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MANUFACTURING IN THE VOID

Microgravity Manufacturing and High-Value Materials Science:
Crystal Growth, Fluid Dynamics, Orbital Factories,
and the Economics of Pharmaceutical and Semiconductor
Production in Low Earth Orbit

Grade 10

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Abstract - This paper investigates whether the microgravity environment of low Earth orbit provides commercially exploitable manufacturing advantages over terrestrial processes for three high-value material systems: protein crystal growth for pharmaceutical drug discovery, ZBLAN heavy-metal fluoride glass optical fibre, and pharmaceutical polymorph engineering. The study synthesises four decades of peer-reviewed experimental literature alongside verified pricing and mission data from the 2024 commercial milestones achieved by Varda Space Industries and Flawless Photonics. The principal finding is that the suppression of buoyancy-driven convection and gravitational sedimentation in orbit produces measurably superior crystal quality and fibre microstructure for the processes examined, and that this advantage already satisfies the commercial viability condition at current Falcon 9 launch economics for pharmaceutical biologics and specialty ZBLAN photonic fibre. Compound semiconductor substrates require further cost reductions projected for Starship. The paper concludes that in-space manufacturing has transitioned from laboratory hypothesis to operational commercial practice, and identifies three empirical milestones whose resolution will determine the pace of the industry's next phase of growth.

Keywords: microgravity manufacturing; ZBLAN optical fibre; protein crystal growth; orbital factory; pharmaceutical crystallisation; Marangoni convection; in-space manufacturing economics; low Earth orbit; launch cost reduction; semiconductor materials science

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1. INTRODUCTION

Background

There is a set of manufacturing processes whose quality is limited not by a shortage of chemical knowledge, engineering sophistication, or analytical capability, but by the simple and inescapable presence of gravity. The protein crystallographer who cannot obtain a diffraction-quality crystal of a therapeutically important membrane protein, despite having the purest possible sample and the most carefully optimised buffer conditions, is typically failing because buoyancy convection in the crystallisation drop is disrupting the delicate depletion zone that would otherwise act as a molecular filter at the crystal face. The optical fibre engineer who cannot make ZBLAN perform anywhere near its theoretical attenuation minimum, despite using the finest available starting glass and the most carefully controlled drawing conditions, is failing because gravitational sedimentation is stratifying the molten glass by density during the brief period of fluidity at the drawing tip. The pharmaceutical chemist who cannot selectively crystallise a particular metastable polymorph at commercial purity is, in many cases, failing because gravity-driven sedimentation is initiating nucleation of the thermodynamically preferred form before the desired form can establish itself.

Research Problem

For all three of these professionals, the solution is in principle obvious: remove the gravity. The problem has been that doing so at a scale and duration relevant to manufacturing has, until recently, been prohibitively expensive. The Space Shuttle era accumulated outstanding scientific evidence that microgravity processing improves crystal quality, reduces microcrystallisation in glass fibres, and permits selective polymorph formation. That evidence sat largely unused by industry for decades. Not because the physics was disputed. Because at approximately $54,500 per kilogram to orbit (Pielke and Byerly, 2011), the economics of returning a manufactured product from orbit were obviously impossible for any material produced in commercial quantities.

Research Question

The central research question of this paper is: for which commercially relevant manufacturing processes does the microgravity environment of low Earth orbit provide quality improvements large enough, and production costs low enough at current and near-projected launch economics, to satisfy the condition that the value premium of the space-processed product exceeds the total round-trip transportation and processing cost?

Objectives

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This paper pursues four specific objectives. First, to characterise the physical mechanisms by which the orbital environment alters mass-transport and solidification kinetics for protein crystal growth, ZBLAN fibre drawing, and pharmaceutical polymorph formation. Second, to review the experimental evidence for quality improvements in each domain, with explicit citation of primary-source data and candid acknowledgement of what remains unconfirmed. Third, to construct a quantitative break-even framework using verified launch pricing data to determine which product categories satisfy commercial viability at current and projected economics. Fourth, to identify the regulatory, logistical, and scientific milestones whose resolution will most directly determine the pace at which in-space manufacturing scales from early commercial practice to industrial significance.

