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NEW TEETH TO BITE THE DUST

TRG035 AND THE SYSTEMIC COSTS OF USAG-1 NEUTRALIZATION: A NAM ANALYSIS

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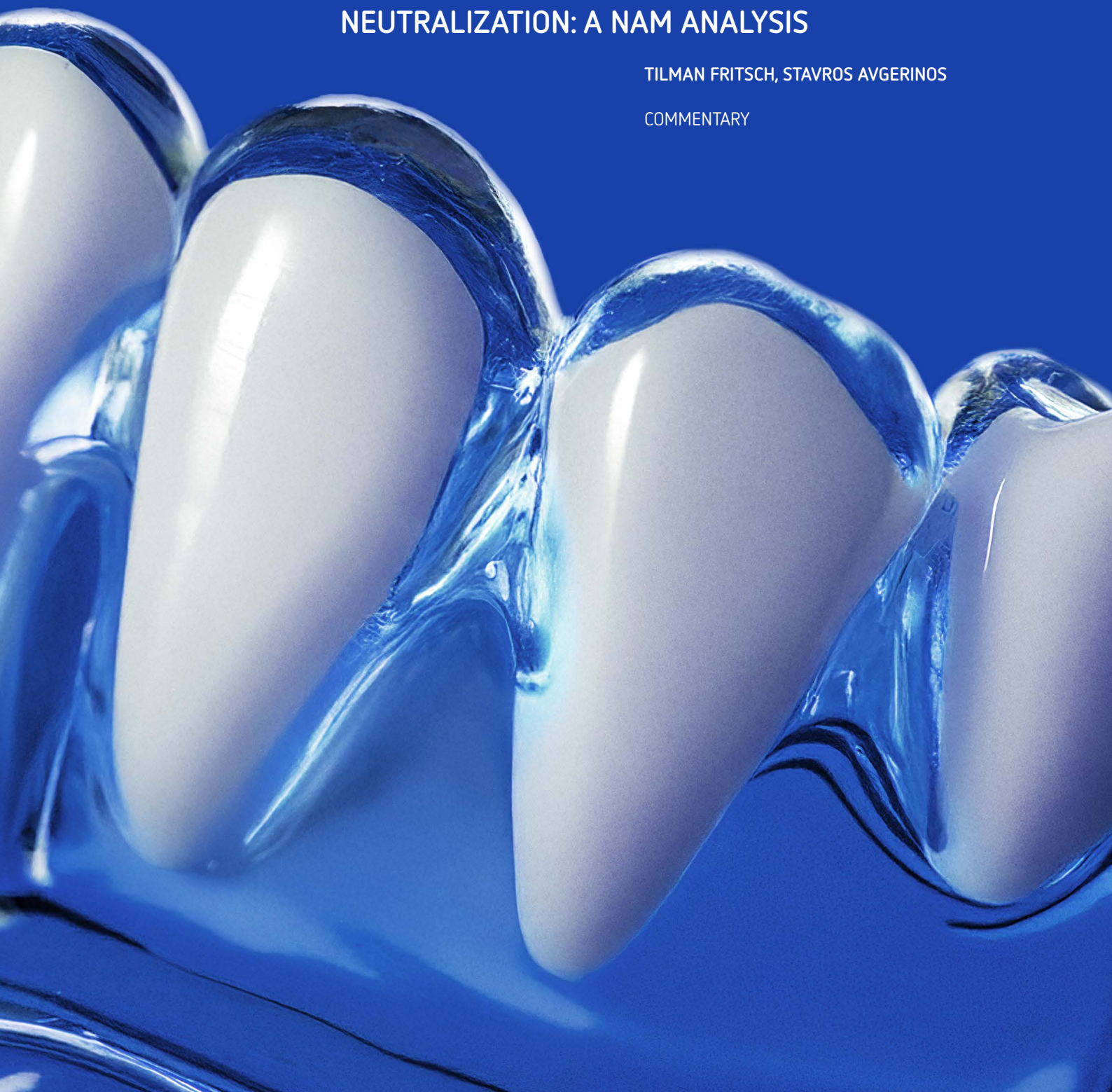
COMMENTARY



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ABSTRACT

TRG035, a humanized monoclonal anti-USAG-1 antibody developed by the Japanese firm Toregem BioPharma, is currently being tested in a Phase I trial (jRCT2051240154) enrolling 30 healthy adult males. Its objective: reactivation of dormant tooth germs through neutralization of the protein USAG-1 (= SOSTDC1). This extended analysis evaluates (a) the pleiotropic risk profile across eight functional domains, (b) an age-class-specific risk stratification for the planned cohorts, and (c) the secondary and tertiary cascade pathways — the "Christmas Tree Cascade" of BMP/Wnt dysregulation.

