CLINIQ

NAD^+

promotes

Stem Cell Renewal and Regenerates Mitochondria

Clinic X receives many inquiries about **stem cell infusion therapies** offered in the United States and other countries.

Our current view from small **human** trials is that there may be a benefit to infusions of **exosomes** that are naturally **secreted** from healthy stem cells.

Stem cell **exosomes** have **regenerative** properties that help restore **functional cells** needed to maintain tissue and organ viability.

Overlooked when considering **exosome** treatments is the ability to **rejuvenate** existing **stem cell pools** utilizing approaches many of you *already* follow.

This includes activating **AMPK** and restoring youthful levels of **sirtuins** and **NAD⁺**.

Increasing **NAD⁺** is a promising way to **selfrenew** existing **stem cells** in order to **extend lifespan** and **prevent disease**.[1-12]

A study published in **June 2019** shows how a **NAD⁺ boosting** supplement called **nicotinamide riboside** increased **stem cell** colonies by **75%** in the gut of aging mice.[13]

Other studies point to the role of **NAD⁺** in restoring **circadian rhythms** needed for restorative **sleep**.[14]

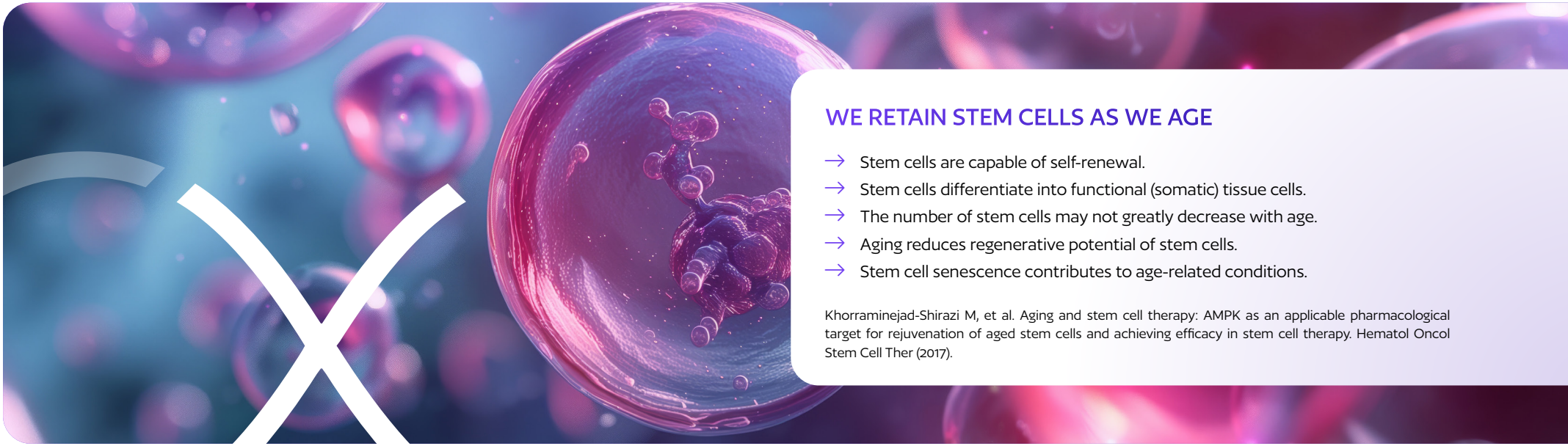
Age-related **sleep deterioration** and **digestive disorders** adversely impact quality of life and accelerate degenerative processes in older individuals.

The most critical role of NAD⁺ is **DNA repair**. Each day, our DNA sustains numerous breaks that are **repaired** by **NAD⁺**-dependent enzymes.

With age, **NAD⁺** levels plummet. Another study published in **2019** showed that a modest dose of **nicotinamide riboside** boosted **NAD⁺** levels by **51%** in overweight **humans**.[15]

We advise holding off on most **stem cell infusions** until more is known about safety and efficacy.

New data reveal how **NAD⁺** improves functionality of existing **stem cells** and replenishes **mitochondria** in cells throughout the body.



WE RETAIN STEM CELLS AS WE AGE

- → Stem cells are capable of self-renewal.
- → Stem cells differentiate into functional (somatic) tissue cells.
- → The number of stem cells may not greatly decrease with age.
- → Aging reduces regenerative potential of stem cells.
- → Stem cell senescence contributes to age-related conditions.