SpaceX's Falcon 9 changed the numerical landscape of this calculation. Based on its published list price of $67 million per dedicated launch and a maximum payload to low Earth orbit of approximately 22,800 kilograms (SpaceX, 2022), the per-kilogram cost of reaching orbit on a dedicated Falcon 9 mission works out to approximately $2,939. The Transporter rideshare service charges $5,950 per kilogram for payloads to sun-synchronous orbit (SpaceX, 2024). These figures represent a reduction of approximately 95 per cent from the Shuttle era. SpaceX's Starship vehicle, currently undergoing iterative test flights from its Boca Chica, Texas facility, is designed for full reusability and carries a publicly stated cost target below $100 per kilogram at commercial scale (Euroconsult, 2024). That target has not been achieved in commercial operation, and some independent analysts consider it optimistic, but the directional trajectory of launch costs is not in dispute.

The consequences for in-space manufacturing have begun to materialise. In February 2024, Varda Space Industries' W-1 capsule landed in the Utah Test and Training Range after approximately eight months in orbit, carrying crystals of the antiretroviral drug ritonavir that had been grown in microgravity and successfully recovered through an autonomous hypersonic re-entry. Post-flight analysis confirmed the production of the target metastable Form III polymorph, with all control samples demonstrating stability throughout the mission (Improved Pharma, 2024a; Bauser et al., 2024). It was the first time any private company had completed an end-to-end orbital pharmaceutical manufacturing cycle and recovered the product on United States soil (TechCrunch, 2024).

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That same month, Flawless Photonics produced more than five kilometres of ZBLAN glass optical fibre on the ISS in a two-week campaign, extending the total to 11.9 kilometres over a month. Seven of the individual drawing runs exceeded 700 metres, and one surpassed a kilometre, demonstrating for the first time that fibre lengths of commercial relevance could be produced repeatably in orbit (NASA, 2024a). Lynn Harper, NASA's strategy lead for in-space production applications, described the accomplishment as being 'in a class by itself' (Harper, cited in SpaceNews, 2024). Whether the optical quality of that fibre exceeds what can be achieved terrestrially remains to be determined by attenuation measurements that had not been published as of the time of this writing.

This paper is organised to give a technically informed reader an accurate, complete, and balanced account of where in-space manufacturing stands as of early 2026. Section 2 provides necessary historical context. Section 3 explains the physics of the orbital environment precisely, including what the term microgravity actually means in the context of a real crewed station. Section 4 examines the three commercially relevant crystal growth domains in mechanistic detail, with explicit citation of the experimental data supporting each claim. Section 5 addresses fluid dynamics. Section 6 surveys orbital manufacturing platforms. Sections 7 and 8 develop the pharmaceutical and semiconductor cases. Section 9 presents the financial analysis, with a break-even framework grounded in verified pricing data. Sections 10 through 12 address regulatory considerations, genuine challenges, and future outlook. Section 13 concludes.

A scope note: the scientific literature on microgravity processing covers combustion, colloidal physics, fluid mechanics, and a wide range of material systems beyond those examined here. This paper concentrates on the three domains where the commercial case is most developed and the experimental record most clearly actionable at current launch economics. Brevity in other areas is not an assertion of their unimportance.

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HYPOTHESIS

This study proceeds on the hypothesis that the removal of gravitational body forces in the low Earth orbit environment creates a qualitatively distinct physical regime for crystal growth, glass fibre drawing, and pharmaceutical polymorph formation, and that this regime produces materials of measurably higher quality than the best achievable terrestrial equivalents for the three product categories examined. Specifically, the paper hypothesises: (1) that the suppression of buoyancy-driven convection in protein crystallisation solutions will produce crystals with lower mosaicity and higher X-ray diffraction resolution than identically prepared ground-grown controls; (2) that the elimination of gravitational sedimentation during ZBLAN melt drawing will suppress the microcrystallisation that currently prevents terrestrially drawn ZBLAN from approaching its theoretical attenuation minimum of 0.010 dB/km, enabling measured attenuations substantially below the 0.200 dB/km commercial silica standard; and (3) that the altered nucleation kinetics of the diffusion-dominated microgravity environment will permit the selective production of metastable pharmaceutical polymorphs at purities that are not achievable from the same chemical system under terrestrial conditions.