Keywords: TRG035, USAG-1, SOSTDC1, tooth regeneration, pleiotropy, tumor suppressor, NK cells, BMP/Wnt cascade, Christmas Tree Cascade, age-risk stratification, NAM-Dentistry Systematic

1. INTRODUCTION

In September 2024, Kyoto University Hospital initiated the world's first clinical trial of an antibody for tooth regeneration [3]. TRG035 (Toregem BioPharma, Kyoto) neutralizes USAG-1, a dual BMP/Wnt antagonist [1]. In animal models, a single administration led to eruption of functional teeth [2]. The Phase I trial enrolls 30 healthy males over 11 months [3]; Phase II studies in children (aged 2–6) are planned; indication expansion to acquired tooth loss (elderly) has been announced. From a NAM perspective [25], three questions arise: (1) What are the direct systemic risks? (2) Are there age-class-specific differences? (3) What downstream cascades are triggered?

2. USAG-1/SOSTDC1: MOLECULAR PROFILE

SOSTDC1 is a 28–32 kDa secreted protein that functions as a dual antagonist of BMP and canonical Wnt signaling pathways via LRP4/5/6 co-receptors [24]. It is highly expressed in skin, intestine, brain, skeletal muscle, lung, kidney, vasculature, bone periosteum, mesenchymal stem cells [24], ocular tissue [20], and Sertoli cells of the infantile testis [18]. The human protein shares 98% identity with its murine ortholog [4].

3. THE EIGHT RISK DOMAINS OF USAG-1 NEUTRALIZATION

3.1 Kidney

USAG-1 exhibits highest expression in renal tubules and modulates TGF-β/BMP-7/Smad balance [17]. Neutralization removes the physiological BMP-7 brake [23].

3.2 Tumor Suppression

SOSTDC1 has been identified as a tumor suppressor in clear cell renal carcinomas [4,5], Wilms tumors (7p21) [6], follicular thyroid carcinomas (via PI3K/Akt, MAPK/ERK) [7], gastric [8], and breast carcinomas [9]. TRG035 simultaneously neutralizes an endogenous tumor suppressor across multiple organs.

3.3 NK Cell Immunity

Sostdc1-knockout mice displayed progressive NK cell accumulation, altered Ly49 repertoire, and hyporesponsiveness against MHC-I-deficient target cells [10]. This directly contradicts the rationale of NK-cell-based immunotherapy protocols.

3.4 Adaptive Immunity (TFH/TFR)

SOSTDC1 is developmentally required for TFR cell generation via WNT-β-catenin blockade [11]. Ablation leads to reduced TFR numbers and enhanced germinal center reactions [11].

3.5 Bone

Pleiotropic paradox: 31% less trabecular bone volume alongside larger cortical bone [12]. He et al. correlated Sostdc1 polymorphisms with low lumbar BMD [13]. Alveolar bone is predominantly trabecular.

3.6 Hair Follicles and Skin

Lymphatic vessels secrete SOSTDC1 as a hair follicle growth factor [14]. Null mice exhibit ectopic teeth, fused molars, and supernumerary nipples [15].

3.7 Vascular Calcification

BMP ligands are enriched in calcific lesions. TGF-β1 upregulates USAG-1 and induces EMT in renal cells [16]. USAG-1 neutralization could amplify BMP-mediated vascular calcification.

3.8 Fertility

SOSTDC1 is predominantly expressed in Sertoli cells of the infantile testis [18]. Its downregulation during puberty is a prerequisite for spermatogenesis [18]. Transgenic rats with persistent expression showed reduced sperm counts due to germ cell apoptosis via pSmad1/5/8 [18].

4. SYNOPTIC RISK MATRIX

Domain	SOSTDC1 Function	Risk Upon Neutralization	Reference
Kidney	BMP-7 modulation, TGF-β/Smad balance	BMP-7 overactivation	[17,23]
Oncology	Tumor suppressor in ≥5 carcinoma types	Loss of endogenous tumor suppression	[4,5,6,7,8,9]
NK Cells	Maturation, Ly49, cytotoxicity	NK hyporesponsiveness	[10]
TFH/TFR	TFR differentiation	GC disinhibition	[11]
Bone	Trabecular/cortical regulation	Trabecular loss	[12,13]
Hair Follicles	Paracrine activation	Follicular alterations	[14,15]
Vasculature	Calcification control	Vascular calcification ↑	[16]
Fertility	Spermatogenesis onset	Germ cell apoptosis	[18]

Table 1. Synoptic risk matrix. Yellow: risk described here for the first time.

5. AGE-RISK STRATIFICATION: NO SAFE WINDOW

The evidence reveals a U-shaped risk profile: children and the elderly carry the highest risks, albeit in entirely different domains. The Phase I cohort (adults aged 30–65) occupies the risk minimum — extrapolation is not permissible.

