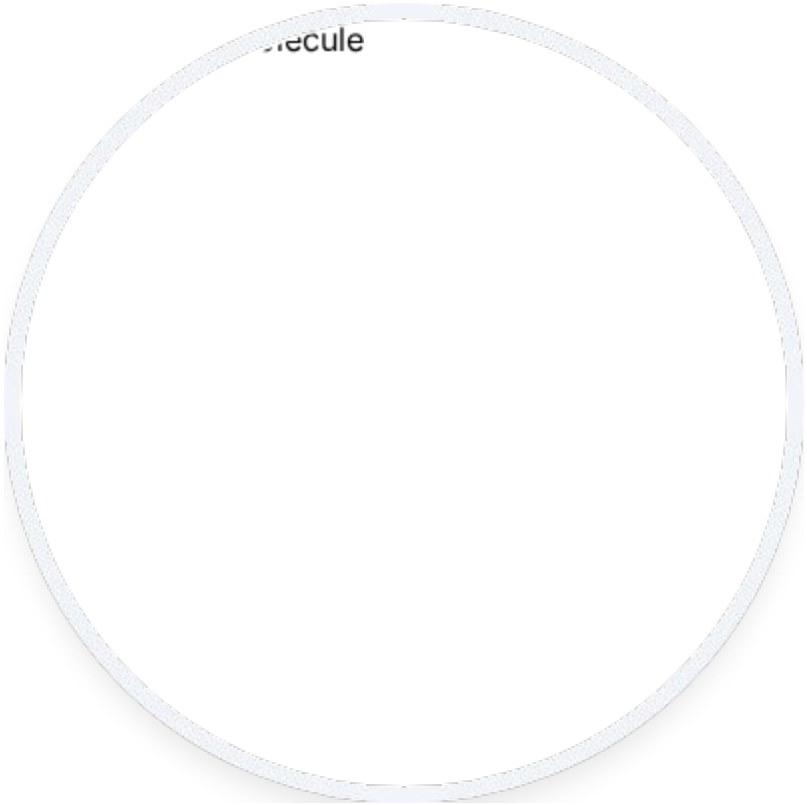
Low-Dose Rapamycin Passes First Human Safety Trial

Insights from the PEARL Trial: A Landmark Year-Long Study

THE DIMMER SWITCH OF AGING



From Transplant to Longevity

Originally discovered in Rapa Nui soil, Rapamycin is an FDA-approved drug traditionally used at high daily doses as an immunosuppressant. Modern geroscience explores its potential at **intermittent low doses** to extend healthspan by modulating the nutrient-sensing mTOR pathway.