Khorraminejad-Shirazi M, et al. Aging and stem cell therapy: AMPK as an applicable pharmacological target for rejuvenation of aged stem cells and achieving efficacy in stem cell therapy. Hematol Oncol Stem Cell Ther (2017).

WHAT IS NAD+?

Nicotinamide adenine dinucleotide (NAD⁺) is a compound found in every living cell. It is critical for **cell energy** production.

Recent research shows **NAD⁺** does much more.[6,8-11,16,17] Hundreds of different **proteins** in each cell *require* **NAD⁺** to work properly.[17]

The most important proteins are the **sirtuins**, cellular guardians that protect against **DNA damage** that leads to many age-related ailments.[18,19]

Sirtuins are an important target for **anti-aging** interventions.[10,11,20-22] Multiple animal studies have demonstrated that *increasing* **sirtuin activity** leads to longer life and reduction in age-related loss of function.[12,23,24]

As **NAD⁺** levels decline with aging, there is reduced sirtuin **activity**. Boosting NAD⁺ helps ramp up **sirtuin** activity.

Increasing NAD⁺ levels can bring additional benefits tied to healthy longevity including:[20,25]

- → *Promoting* **AMPK activity**, an enzyme that improves metabolism and helps protect against obesity and diabetes,
- → *Modulating* **p53**, a tumor suppressor gene that repairs damaged DNA and protects against cancer initiation,
- → *Inhibiting* **NF-kB** (nuclear factor-kappa B), a protein that induces the chronic inflammation tied to many diseases and premature aging, and
- → *Inhibiting* **mTOR**, a molecular complex whose abnormal activation contributes to many chronic diseases of aging.

HOW OLD STEM CELLS MAY BE REJUVENATED

- → *Boost cellular AMPK*
- → *AMPK lowers excess mTORC1*
- → *Replenish NAD+ cell levels*
- → *Activate sirtuins (with resveratrol)*

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NICOTINAMIDE RIBOSIDE AND RESVERATROL: A POWERFUL ANTI-AGING DUO

Resveratrol is a plant compound found in red grapes, red wine, and other darkly colored fruits.

Among its many benefits, it activates **sirtuins**, the key defender proteins linked to longer, healthier life.[47-49]

But resveratrol can't do this if cells are low in **NAD⁺**. That's because **NAD⁺** is required for sirtuins to work properly. It would be like pressing the accelerator in your car when your gas tank is empty.

The solution is to increase intake of **nicotinamide riboside** to boost **NAD⁺** levels at the same time as promoting sirtuin activity with **resveratrol**. This combination ensures that the enhanced sirtuin activity can have its maximum beneficial effect on health and aging.

NICOTINAMIDE RIBOSIDE BOOSTS NAD+

Higher levels of NAD⁺ correlate with improved health and a lower occurrence of age-related disorders.

Lower NAD⁺ levels contribute to many diseases of older age, including sleep disturbances, metabolic disorders, diabetes, cardiovascular disease, and cognitive decline.[7,9-11,14,26]

An easy way to boost NAD⁺ levels is with **nicotinamide riboside**, which converts to NAD⁺ in your body. In human subjects, a **300 mg** dose of **nicotinamide riboside** increased cellular NAD⁺ levels by **51%**.[15]

Nicotinamide riboside is highly absorbable, or **bioavailable**, when taken orally.[27]

REMARKABLE NEW FINDINGS

Recent studies of NAD⁺ and nicotinamide riboside have shown two primary ways in which they improve health.

1. Replacing Old Mitochondria and Improving Mitochondrial Function

Mitochondria are the power suppliers of every cell, breaking down nutrients like sugars and fats into energy the cell can use to do work. When mitochondria age, they become dysfunctional, contributing to many illnesses.

Evidence indicates that **sirtuins** perform **cellular housekeeping** that includes replacing old and damaged mitochondria with healthy, new ones.[28] This process rejuvenates cells and improves their metabolism while maintaining their optimal function.