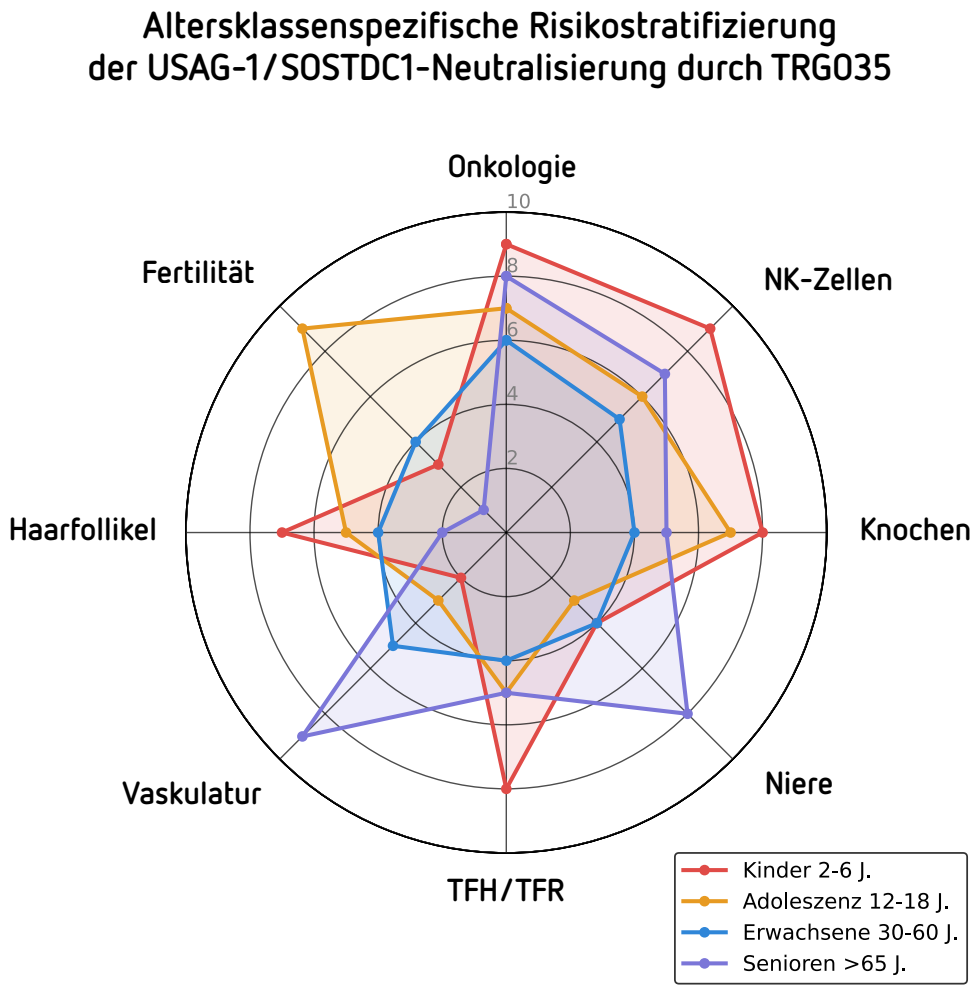

Figure 1. Age-class-specific risk stratification (radar diagram). Scores 1–10 based on published evidence for SOSTDC1 expression, pathway activity, and organ vulnerability per age group. Red: children 2–6; Orange: adolescence; Blue: adults; Purple: elderly.

5.1 Children (Aged 2–6)—Planned Phase II Cohort

Overall risk: Maximum. BMP/Wnt maximally active (growth) [24]. Tumor suppressor loss at highest cell division rate + longest remaining lifespan for latency development. Wilms tumor (SOSTDC1 deletion 7p21) = pediatric tumor [6]. NK immunity immature [21,22]. Germinal center reactions still developing [11]. Sostdc1/Sost double knockout: polydactyly [19].

5.2 Adolescence (Aged 12–18)

Dominant risk: Fertility. SOSTDC1 downregulation = spermatogenesis onset [18]. Concurrent: peak bone mass [13], testicular germ cell tumors (most common tumor in males aged 15–40), NK repertoire still maturing [22].

5.3 Adults (Aged 30–65)—Phase I Cohort

Lowest acute risk. Mature immune system [22], completed puberty [18]. However: accumulating mutations, incipient GFR decline, early vascular calcification. The trial is conducted in the lowest-risk population [3].

5.4 Elderly (>65 J.) – Zielgruppe Zahnverlust

Overall risk: Maximum in other domains. Immunosenescence (NK ≈ neonatal) [22], highest mutational burden [4,5], advanced vascular calcification [16], CKD prevalence 25–30% [17]. The announced indication expansion targets precisely this population.

Domäne	Children	Adolescence	Adults	Senioren
Onkologie	9 – CRITICAL	7	6	8
NK-Zellen	9 – KRITISCH	6	5	7
Knochen	8	7	4	5
Niere	5	4	5	8 – CRITICAL
TFH/TFR	8	6	4	5
Vaskulatur	2	3	5	9 – KRITISCH
Fertilität	3	9 – KRITISCH	4	1
Haarfollikel	7	5	3	2

Table 2. Age-class-specific risk scores (1–10). Red: critical (≥8). Orange: elevated (≥7).