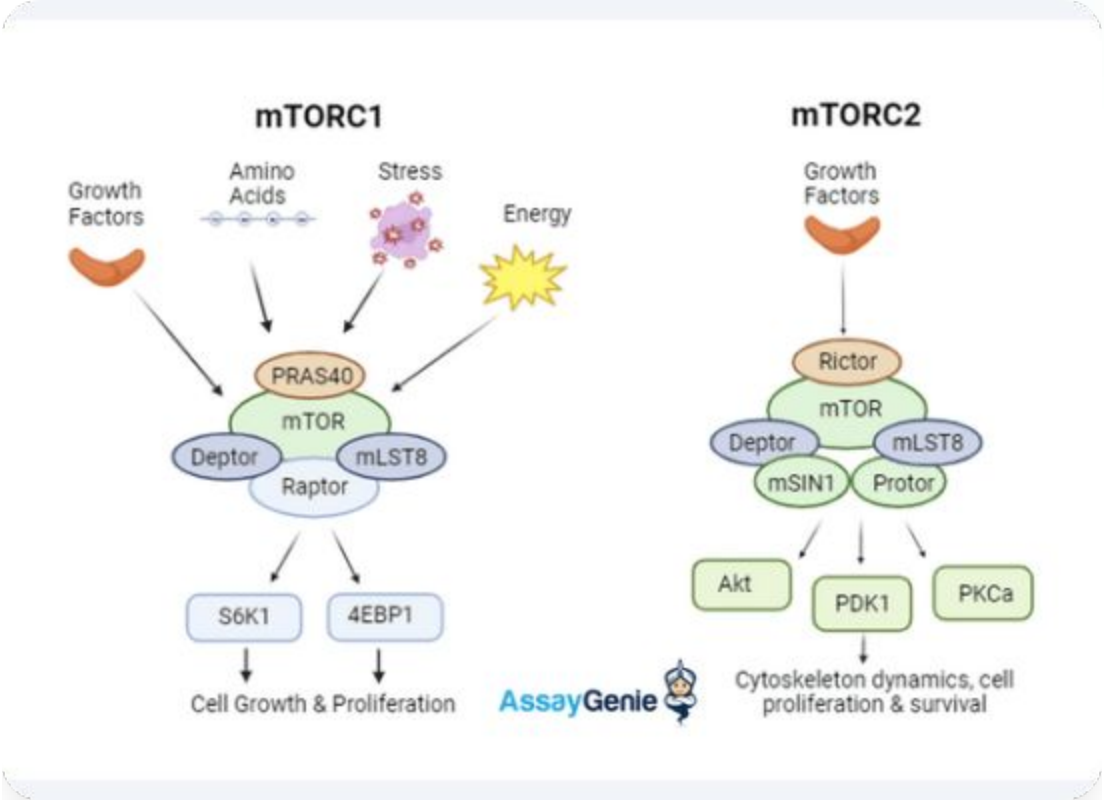
THE PEARL STUDY DESIGN

Parameter	Clinical Details
Study Type	Randomized, Double-Blind, Placebo-Controlled (48 Weeks)
Participants	114 Healthy Adults (Aged 50–85)
Dosing Groups	Placebo vs. 5mg Weekly vs. 10mg Weekly (Compounded)
Primary Goal	Evaluate Long-Term Safety and Visceral Adiposity Changes

