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NEWS RELEASE

Niagen Bioscience Announces First-Ever Peer-Reviewed Pilot Clinical Study on Mitochondrial DNA Disease Demonstrating Safety and Tolerability of High-Dose Niagen with Early Signals in One Mobility Measure and Favorable Trends in Mitochondrial Measures

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Findings from this small, open-label exploratory study add to a growing body of evidence showing favorable effects of NR on mitochondrial biology, including increased muscle mitochondrial biogenesis

LOS ANGELES--(BUSINESS WIRE)-- **Niagen Bioscience, Inc.** (NASDAQ: NAGE), the global authority on NAD+ (nicotinamide adenine dinucleotide) with a focus on the science of healthy aging, today announces the publication of a first-of-its-kind independently conducted clinical study of Niagen® (patented nicotinamide riboside, or NR) in people with mitochondrial DNA (mtDNA) disease, a group of inherited conditions that devastate multi-organ systems by disrupting how cells make energy. Led by researchers at the University of Cambridge and published in the peer-reviewed journal **Genome Medicine**, the four-week, open-label exploratory study of eight adults is the first clinical study of Niagen in mtDNA disease. High-dose Niagen (1,250 to 2,000 mg per day) was well tolerated and, as reported by **Cambridge University**, "participants with large-scale mitochondrial DNA deletions showed promising biological signs of improved mitochondrial health, including extra healthy mitochondria and better muscle function markers.” This study supports further investigation of NAD+ augmentation with Niagen as a therapeutic strategy in rare mtDNA disease.

Katherine R. Schon, PhD, Assistant Professor in the Department of Medical Genetics and Honorary Consultant in Clinical Genetics and Genomic Medicine, and Patrick F. Chinnery, Professor of Neurology and Head of the

Department of Clinical Neurosciences, both at the University of Cambridge, authored the publication. The study was independently conducted. Niagen Bioscience did not fund, design, or conduct the study and donated the Niagen material through the Niagen Research Program. The authors reported no conflicts of interest.

“Mitochondria are central to cellular health, and NAD+ is essential to how they work,” Rob Fried, Chief Executive Officer at Niagen Bioscience, remarked. “This first-of-its-kind independent study from the University of Cambridge is early and exploratory, but shows leading institutions are choosing Niagen to tackle some of the hardest problems in human health.”

Mitochondrial Health & NAD+

Mitochondria generate the energy cells need to function and are essential for cellular and overall health. NAD+ is an essential coenzyme in that process, including as a required fuel for sirtuin enzymes that help regulate the creation of new mitochondria. NAD+ declines with age and exposure to metabolic stress, and mitochondrial dysfunction is recognized as a hallmark of aging (**López-Otín et al., 2023**). Mitochondrial disorders are common (**Gorman et al., 2015**) and can affect many different organ systems (**Chinnery & Hudson, 2013**), hindering quality and duration of life (**Kaufmann et al., 2011**). Primary mtDNA disease is a distinct inherited condition rather than a product of aging, and the findings from this study should not be extended to healthy individuals.

Understanding how NAD+ augmentation with NR affects mitochondrial biology across human conditions is therefore central to Niagen Bioscience’s healthspan research. These findings add to an existing body of evidence showing favorable effects of NR on mitochondrial biology, including increased muscle mitochondrial biogenesis and improved mitochondrial respiration (**Lapatto et al., 2023**).

Dr. Schon noted, “The muscle biopsy changes were particularly promising in people with mitochondrial DNA deletions, and we are designing a new clinical trial for this group.”

Study Highlights

This four-week, open-label, single-arm study included eight adults (3 women and 5 men; mean age 53.5 yrs) with genetically confirmed mtDNA disease, recruited from mitochondrial clinics in Cambridge and London. Five participants had the m.3243A>G/T variant and three had a single large-scale mtDNA deletion. Participants took Niagen at 20 mg/kg per day, split into two doses, for four weeks (final doses of 2,000 mg/day in three participants and 1,250 mg/day in five), with clinical testing and muscle biopsies at baseline and at week four.

Key Clinical and Quality of Life Findings

- Safety (primary outcome): High-dose Niagen was well tolerated.
- Mobility (secondary outcomes): Secondary outcomes measuring mobility with the Timed Up and Go test showed a significant 16.3% improvement in time, from 11.9 seconds at baseline to 9.96 seconds at week four. Additional secondary outcomes measuring six-minute walk distance, grip strength, and SF-36 quality-of-life scores did not change significantly.

Key Muscle Mitochondrial Function Findings

- Muscle mitochondria in the three participants with mtDNA deletions (post hoc analysis)
    - Muscle biopsies showed favorable changes, but none reached statistical significance due to the small sample size. More specifically:
        - In one participant, the share of muscle fibers with visibly damaged mitochondria fell from 6.47% to 2.29%, while the other two stayed below 1%.
        - Citrate synthase activity, an enzyme commonly used as a marker of how many mitochondria a muscle cell contains, rose overall in the group.
        - The proportion of mitochondrial DNA carrying the disease-causing mutation decreased in all three participants, and total muscle mitochondrial DNA increased in two of three; in two participants, healthy mitochondrial DNA rose by 84% on average.
        - Phosphocreatine recovery, a measure of how quickly muscle restores its energy supply, also increased overall in the group.
- Differences by genetic diagnosis
    - Muscle appeared different at baseline depending on diagnosis. Participants with mtDNA deletions had more muscle fibers lacking a key energy-producing enzyme (cytochrome c oxidase), while those with the m.3243A>G/T variant had more fibers with dysfunctional mitochondria. The favorable trends above were not seen in the m.3243A>G/T group.
- Blood biomarkers
    - FGF-21 and GDF-15, two proposed blood markers of mitochondrial disease severity, showed a non-significant trend toward lower levels in both genetic groups.