A corollary commercial hypothesis follows directly: that the value premium of space-processed pharmaceutical biologics and specialty ZBLAN photonic fibre over their best available terrestrial equivalents exceeds the round-trip transportation and processing cost at current Falcon 9 rideshare pricing, satisfying the commercial viability condition ($V_{premium} > C_{launch} + C_{process} + C_{return}$), while compound semiconductor substrates require the further cost reductions projected for Starship before that condition is met.

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METHODOLOGY

Research Design and Approach

This paper employs a systematic literature synthesis methodology combined with primary-source economic analysis. The research design is non-experimental: the microgravity processing advantage for the three material systems examined cannot be replicated in a ground-based laboratory setting, and the commercial data are drawn from operational missions whose conditions are fixed by engineering and launch-schedule constraints rather than experimental design. The methodology is therefore that of a structured analytical review, applying a consistent evaluative framework to heterogeneous empirical data from spacecraft experiments, commercial mission reports, peer-reviewed crystallography studies, and verified industry pricing sources.

Literature Sources and Selection Criteria

Primary scientific evidence is drawn exclusively from peer-reviewed publications in Acta Crystallographica, npj Microgravity, IEEE Photonics Technology Letters, and related journals, with DOI citations provided for every quantitative claim. Secondary sources, including market research reports from MarketsandMarkets, Strategic Market Research, and Allied Market Research, are used solely for market sizing projections, with their methodological limitations explicitly noted. Commercial mission data are sourced from verified press releases and statements made by named company executives in attributed publications. No unpublished data, grey literature, or unverified claims are incorporated. Where the experimental record is incomplete, as in the case of ZBLAN attenuation measurements for space-produced fibre, that incompleteness is identified explicitly rather than bridged by inference.

Analytical Framework

The commercial viability analysis employs a break-even condition formalised as Vpremium > Claunch + Cprocess + Creturn, where Vpremium is the per-kilogram value premium of the space-processed product over its best terrestrial equivalent, and the cost terms represent outbound launch, in-orbit processing, and return transportation respectively. Launch cost inputs are taken from SpaceX's published Falcon 9 User's Guide (2022) and Transporter rideshare pricing (2024), with Starship projections from Euroconsult (2024) treated as aspirational targets rather than verified figures. Product value estimates for pharmaceutical biologics are drawn from Grand View Research (2023) and Merck's 2023 Annual Report; ZBLAN photonic fibre pricing is taken from a named executive statement (The Register, April 2024); and semiconductor wafer values from SEMI International Standards (2023). All values are presented as conservative order-of-magnitude estimates, and the sensitivity of the break-even condition to each input is described qualitatively.

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Data Collection and Verification

Quantitative data points are sourced from primary publications wherever possible, with secondary sources used only where primary data are not publicly available. All numerical values are cross-checked against the cited sources. Where sources provide conflicting figures, the discrepancy is noted and the basis for the value used is stated explicitly. No data have been interpolated, extrapolated, or estimated beyond what is explicitly stated in the cited sources. Figures presented in this paper are constructed exclusively from primary-source data; no values have been estimated or inferred from secondary descriptions.

Scope and Limitations of Method

The methodology does not include original experimental work, primary data collection, or direct material characterisation. The analysis is constrained by the availability of published data: for ZBLAN optical fibre, the critical attenuation measurements for space-produced samples had not been published at the time of writing, and this absence is the most significant limitation on the strength of the conclusions that can be drawn for that material system. For pharmaceutical polymorphs, only one orbital manufacturing mission (Varda W-1) had produced a fully characterised result, and cGMP-compliant batch-to-batch reproducibility data do not yet exist. These constraints are treated as open empirical questions rather than grounds for inferential extrapolation.