MECHANISM: THE MTOR PULSE

mTORC1 vs. mTORC2

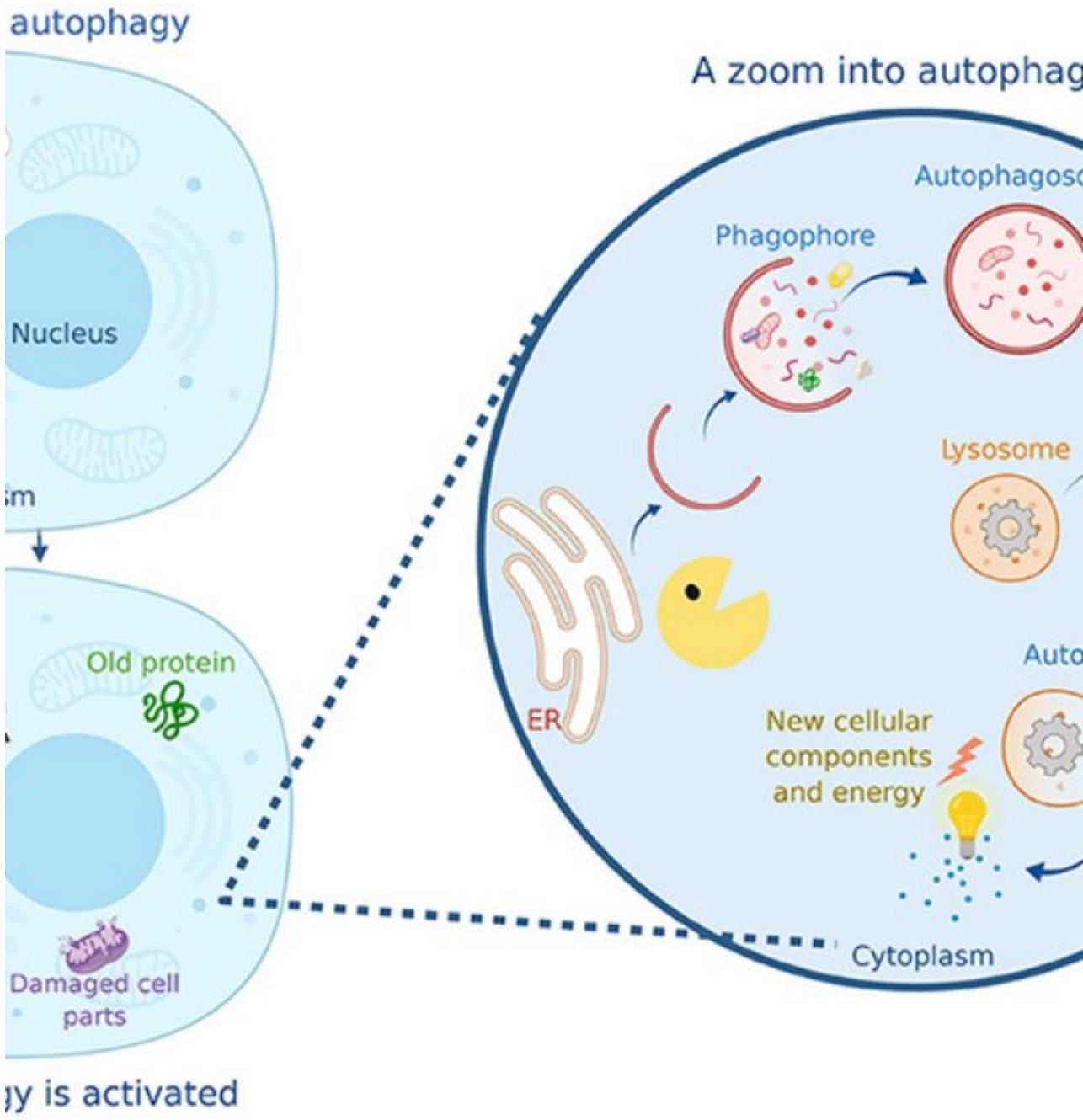
High-dose daily use inhibits both complexes, leading to immunosuppression. The weekly **"pulse" protocol** selectively suppresses **mTORC1** (nutrient sensing) while leaving **mTORC2** (immune integrity) largely intact, allowing for periodic recovery.