This was a carefully designed exploratory study, and the authors are appropriately measured in their conclusions. The most encouraging signals were seen in the three participants with large-scale mtDNA deletions and were not seen in those with the m.3243A>G/T variant. The investigators concluded that larger randomized controlled trials are needed to determine whether the biological changes translate into meaningful clinical benefit.

Additional information on this study can be found on the Cambridge Clinical Mitochondrial Research Group website, **Nicotinamide Riboside (NR) Study Paper published in Genome Medicine**, and on the About NAD+

website, **Nicotinamide Riboside and Mitochondrial DNA Disease: Early Findings From a Human Study**.

For more information on the Niagen Research Program and patented Niagen ingredient, visit **www.niagenbioscience.com**.

About Niagen Bioscience

Niagen Bioscience, Inc. (NASDAQ: NAGE) is the global authority in healthy aging and NAD+ (nicotinamide adenine dinucleotide) science. As a trusted pioneer of NAD+ discoveries, Niagen Bioscience™ is dedicated to advancing healthspan through precision science and innovative NAD+-boosting solutions.

The Niagen Bioscience team, composed of world-renowned scientists, works with independent investigators from esteemed universities and research institutions around the globe to uncover the full potential of NAD+. A vital coenzyme found in every cell of the human body, NAD+ declines with age and exposure to everyday lifestyle stressors. NAD+ depletion is a key contributor to age-related changes in health and vitality.

Distinguished by state-of-the-art laboratories, rigorous scientific and quality protocols, and collaborations with leading research institutions worldwide, Niagen Bioscience sets the gold standard for research, quality, and innovation. There's a better way to age.

At the heart of its clinically tested product portfolio is Niagen® (patented nicotinamide riboside, or NR), the most efficient, well-researched, and high-quality NAD+ booster available. Niagen powers the Company's consumer supplement, Tru Niagen®, the number one NAD+ boosting oral supplement in the United States† (available at **www.truniagen.com**), and Niagen™ Plus, featuring pharmaceutical-grade intravenous (IV) and injectable Niagen products (**www.niagenplus.com**). Pharmaceutical-grade Niagen IV and injections are compounded and distributed by U.S. FDA-registered 503B outsourcing facilities and are available exclusively at clinics with a prescription. NAD Pharmaceuticals Corp., the Company's wholly owned subsidiary focused on developing therapies for accelerated aging and rare genetic diseases, is conducting research on NB4168, a differentiated small molecule.

Niagen Bioscience's robust patent portfolio protects NR and other NAD+ precursors. Niagen Bioscience maintains a website at **www.niagenbioscience.com**, where copies of press releases, news, and financial information are regularly published.

† Based on revenue per largest U.S. e-commerce marketplace (Jan. 2025 – Dec. 2025)

Forward Looking Statements:

This release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, and Section 21E of the Securities Exchange Act of 1934. 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,” “predicts,” “projects,” “continue,” “would” or the negative of such terms or other similar expressions.

Forward-looking statements are based on current expectations and assumptions and are subject to risks and uncertainties that could cause actual results to differ materially from those described. These risks and uncertainties include, but are not limited to, statements regarding the results of small, open-label exploratory studies, including the study described in this release, may not be replicated in larger randomized controlled trials, Niagen Bioscience's NB4168 pharmaceutical development program; planned preclinical, IND-enabling and clinical development activities; the potential timing of an IND submission or first-in-human study; the potential bioavailability, exposure, safety, tolerability, efficacy, pharmacodynamic or clinical profile of NB4168; and the Company's ability to translate its NAD+ platform into pharmaceutical products; inflationary conditions and adverse economic conditions; our history of operating losses; the growth and profitability of our product sales; our ability to maintain and grow sales, marketing and distribution capabilities; changing consumer perceptions of our products; our reliance on a single or limited number of third-party suppliers; risks of conducting business in China; including unanticipated developments in and risks related to the Company’s ability to secure adequate quantities of pharmaceutical-grade Niagen in a timely manner; the Company’s ability to obtain appropriate contracts and arrangements with U.S. FDA-registered 503B outsourcing facilities required to compound and distribute pharmaceutical-grade Niagen to clinics; the Company’s ability to remain on the U.S. FDA Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act Category 1 list; the Company’s ability to maintain and enforce the Company’s existing intellectual property and obtain new patents; whether the potential benefits of NRC can be further supported; further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials; determinations made by the FDA and other governmental authorities, including with respect to products seeking to compete in our market; mislabeling or other misleading marketing practices by competitors; economic and market instability, including as a result of tariffs or trade conflicts; and the risks and uncertainties associated with our business and financial condition in general, described in our filings with the Securities and Exchange Commission (SEC), including, without limitation, our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q as filed with the SEC.

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 Niagen Bioscience

undertakes no obligation to revise or update this release to reflect events or circumstances after the date hereof.

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