Because **sirtuin activity** is dependent on **NAD⁺** (which plummets with age), supplementation with **nicotinamide riboside** can help preserve cellular functions. Replenishing **NAD⁺** levels with nicotinamide riboside resulted in enhanced mitochondrial function that:

- Rejuvenated aging **bone marrow cells**, helping to maintain **immune function** and prevent bone marrow failure and related diseases,[29,30]
- Improved muscle function and reduced muscle pathology in an animal model of **muscular dystrophy**,[31] and
- Lessened **liver inflammation** and induced mitochondrial biogenesis, the formation of new mitochondria, in mice liver cells.[32]

2. Rejuvenating Stem Cells

Healthy **stem cells** in tissues are needed to replace dead or dying **functional cells** with new ones. But stem cells age and become dysfunctional over time, causing tissues to deteriorate and increasing risk for disease.[33]

Nicotinamide riboside intake can help prevent this. In a study on elderly mice, nicotinamide riboside replenished NAD⁺ levels, which improved mitochondria function that **rejuvenated stem cells** in muscles. It also prevented the deterioration of muscle, skin, and brain stem cells.[24]

This prolonged the lifespan of old mice by approximately **5%**. Though this number may not seem huge, the supplementation only began when the mice were already two years old, the equivalent of about **80 years** in humans.[34]

WHAT YOU NEED TO KNOW

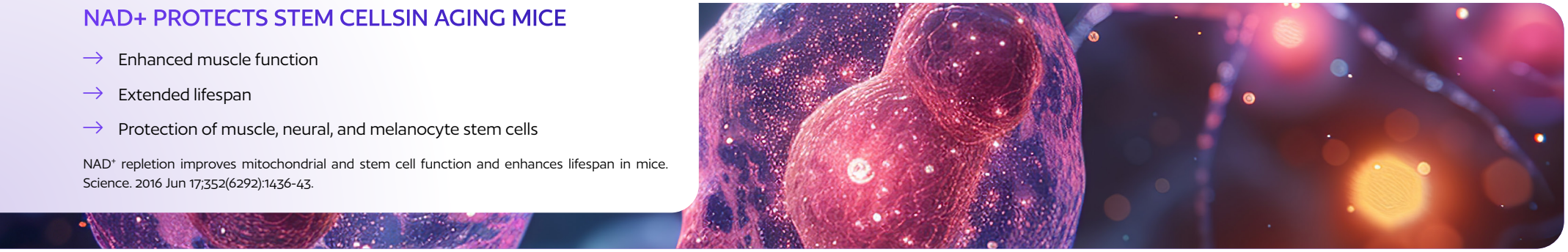
NAD⁺ FOR HEALTHY LONGEVITY

- NAD⁺ (nicotinamide adenine dinucleotide) is an essential cofactor for hundreds of cellular processes.
- Sirtuins, cellular defenders linked to longer life and protection from disease, require optimal NAD⁺ levels to function.
- Levels of NAD⁺ drop with age, accelerating aging. Nicotinamide riboside helps replenish NAD+ levels.
- Boosting NAD⁺ has been tied to improved mitochondrial function, healthier stem cells that rejuvenate tissues, and increased longevity.
- Maximizing NAD⁺ also protects tissues from the effects of age and may reduce risk for age-related diseases such as cognitive decline, cardiovascular disease, and metabolic disease.

NAD+ PROTECTS STEM CELLSIN AGING MICE

- → Enhanced muscle function
- → Extended lifespan
- → Protection of muscle, neural, and melanocyte stem cells

NAD⁺ repletion improves mitochondrial and stem cell function and enhances lifespan in mice. Science. 2016 Jun 17;352(6292):1436-43.



A more significant effect may occur if NAD⁺ is boosted *earlier* in life, and combined with interventions like **resveratrol** that prompts cells to express **sirtuin proteins** that **NAD⁺** then **activates**.

New studies corroborate a beneficial impact of NAD⁺ on other **stem cells**.[13,29] In one study, researchers looked at adult mice gut **stem cells**, which typically dwindle in older age.[13] Injuries to the gut of these older animals have a difficult time healing.
Nicotinamide riboside increased these digestive tract **stem cell** colonies by approximately **75%**, improving the ability to recover from injury. This finding has favorable implications for older individuals suffering from **digestive tract** discomforts.

WIDE-RANGING BENEFITS OF NAD+

Boosting NAD⁺ levels can have a positive impact on multiple areas of health.