CELLULAR CLEANUP

Inducing Autophagy

By temporarily braking mTORC1, cells enter a self-cleaning mode known as **autophagy**. This process recycles damaged proteins and organelles, reducing the "toxic burden" that accumulates with age and driving cellular rejuvenation.



SAFETY PROFILE: ADVERSE EVENTS

∗Adverse events were mild and similar across groups. Most common side effect was transient gastrointestinal discomfort. No major metabolic derangement or immunosuppression observed.

KEY FINDING: LEAN MUSCLE MASS

Benefits in Women

Statistically significant improvement in lean tissue mass observed in women using the 10mg weekly dose.

DXA Validation

DEXA scans confirmed muscle preservation, suggesting rapamycin may combat sarcopenia (age-related muscle loss).

Proteostasis

Improved muscle quality via enhanced protein folding and clearance of aggregate damage.

SIGNIFICANT PAIN REDUCTION

p=0.01

Self-Reported Pain Improvement

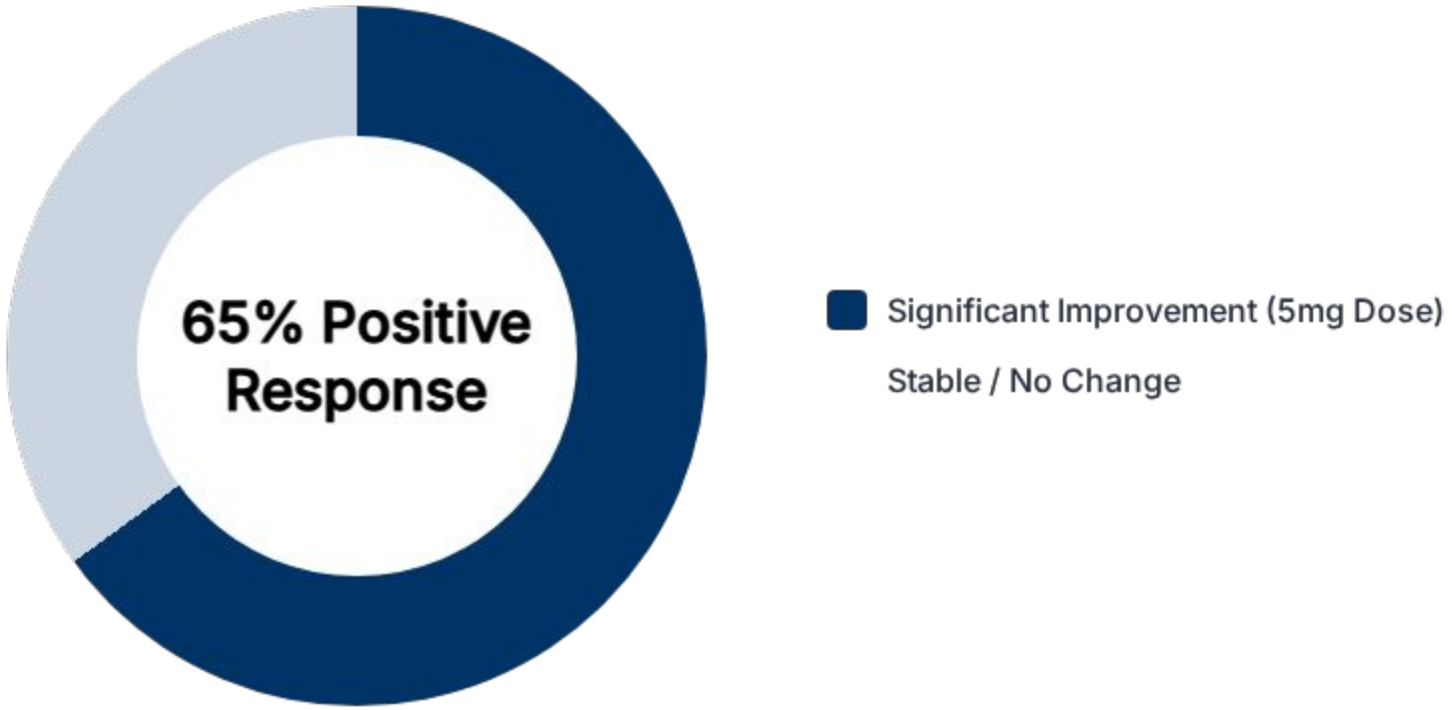
5

Gender-Specific Efficacy

The 10mg dose group showed a marked reduction in chronic pain signals, particularly in women. This aligns with previous anecdotal reports and suggests anti-inflammatory benefits at the joint and systemic level.

Researchers noted a medium-to-large effect size ($\eta p^2 = 0.168$), indicating a clinically meaningful impact on quality of life.

EMOTIONAL WELL-BEING SCORES



Participants in the 5mg weekly group reported improved emotional health and general well-being (p = 0.023).

INTERMITTENT DOSING PROTOCOLS

- **The Pulse Method:** Weekly administration allows the drug to clear the system (Trough < 5 ng/mL) before the next dose.
- **Bioavailability Lesson:** Compounded rapamycin was found to be 1/3 as bioavailable as generic formulations.
- **Clinical Supervision:** Despite safety, protocols should be monitored to manage potential minor lab shifts (e.g., HbA1c).
- **Personalization:** Dose-response varies; TROUGH levels are key to avoiding chronic mTORC2 inhibition.

AGING METRICS & FUTURE OUTLOOK

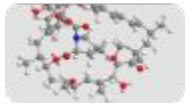
Projected impact: Scaling from pilot RCTs to large-scale bio-marker tracking for human longevity.

Questions?

The PEARL trial proves that low-dose, intermittent rapamycin is safe for healthy adults, paving the way for the first true gerotherapeutic interventions.

Reference: Moel et al. (2025). Aging-US Vol 17, Iss 4.

IMAGE SOURCES



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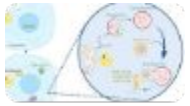

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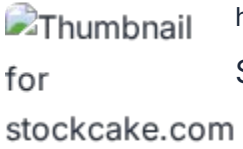

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