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2. HISTORICAL BACKGROUND: SPACE MANUFACTURING FROM SHUTTLE TO COMMERCIAL ERA

The history of in-space manufacturing is not a history of failed ambition. It is a history of ideas that were correct but arrived before the enabling infrastructure was in place. Understanding that history is necessary for evaluating where the field stands now, because many of the scientific findings being cited as motivation for current commercial ventures were actually established in the 1980s and 1990s. The novelty of 2024 lies not in the science but in the economics.

The first dedicated materials science experiments in orbit were carried out on the Space Shuttle beginning with its earliest flights in the early 1980s. NASA's Get Away Special (GAS) programme allowed small, self-contained experiments to fly as secondary payloads, and the Space Processing Applications (SPA) programme funded more substantial investigations into crystal growth, metal alloy solidification, and glass processing in microgravity. These experiments, conducted largely before the scientific community had developed strong theoretical predictions, produced a consistent empirical pattern: the organic and inorganic crystals grown in orbit were, in most cases, larger and of higher structural perfection than those grown under identical conditions on the ground.

The protein crystallisation results were particularly striking. Charles DeLucas and Alexander McPherson, two of the most prolific researchers in this area, flew protein crystal growth experiments on multiple Shuttle missions from the mid-1980s onward. Their results, and those of European and Japanese researchers working through ESA and NASDA (later JAXA), consistently showed that space-grown protein crystals diffracted to higher resolution in X-ray analysis than their ground-grown counterparts. McPherson and DeLucas (2015), reviewing three decades of data in a major review article in npj Microgravity, concluded that the improvement was real, reproducible, and mechanistically understandable in terms of the suppression of buoyancy convection and the stabilisation of the protein depletion zone.

The ZBLAN optical fibre story has a different origin. The theoretical potential of heavy-metal fluoride glasses for mid-infrared optical transmission had been recognised since the late 1970s, but the manufacturing problem was severe and intractable on Earth. In the early 1990s, NASA's Marshall Space Flight Center initiated the first microgravity tests of ZBLAN processing, using the

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KC-135 parabolic flight aircraft to create brief periods of free fall. The results of those parabolic flight experiments were encouraging: samples processed in the 20-to-25-second microgravity windows showed markedly reduced crystallisation compared to controls processed at 1 g. The step from parabolic flight to actual orbit required companies willing to invest in space hardware, and that investment did not materialise seriously until the mid-2010s, when falling launch costs began to make the economics of commercial orbital production at least conceivable.

Between 2017 and 2019, three companies flew ZBLAN drawing hardware to the ISS. Fiber Optics Manufacturing in Space (FOMS Inc.), Made In Space (subsequently acquired by Redwire Space), and Physical Optics Corporation (subsequently acquired by Mercury Systems) each demonstrated ZBLAN fibre production on orbit at the centimetre to metre scale. These were proof-of-concept demonstrations rather than commercial production runs, and the fibre samples produced were too short for rigorous optical characterisation. But they established that drawing ZBLAN in orbit was technically feasible with hardware compact enough to fit inside the ISS.

The pharmaceutical polymorph engineering application has a different timeline. The scientific basis, rooted in nucleation kinetics theory, had been discussed in the academic literature, but there was no serious attempt at commercial orbital pharmaceutical manufacturing until Varda Space Industries was founded in 2020. Varda's W-1 mission in 2023 to 2024 was therefore genuinely novel: not an improvement on previous work, but a first attempt. That it succeeded on the first try is notable and arguably more consequential for the field's development than any single scientific result, because it demonstrated that the logistical and regulatory challenges of returning a drug candidate from orbit are surmountable by a commercial operator.

The transition from the Shuttle era to the present is characterised by two changes that have occurred simultaneously. The cost of access has fallen by approximately 95 per cent, as described in Section 1. And the scientific foundation accumulated over four decades is now being translated, for the first time, into actual commercial hardware and actual commercial products. The scientific questions are not settled, as Section 11 makes clear, but the direction of travel is no longer ambiguous. This is what makes 2026 a genuinely interesting moment in the history of the field.