LONGEVITY

Studying the effect of a supplement on human longevity is difficult, because of the long average lifespan of humans. But many studies show that increasing NAD⁺ **prolongs the life** of a variety of organisms.[12,23,24,35]
In yeast, a single-cell organism with a short lifespan, **nicotinamide riboside** increased lifespan as demonstrated by improved cell **replicative capacity**.[23]
Studies of worms show that nicotinamide riboside can prolong their life by at least **10%**.[35] These effects extend to mammals as well.[12,24]

PHYSICAL PERFORMANCE

In a recent study of older men, levels of NADH, the reduced form of NAD⁺ were significantly increased by **59%** only two hours after taking one dose of **nicotinamide riboside**, while markers of oxidative stress were decreased.[15]

The men in this study had an **8%** improvement in peak isometric muscle torque (a measure of muscle force) and a **15%** improvement in fatigue associated with exercise.

BRAIN HEALTH

Studies of mouse models of **Alzheimer's** disease have shown improvements with nicotinamide riboside supplementation.[36,37]
In the most recent study, it reversed the cognitive deficits in mice, improving memory.[37]
The pathology observed in the brains of Alzheimer's disease patients, **amyloid plaques**, was also reduced in the brains of these animals. A previous study had similar findings.[36]

OBESITY AND METABOLIC DISORDERS

Sirtuins improve metabolism and can be helpful guardians against weight gain, metabolic syndrome, and type II diabetes.[38-43]
By boosting **sirtuin activity**, nicotinamide riboside enhanced metabolism and prevented excessive **weight gain** in mice.[44]
In animal models of **type II diabetes**, this improved metabolism helped control blood sugar levels and shield against the damage done by high blood glucose.[42]

CARDIOVASCULAR HEALTH

Improved metabolism and lower body weight help to reduce risk for cardiovascular disease.

But nicotinamide riboside does even more to protect the cardiovascular system.
One recent study focused on mice with **heart disease** that had a **30%** reduction in NAD⁺ levels.[45] Untreated, they typically developed heart failure. But nicotinamide riboside attenuated the decline in cardiac function.

People **aged 50** have about **40%** less NAD^+ whereas 80-year-old people can have **90%-98%** lower levels of NAD^+ compared to 21-year-olds.

Heart failure risk increases as people grow older.

Recent studies show that **nicotinamide riboside** protects the organs of the cardiovascular system and protects other tissues from the effects of cardiovascular disease.

Normally, if blood flow to a tissue is compromised due to disease, the tissue dies, as happens in a **myocardial infarction** or a **stroke**. Preclinical studies show that **nicotinamide riboside** improves the response of tissues to this type of injury, reducing damage and encouraging recovery of the tissue.[5,46]

UNIFIED THEORY OF STEM CELL REJUVENATION

- Adult stem cells lose ability to repopulate tissues with functional cells.
- Systemic deterioration occurs as functional cells degenerate/die.
- How your stem cells may be renewed:
  - Boost cellular AMPK
  - Suppress excess mTORC1
  - Replenish NAD+ cell levels
  - Activate sirtuin proteins

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HOW NAD+ IMPROVES SLEEP

It's no secret that sleep patterns become disrupted with age.
Much of this problem is due to a disruption in circadian rhythms that govern our sleep/wake cycle.

NAD^+ has shown the ability to rebalance circadian rhythms through its stimulation of a vital cell protein called SIRT1.

In an animal study, mice deficient in SIRT1 experienced decreased quality of sleep.[14]
Increasing NAD^+ levels can help increase SIRT1 and other sirtuins, helping to restore normal sleep/ wake cycles.

SUMMARY

NAD^+ is a critical component of a healthy aging program.
Every cell requires it for hundreds of processes. These include **activity** of **sirtuins**, cellular guardians linked to prolonged lifespan and healthspan.

NAD^+ levels and sirtuin expression diminish with advancing age, accelerating aging processes and degenerative disease risk.

Nicotinamide riboside is a compound that increases cellular NAD^+ levels, enhancing sirtuin activity. New research has found that maintaining more youthful NAD^+ levels can slow certain aspects of biological aging.

NAD^+ also improves the health of **stem cells** that can replace dead and dying cells and keep vital tissues functioning.

