releases as well as additional and financial information about the Company.

Forward-Looking Statements:

This release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities and Exchange Act of 1934, as amended, including statements related to whether these findings contribute to the mounting evidence indicating that NR may serve as a proactive safeguard against inflammatory cytokines in healthy adults and those with inflammation-related disorders. Statements that are not a description of historical facts constitute forward-looking statements and may often, but not always, be identified by the use of such words as "expects," "anticipates," "intends," "estimates," "plans," "potential,"

"possible," "probable," "believes," "seeks," "may," "will," "should," "could" or the negative of such terms or other similar expressions. Risks that contribute to the uncertain nature of these forward-looking statements include the impact of the COVID-19 pandemic on our business and the global economy; our history of operating losses and need to obtain additional financing; the growth and profitability of our product sales; our ability to maintain sales, marketing and distribution capabilities; changing consumer perceptions of our products; our reliance on a single or limited number of third-party suppliers; and the risks and uncertainties associated with our business and financial condition. More detailed information about ChromaDex and the risk factors that may affect the realization of forward-looking statements is set forth in ChromaDex's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, ChromaDex's Quarterly Reports on Form 10-Q and other filings submitted by ChromaDex to the SEC, copies of which may be obtained from the SEC's website at **www.sec.gov**. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and actual results may differ materially from those suggested by these forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement and ChromaDex undertakes no obligation to revise or update this release to reflect events or circumstances after the date hereof.

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