6. THE CHRISTMAS TREE CASCADE: SECONDARY AND TERTIARY PATHWAY EFFECTS

The preceding analysis describes level-1 effects (direct SOSTDC1 functional losses). However, SOSTDC1 is a dual antagonist of two fundamental signaling pathways that feed into cascades of downstream effectors. A single intervention at the trunk (USAG-1) generates branching effects at every subsequent level—the Christmas Tree Cascade.

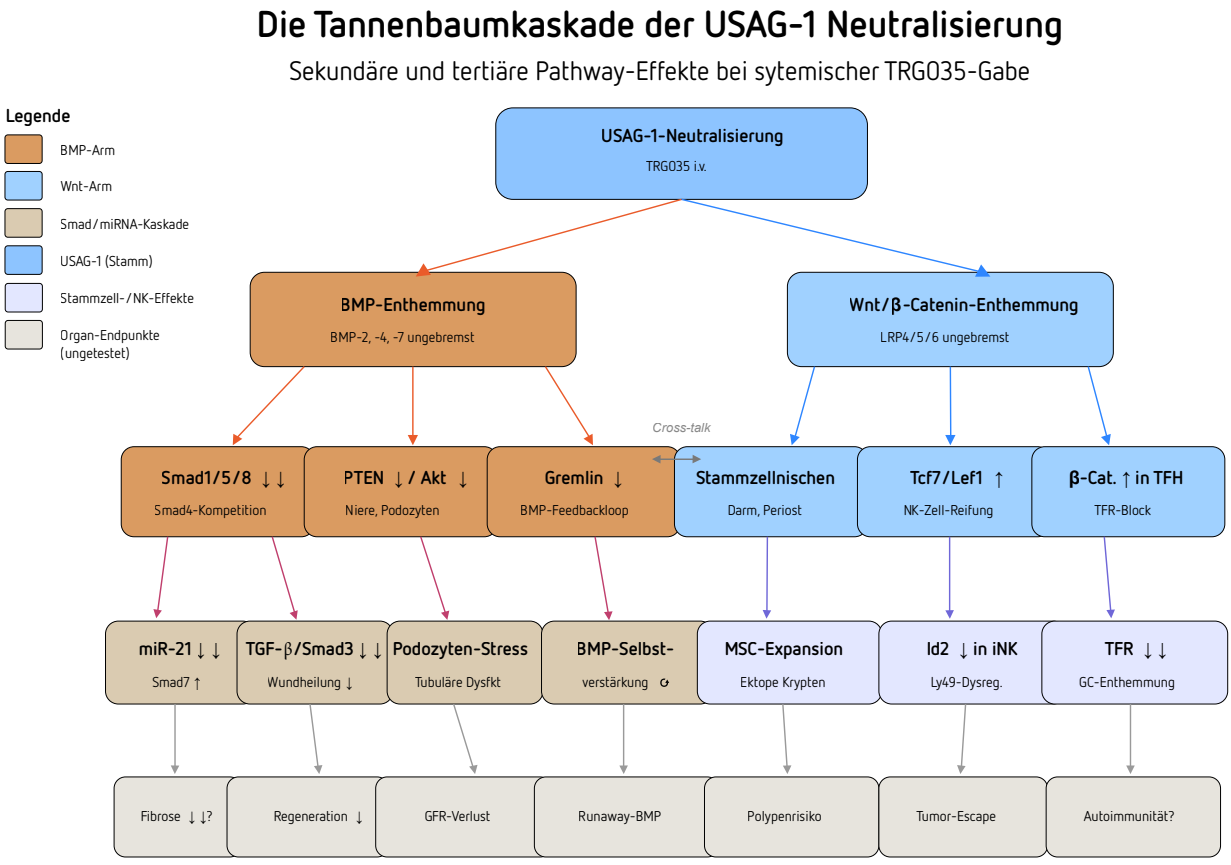

Figure 2. The Christmas Tree Cascade of USAG-1 neutralization. Five levels: trunk (USAG-1), main branches (BMP/Wnt), side branches (Smad competition, stem cell niches), secondary cascade (miRNA, feedback loops, NK reprogramming), organ end-points (untested in Phase I). Red-orange: BMP arm; Blue: Wnt arm; Pink: Smad/miRNA cascade; Purple: stem cell/NK effects; Gray: untested endpoints.

6.1 The BMP Arm

Level 1: USAG-1-Neutralisierung → BMP-7-Enthemmung in Nierentubuli [17]. Level 2: Smad1/5/8-Überaktivierung konkurriert mit TGF-β/Smad2/3 um Smad4 [17]; BMP-7 hochreguliert PTEN, inhibiert PI3K/Akt [23]. Level 3: BMP-7 supprimiert miR-21 → Smad7 steigt → TGF-β-Signaling übermäßig blockiert → Verlust wundheilungsrelevanter TGF-β-Signale [17]. Level 4: Gremlin (BMP antagonist) is suppressed → positive feedback loop of BMP activation [17].