This not only extends lifespan, but also helps reduce the risk for metabolic disease, obesity, cardiovascular disease, cognitive dysfunction, and more.

If you have any questions on the scientific content of this article, please contact a **Clinic X** Specialist.

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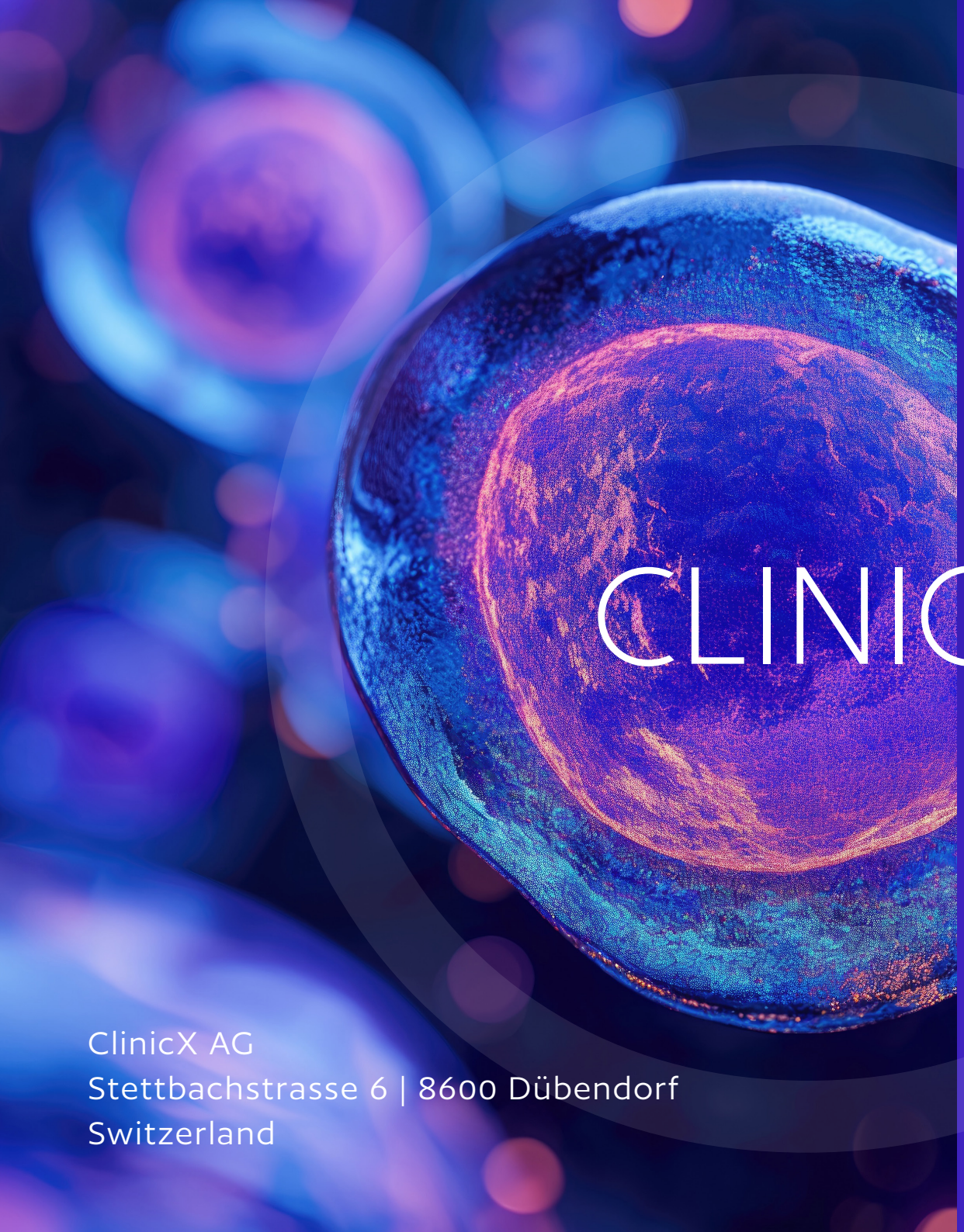

CLINICX

ClinicX AG
Stettbachstrasse 6 | 8600 Dübendorf
Switzerland

www.clinicx.ch