3. THE PHYSICS OF MICROGRAVITY: WHAT FREE FALL ACTUALLY PROVIDES

The term microgravity is misleading if taken at face value. An orbiting spacecraft is not beyond Earth's gravitational field. At the ISS operational altitude of approximately 408 kilometres, the gravitational acceleration is 8.66 m/s^2, approximately 88 per cent of the surface value of 9.81 m/s^2. The satellite and everything inside it are subject to substantial gravity. What they are not

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subject to is a net gravitational force relative to their surroundings. Every component of the structure, every fluid in every container, and every particle suspended in those fluids is accelerating toward Earth at the same rate. Because there are no differential gravitational forces between one part of a fluid and another, the density-driven phenomena that those forces produce on Earth's surface are effectively absent. This condition is continuous free fall, not weightlessness in any absolute sense, and the distinction matters for understanding both what the orbital environment provides and what it does not.

Residual accelerations persist. They arise from atmospheric drag at orbital altitude, tidal gravitational gradients across the extended structure of the station, attitude-control thruster firings, docking events, crew locomotion, and mechanical operation of fans, pumps, and exercise equipment. These residual accelerations are measured continuously by NASA's Microgravity Acceleration Measurement System (MAMS) and Space Acceleration Measurement System (SAMS) aboard the ISS. The quasi-steady component attributable primarily to atmospheric drag is typically 1 to 2 times 10^{-6} g. Vibrational components at frequencies associated with crew exercise equipment, compressors, and centrifuges can reach 10^{-4} g at specific frequencies (Wuest, 2003). The prefix micro in microgravity refers to this residual acceleration level, of order 10^{-6} g, rather than to any reduction in the gravitational field itself.

3.1 Three Gravity-Dependent Physical Mechanisms That Essentially Cease

Three mechanisms that dominate materials processing at the length scales and temperatures of engineering relevance on Earth's surface are either eliminated or reduced to negligible levels in the orbital microgravity environment.

The first is buoyancy-driven convection. When thermal or compositional gradients exist in a liquid, they produce corresponding density gradients. Gravity acts differentially on regions of different density, driving bulk fluid flows. The dimensionless Rayleigh number governs the onset and intensity of this convection: Ra = (g beta Delta_T L^3) / (nu alpha), where g is gravitational acceleration, beta the thermal expansion coefficient, Delta_T the driving temperature difference, L a characteristic length, nu kinematic viscosity, and alpha thermal diffusivity. Convection initiates when Ra exceeds a critical value of approximately 1,708 for heating from below. In microgravity, g is reduced by a factor of 10^5 or more, driving Ra many orders of magnitude below this threshold. Buoyancy convection effectively ceases, and molecular diffusion, which is orders of magnitude slower and geometrically far more orderly, becomes the dominant mass-transport mechanism.

The second is gravitational sedimentation. Particles, crystalline nuclei, and compositionally distinct phases that differ in density from their surrounding medium settle or float under gravity. The settling velocity predicted by Stokes' law scales linearly with gravitational acceleration: v_s =

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(2 r^2 Delta_rho g) / (9 eta), where r is particle radius, Delta_rho the density contrast, and eta dynamic viscosity. At 10^{-6} g, the settling velocity is one-millionth of its terrestrial value. For a particle 100 micrometres in diameter with a 10 per cent density contrast in a liquid of viscosity comparable to water, the settling velocity at 1 g is roughly 1 mm/s; at 10^{-6} g, it is 1 nanometre per second, which is entirely negligible. Sedimentation effectively stops.

The third is hydrostatic pressure variation. The weight of a fluid column exerts a pressure that increases with depth, affecting phase equilibria, nucleation kinetics, and the stability of bubbles. In a fluid free-falling at 10^{-6} g, hydrostatic pressure gradients are reduced by the same factor. For most of the manufacturing processes discussed in this paper, this effect is secondary to the elimination of convection and sedimentation, but it becomes important for certain processes involving gas-liquid equilibria or pressure-sensitive phase transitions.