6.2 The Wnt Arm

Level 1: Wnt/β-Catenin-Enthemmung in multiplen Stammzellnischen [24]. Level 2: Intestinal crypt base: Wnt ↑ + BMP ↑ — net effect context-dependent on SMAD4/p53 status. With SMAD4 loss: BMP paradoxically activates Wnt [24]. Level 3: Tcf7/Lef1 ↑ in NK-Zellen, Id2 ↓ in unreifen NK-Zellen → transkriptionelle Reprogrammierung der NK-Entwicklung [10]. Level 4: MSC-Quieszenz-Verlust im Periost (>2× MSCs in Frakturen) [12]. Unkontrollierte Proliferation bei reduzierter Tumorsuppression.

6.3 Cross-talk BMP × Wnt

The two arms interact: BMP normally inhibits Wnt in intestinal homeostasis [24]. Sost and Sostdc1 define non-overlapping expression domains — a double knockout produces polydactyly and syndactyly through Wnt overactivation and SHH misregulation [19]. The Christmas Tree Cascade is not a linear scheme but an interconnected system with feedback loops.

7. NAM PERSPECTIVE

The NAM-Dentistry Systematic [25] classifies therapeutic interventions along three pillars. TRG035 impacts all three simultaneously: Pillar 1 (Toxification) – iatrogenic BMP/Wnt signal disruption; Pillar 2 (Silent Inflammation) – TFH/TFR destabilization and NK hyporesponsiveness; Pillar 3 (Dynamic Function) – trabecular bone loss in alveolar bone + MSC expansion without tumor suppression.

The Christmas Tree Cascade demonstrates that USAG-1/SOSTDC1 branching depth extends at least four levels deep, with cross-talk between the BMP and Wnt arms. No Phase I design can capture this pattern.

Methodological Note: Knockout vs. Antibody. The evidence presented here regarding NK cells [10], TFH/TFR [11], bone [12], hair follicles [15], fertility [18], and polydactyly [19] derives predominantly from Sostdc1-knockout mice — i.e., lifelong, complete gene ablation. TRG035 is a transient monoclonal antibody with a

defined half-life. Pharmacological equivalence between knockout and temporary neutralization cannot be assumed. Three arguments nonetheless support the relevance of knockout data: (1) No published pharmacokinetic data exist for TRG035 regarding tissue penetration, half-life, or dose-dependence of systemic effects — knockout data provide the only available evidence for the pleiotropic risk profile. (2) The announced indication expansion to acquired tooth loss implies cumulative repeat dosing over months to years — an exposure pattern that approximates the knockout phenotype. (3) For a protein with tumor suppressor function in ≥5 organ systems, the precautionary principle demands that knockout evidence be considered a risk signal until pharmacokinetic dose-response studies provide clearance.

8. PLANETARY HEALTH, NAM-BIAS, AND THE NOIS OF TOOTH REGENERATION RESEARCH

8.1 The Illich Question in the 21st Century

Ivan Illich formulated the concept of social iatrogenesis in 1976 [26]: the medicalization of life situations for which functioning solutions already exist generates more harm than the problem itself. TRG035 is a paradigm case of this logic. Age-related tooth loss is not an intractable problem — it has identifiable causes (periodontitis, caries, material toxification, occlusal trauma) that the NAM-Dentistry Systematic [25] addresses through three pillars, and it has proven prosthetic solutions (implants, bridges, dentures) that act locally and do not trigger a systemic Christmas Tree Cascade.

The question is not: Can we regrow teeth? The question is: Does humanity need a drug that neutralizes a pleiotropic master regulator across eight organ systems to solve a problem already addressed by prevention and existing prosthetics?

8.2 The Planetary Cost Accounting

Monoclonal antibody production ranks among the most resource-intensive industrial processes. Life-cycle assessments reveal a CO2 footprint of approximately 22.7 tonnes CO2-equivalent per kilogram of drug substance in a 2000-L process [29]. The primary source: energy consumption for HVAC, bioreactors, and GMP environments [30]. Globally, the healthcare sector emits greenhouse gases equivalent to 514 coal-fired power plants — if it were a country, it would be the fifth-largest emitter worldwide [30].

The footprint of TRG035 consists of three multiplicative layers: (1) Production (mAb manufacturing, cold chain, i.v. infrastructure), (2) Monitoring (lifelong screening across ≥5 organs: oncology, NK cells, kidney, bone, vasculature), and (3) Adverse effect management (treatment of the iatrogenic cascade arising from the Christmas Tree branching). Each layer carries its own resource footprint, and all three multiply with patient numbers.

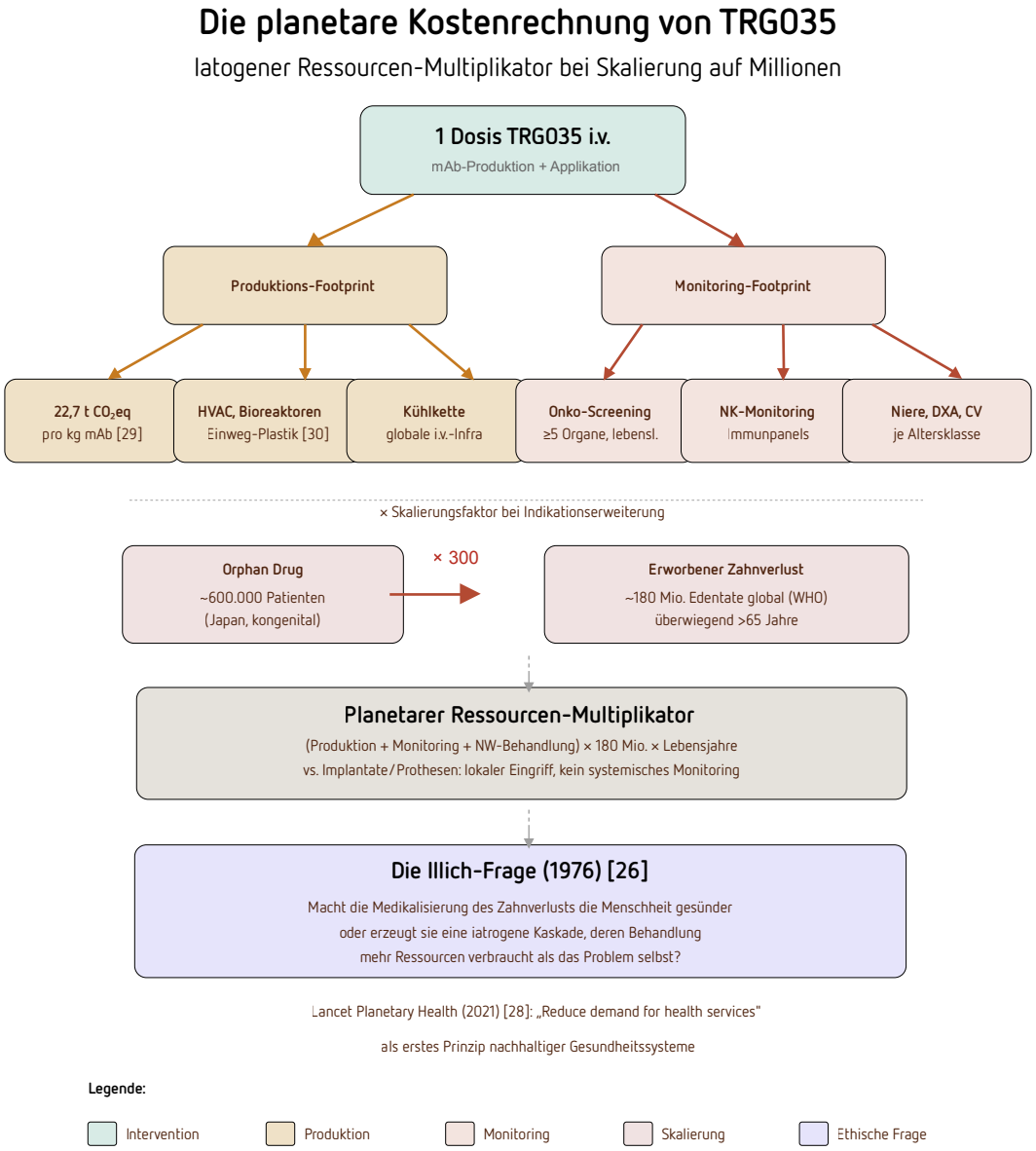

Figure 3. The planetary cost accounting of TRG035. Iatrogenic resource multiplier: production footprint (22.7 t CO_2 eq/kg mAb) + monitoring footprint (≥5 organs lifelong) × scaling from 600,000 (orphan) to 350 million (acquired tooth loss). Bottom: The Illich question [26] and the Lancet Planetary Health principle [28].

8.3 The Scaling Shock: From Orphan to Mass Market

Orphan drug designation for severe congenital hypodontia covers approximately 600,000 patients in Japan. Within this framework, the benefit-risk calculus and planetary footprint may be justifiable — a rare disease without alternatives, a manageable population. Toregem's announced indication expansion to acquired tooth loss shifts this calculus by orders of magnitude: GBD 2021 data (Lancet 2025) and the WHO Oral Health Data Portal estimate the global prevalence of complete edentulism at approximately 350 million individuals [32], predominantly aged over 65. The scaling from 600,000 to 350 million — a factor of ≈580 — transforms a manageable orphan drug footprint into a planetary resource burden encompassing production, monitoring, and adverse effect management.

Das Lancet Planetary Health framework (2021) identifies as its first principle for sustainable health systems [28]: Reduce demand for health services. TRG035 as a mass-market drug for acquired tooth loss produces exactly the opposite: a massive new demand for lifelong monitoring among millions of patients previously managed with local, monitoring-free solutions. The AMA Journal of Ethics [31] articulates the ethical obligation to evaluate clinical decisions through a climate lens and reduce unnecessary interventions.