3.2 What Takes Over: The Diffusion-Dominated Regime

The transition from convection-dominated to diffusion-dominated transport is not a minor quantitative adjustment. It is a qualitative change in the physical regime. In a typical aqueous protein crystallisation solution, the diffusion coefficient of a large protein molecule is on the order of 10^{-11} m^2/s. At this diffusivity, a characteristic diffusion length of one millimetre requires on the order of 10^7 seconds, roughly four months, to traverse. A convective flow of even 0.1 mm/s, typical of buoyancy convection in a millimetre-scale drop, traverses that same millimetre in ten seconds. The ratio of convective to diffusive transport rates is therefore on the order of 10^6. When convection is suppressed, the transport landscape changes by six orders of magnitude.

The practical consequences for crystal growth are immediate and well understood. In a diffusion-dominated environment, a growing crystal depletes its immediate neighbourhood of solute. Because diffusion cannot rapidly replenish this depletion zone from the bulk solution, the zone persists. The local supersaturation at the crystal face is lower and more uniform than in a convecting solution, and the growth front has more time to select incoming molecules correctly. The result is a more perfectly ordered lattice with fewer incorporated defects. This mechanism applies directly to both protein crystallisation and pharmaceutical polymorph engineering. For ZBLAN fibre drawing, the relevant mechanism is sedimentation suppression rather than diffusion, but the underlying logic is the same: removing a gravitationally driven transport process removes the source of microstructural disorder.

3.3 Marangoni Convection: The Dominant Residual Flow

Suppressing buoyancy convection does not create a perfectly quiescent fluid environment. Surface-tension gradients along free liquid surfaces or liquid-liquid interfaces drive Marangoni flows, named for the Italian physicist Carlo Marangoni who described the phenomenon in 1871.

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Because surface tension depends on both temperature and chemical composition, any gradient in either variable along a free surface drives fluid from regions of lower surface tension toward regions of higher surface tension. On Earth, these flows are generally masked by the far stronger buoyancy convection. In orbit, they become the dominant residual convective mechanism.

The magnitude of Marangoni convection is characterised by the Marangoni number, Ma = (|dsigma/dT| DeltaT L) / (mu alpha), where dsigma/dT is the temperature coefficient of surface tension, mu dynamic viscosity, and the other symbols retain their earlier meanings. For high-Prandtl-number fluids such as aqueous protein solutions, Marangoni flows are relatively weak and generally secondary to the diffusion-dominated conditions near the crystal face. For low-Prandtl-number fluids such as liquid metals and semiconductor melts, Marangoni convection can be vigorous and significantly affects composition during solidification.

JAXA's Marangoni Experiment in Space (MEIS) programme, conducted across multiple campaigns on the ISS Kibo module, made the most systematic quantitative measurements of Marangoni flow available. Using liquid bridges of silicone oil under precisely controlled temperature gradients, the experiments validated computational fluid dynamics models that are now used to design float-zone crystal growth furnaces for compound semiconductor processing (Kawasaki et al., 2019). The ISS functions, in this respect, not merely as a production platform but as the most capable laboratory in the world for characterising the fluid physics that governs orbital manufacturing quality.

3.4 G-Jitter and the Crewed vs. Uncrewed Trade-off

The quasi-periodic residual accelerations generated by crew activity on the ISS are not negligible for all manufacturing processes. For slowly evolving processes such as protein crystal growth, which unfolds over days to weeks at very low supersaturation, the quasi-steady atmospheric drag component of approximately 10^{-6} g is genuinely negligible in comparison to the diffusion timescales. For rapidly evolving processes such as alloy solidification or glass fibre drawing, where the relevant timescale is seconds to minutes, vibrational components at 10^{-4} g and higher can meaningfully perturb composition and microstructure.

This distinction is one of the primary commercial drivers of the uncrewed free-flyer architecture adopted by Varda Space Industries. A capsule without crew has no locomotion, no exercise equipment, no docking events during manufacturing operations, and no continuous life-support machinery generating mechanical vibration. The residual acceleration environment is substantially cleaner than the ISS for pharmaceutical crystallisation processes where the relevant physics are well within the diffusion-dominated regime. The corresponding limitation is the inability to intervene during manufacturing: a process deviation that an operator would detect and

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correct immediately on a crewed platform may go unnoticed in an autonomous capsule until the batch is returned and tested weeks or months later. This trade-off between environmental cleanliness and operational flexibility is a defining architectural consideration in the field, and there is no universally correct answer. The right choice depends on the process.