8.4 NAM-BIAS: Substance-Ontological Bias in Tooth Regeneration Research

The NAM-BIAS framework (NAM-Bias-Awareness-Systematic) classifies scientific biases at four levels: Ebene 1 (study bias per Sackett), Ebene 2 (systemic bias per Ioannidis/Sismondo), Ebene 3 (substance-ontological bias with eight NAM-BIAS types), and Ebene 4 (cognitive engine per Kahneman). TRG035 research displays characteristic distortions at every level:

Level 1: The Phase I trial is by design unsuitable for addressing the documented systemic risks. Thirty subjects, 11 months, healthy males — none of the target populations, none of the critical endpoints, none of the latency periods.

Level 2: Orphan drug status, AMED funding, and media attention generate a systemic bias that marginalizes critical questions about pleiotropy. The research direction is dictated by economic and media incentives, not by systems biology logic.

Level 3: The substance-ontological bias manifests in the reduction of USAG-1/SOSTDC1 to a "tooth inhibition switch". The seven non-dental functional domains are not mentioned in the Toregem literature. The protein is reduced to its tooth-relevant function — an ontological narrowing that obscures its systemic

identity.

Level 4: The cognitive engine — Kahneman's System 1 — generates the appeal: "Regrowing teeth" is an emotionally compelling narrative that suppresses critical inquiry (System 2). No patient asks: "Which seven other organ systems does the antibody affect?"

8.5 NOIS: The Collective Noise of Tooth Regeneration Research

Kahneman, Sibony, and Sunstein defined NOIS [27] as unsystematic variability in judgments given identical case facts — complementary to bias, which describes systematic directional deviation. Extending this concept to the meta-scientific level, TRG035 research reveals an analogous pattern: an entire research community pursues the same direction (tooth regeneration via USAG-1 neutralization) without questioning the fundamental logic.

The pattern: The same researchers publish the preclinical data, found the spin-off (Toregem), obtain orphan drug status and AMED funding, design the Phase I trial, and announce the indication expansion. The independent literature on SOSTDC1 — tumor suppression, NK cells, TFH/TFR, bone, hair follicles, vasculature, fertility — is published by entirely different research groups with no connection to tooth regeneration research. No integrating forum exists to bring both together. This is NOIS at the systemic level: not the variability of individual judgments, but the collective noise of a research landscape operating in siloed specializations.

In NAM-BIAS terms: NOIS and bias converge. Bias narrows SOSTDC1 to the tooth switch. NOIS distributes knowledge of the seven other functional domains across research groups that never communicate. The result is a research program that no one on earth needs: a systemic antibody against a problem solvable by prevention and prosthetics, whose adverse effect cascade can generate more disease than the tooth loss itself, and whose planetary footprint upon scaling exceeds the benefit manifold.

8.6 The NAM Alternative: Prevention Over Regeneration

The NAM-Dentistry Systematic [25] offers the diametrically opposite model: tooth loss is not treated as an endpoint to be reversed by molecular intervention, but as the result of preventable causal chains (Pillar 1: Toxification from dental materials, Pillar 2: Silent Inflammation from periodontitis/PA/PPA, Pillar 3: Dynamic Dysfunction from occlusal trauma). Preventing these causal chains requires no systemic antibody, no lifelong monitoring, and no planetary resource consumption. It requires clinical competence, materials expertise, and a systemic understanding of the Mouth-Brain-Body Connection.

This is not a romantic return to basics, but the logical consequence of a Planetary Health ethic: the best tooth regeneration is the tooth that was never lost.

9. CONCLUSION

This analysis documents (1) eight direct functional domains of USAG-1 neutralization [4–18,24], (2) a U-shaped age-risk profile with maximal risks in children [6,19,21] and the elderly [16,17,22] — the target populations for Phase II and indication expansion, (3) a multi-level Christmas Tree Cascade of secondary and tertiary pathway effects [17,23,24], (4) a planetary cost accounting [28–31] that upon scaling to acquired tooth loss exceeds the benefit manifold, and (5) a convergence of BIAS and NOIS [27] that explains how an entire research direction can miss the systemic logic.

TRG035 is a research program that no one on earth needs. Not because the science is poor — the preclinical work by Takahashi et al. [2] is methodologically sound. Rather, because the question is wrong. The right question is not: How can we replace lost teeth? The right question is: Why do people lose their teeth — and how do we prevent it? [25]

Those who treat the mouth only as a mouth lose sight of the body. Those who regrow teeth without addressing the cause of loss create patients who have new teeth — and new diseases along with them.

REFERENCES

[1] Murashima-Suginami A et al. Anti-USAG-1 therapy. Sci Adv. 2021;7(7):eabf1798.
[2] Takahashi K et al. Antibody drug for congenital tooth agenesis. J Oral Biosci. 2024;66(4):1–9.
[3] Toregem BioPharma. Phase I TRG-035. jRCT2051240154. 2024.
[4] Blish KR et al. BMP antagonist down-regulated in renal cancer. Mol Biol Cell. 2008;19(2):457–464.
[5] Blish KR et al. LOH and SOSTDC1 in renal tumors. J Exp Clin Cancer Res. 2010;29:147.
[6] Ohshima J et al. MEOX2 and SOSTDC1 in Wilms tumor. Genes Chromosomes Cancer. 2009;48(12):1037–1050.
[7] Zhou Q, Chen J, Feng J, Xu Y, Zheng W, Wang J. SOSTDC1 inhibits follicular thyroid cancer cell proliferation, migration, and EMT via suppressing PI3K/Akt and MAPK/Erk signaling pathways. Mol Cell Biochem. 2017;435(1-2):87–95.
[8] Cui Y, Zhang Y, Zhao H et al. The BMP antagonist, SOSTDC1, restrains gastric cancer progression via inactivation of c-Jun signaling. Am J Cancer Res. 2019;9(11):2331–2348.
[9] Clausen KA, Blish KR, Birse CE et al. SOSTDC1 differentially modulates Smad and beta-catenin activation and is down-regulated in breast cancer. Breast Cancer Res Treat. 2011;129(3):737–746.
[10] Millan AJ et al. Sostdc1 regulates NK cell maturation. J Immunol. 2019;202(8):2296–2306.
[11] Wu X et al. SOSTDC1-producing TFH promote TFR differentiation. Science. 2020;369:984–988.
[12] Collette NM et al. Sostdc1 deficiency accelerates fracture healing. Bone. 2016;88:20–30.
[13] He JW, Yue H, Hu WW, Hu YQ, Zhang ZL. Contribution of the sclerostin domain-containing protein 1 (SOSTDC1) gene to normal variation of peak bone mineral density in Chinese women and men. J Bone Miner Metab. 2011;29(5):571–581.
[14] Togo Y et al. Sostdc1 from lymphatic vessels. Curr Issues Mol Biol. 2022;44(5):146.
[15] Närhi K et al. Sostdc1 defines skin appendage placodes. Dev Biol. 2012;364(2):149–161.
[16] Lu L et al. TGF-β1-induced EMT via USAG-1. Mol Med Rep. 2019;19(3):1694–1704.
[17] Meng XM et al. TGF-β/BMP-7/Smad in renal diseases. Clin Sci. 2013;124:243–254.
[18] Pradhan BS, Bhattacharya I, Sarkar R, Majumdar SS. Downregulation of Sostdc1 in testicular Sertoli cells is prerequisite for onset of robust spermatogenesis at puberty. Sci Rep. 2019;9:11458.
[19] Collette NM et al. Sost and Sostdc1 coordinate digit number. Dev Biol. 2013;383(1):90–105.
[20] Simon-Chazottes D et al. Sostdc1 in mammalian eyes. Graefes Arch. 2019.
[21] Syrimi E et al. NK cell immunity in pediatric cancer. iScience. 2024;27(9):110839.
[22] Simon AK et al. Immune system from infancy to old age. Proc Biol Sci. 2015;282:20143085.
[23] Higgins DF et al. BMP-7-induced PTEN inhibits Akt. BBA Mol Basis Dis. 2017;1863:3095–3104.
[24] Xiao S et al. Sostdc1 in skeletal biology and cancer. Front Physiol. 2022;13:1029646.
[25] Fritsch T, Avgerinos S, Jacob U, Muss C. 80 Jahre NAM-Zahnheilkunde [80 Years of NAM Dentistry]. NAM-Journal 2025. doi:10.64447/2025nam0007.

[26] Illich I. Medical Nemesis: The Expropriation of Health. London: Calder & Boyars; 1976.
[27] Kahneman D, Sibony O, Sunstein CR. Noise: A Flaw in Human Judgment. New York: Little, Brown Spark; 2021.
[28] Lancet Planetary Health. Planetary health care: a framework for sustainable health systems. Lancet Planet Health. 2021;5(2):e66–e68.
[29] Budzinski K, Constable D, D'Aquila D et al. Streamlined life cycle assessment of single use technologies in biopharmaceutical manufacture. N Biotechnol. 2022;68:28–36.
[30] Sherman JD et al. The Green Print: Advancement of Environmental Sustainability in Healthcare. Resour Conserv Recycl. 2020;161:104882.
[31] J Ethics AMA. How should we respond to health care generating environmental harm? 2022;24(10):E986–E993.
[32] GBD 2021 Oral Disorders Collaborators. Trends in the global, regional, and national burden of oral conditions from 1990 to 2021. Lancet. 2025;405(10477):e8–e20. WHO Oral Health Data Portal: Complete tooth loss affects 350 million people. who.int/data/gho/data/themes/oral-health-data-portal.
[33] Fritsch T. Neue Zähne, um damit ins Gras zu beißen – TRG035 und die systemischen Kosten der USAG-1-Neutralisierung. Kommentar NAM-Journal März 2026.DOI: 10.64447/2026nam0010

Conflict of Interest: TF is founder/director of the NAM Institute, President of ÖGSZM/SBMC. SA is affiliated with the NAM Institute. Neither author has any connection to Toregem BioPharma.

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