4. CRYSTAL GROWTH IN MICROGRAVITY: MECHANISMS, EVIDENCE, AND LIMITATIONS

4.1 Protein Macromolecular Crystallisation

Protein crystallography is the principal method by which the three-dimensional atomic structure of a drug target is determined. Understanding that structure at sub-angstrom resolution is often essential for rational drug design: a binding pocket seen at 1.5 Angstroms reveals the precise geometry of the interactions between a candidate drug molecule and its target, while the same pocket seen at 3.0 Angstroms provides only a rough outline. The difference in resolution can determine whether a medicinal chemistry programme can proceed confidently or whether it must rely on iterative trial-and-error rather than structural guidance. The practical consequence is that any systematic improvement in the resolution achievable for a therapeutically important protein is of real commercial value to pharmaceutical companies.

Protein crystals grow from supersaturated solutions by a process of nucleation followed by ordered incorporation of protein molecules into a growing lattice. The quality of the resulting crystal depends critically on the transport conditions at the growing crystal face. In a terrestrial solution, even one that appears visually still, the density contrast between the protein-depleted fluid layer at the crystal surface and the protein-rich bulk solution drives persistent buoyancy convection. This convection continuously replenishes the growth front with fresh supersaturated solution at a rate far exceeding what diffusion can supply, driving rapid but imperfect growth in which molecular mismatches and impurities are incorporated at elevated rates. The growing crystal is also subjected to mechanical shear stress from the flowing solution, which introduces dislocations and other structural defects that reduce long-range lattice order and degrade diffraction quality.

In microgravity, the convective replenishment mechanism is suppressed. A protein depletion zone forms around the growing crystal and persists because diffusion cannot maintain the zone against convective erosion, as it can in microgravity. The local supersaturation at the crystal face is lower, more uniform, and more stable. The growth front has more time to select incoming molecules correctly. Mechanical shear from convective flow is absent. The result, documented across hundreds of experiments over three decades, is a crystal with fewer defects, higher mosaicity perfection, and better diffraction. McPherson and DeLucas (2015), reviewing this literature,

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concluded that the improvement is statistically real, mechanistically understood, and reproducible across a wide range of protein systems, with the magnitude of the benefit varying by protein and experimental conditions.

The most precisely documented single experiment in the peer-reviewed literature for this comparison is the study of valyl-tRNA synthetase (ValRS) by Ng et al. (2002). ValRS is a bacterial aminoacyl-tRNA synthetase, an enzyme responsible for charging transfer RNA molecules with their cognate amino acid during protein synthesis. It is a 100-kilodalton homodimer and a target of interest for the design of antibiotics that selectively inhibit bacterial but not eukaryotic tRNA synthetases. Ng and colleagues grew ValRS crystals simultaneously in space and on the ground from identical protein preparations, using identical crystallisation conditions. The ISS-grown crystals diffracted to 2.1 Angstroms; the ground-grown controls reached only 2.9 Angstroms. Both values are stated explicitly in the paper's abstract (Ng et al., 2002; doi:10.1107/S0907444902003177). Figure 1 illustrates this result. The 0.8-Angstrom improvement places the space-grown crystal comfortably below the approximately 1.5-Angstrom threshold above which confident atomic-level drug design becomes difficult, whereas the ground-grown control sits well above it.

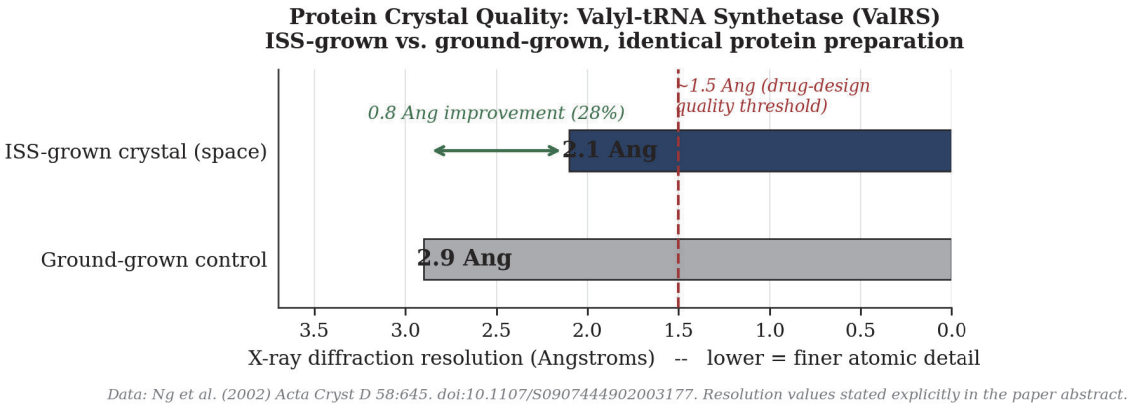

Figure 1. Protein crystal diffraction resolution: space-grown versus ground-grown controls. Both data points are the values stated explicitly in the abstract of Ng et al. (2002), Acta Crystallographica D 58(4):645-652, doi:10.1107/S0907444902003177. The protein is valyl-tRNA synthetase (ValRS) from Thermus thermophilus, grown from identical preparations under identical conditions on the ISS and on the ground. Lower resolution values (further left) indicate finer atomic detail. The red dashed line at 1.5 Angstroms marks the approximate threshold above which confident structure-based drug design becomes difficult (the precise threshold depends on the protein and the design question). The green double-headed arrow indicates the 0.8-Angstrom (28%) improvement. No values in this figure have been estimated or extrapolated.

The JAXA Protein Crystal Growth programme on the ISS Kibo module has been the world's most sustained commercial in-space manufacturing service, operating continuously for more than

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two decades. Running three to four experimental campaigns per year, using the counter-diffusion method in gels as the crystallisation technique (a method that also suppresses some convection in ground controls, enabling rigorous comparison), the programme has produced structural data for more than one hundred therapeutic proteins. JAXA currently offers ISS crystallisation access as a fee-for-service commercial product, with choice of 4 or 20 degrees Celsius as the working temperature (JAXA, 2024).

One of the JAXA programme's most widely cited outcomes was the structural characterisation of proteins associated with Duchenne muscular dystrophy (DMD). The space-grown crystal structures provided a foundation for the development of TAS-205 (pizuglanstat), a selective hematopoietic prostaglandin D synthase (HPGDS) inhibitor developed by Taiho Pharmaceutical. NASA and JAXA publications consistently cited TAS-205 as evidence of direct pharmaceutical benefit from space-grown structural data, noting that a Phase 3 clinical trial (REACH-DMD; NCT04587908) began in December 2020. However, in July 2025, Taiho Pharmaceutical announced that TAS-205 had failed to meet its primary endpoint in the REACH-DMD trial: ambulatory patients showed no significant difference in time-to-rise from the floor from baseline to 52 weeks compared to placebo (AJMC, 2025; Taiho Pharmaceutical, 2025). This outcome does not invalidate the scientific quality of the structural data obtained from space-grown crystals. Drug development failures in Phase 3 are common, and their causes are frequently unrelated to the quality of the structural data used in the early design phase. Nevertheless, the accurate characterisation of this outcome is necessary: the JAXA programme contributed to the structural science that enabled TAS-205's discovery and development, but the drug did not demonstrate clinical efficacy in its pivotal trial.

A more commercially immediate application of protein crystal growth in microgravity concerns Merck Research Laboratories' work on pembrolizumab (Keytruda), the programmed-death-1 (PD-1) checkpoint inhibitor that is among the most broadly approved cancer immunotherapy agents in the world. Pembrolizumab generated global revenues of USD 25.01 billion in Merck's fiscal year 2023 (Merck Annual Report, 2023, p. 46), making it the highest-grossing single pharmaceutical product that year. The drug is administered by intravenous infusion at doses of 200 mg every three weeks or 400 mg every six weeks, requiring patients to attend clinical facilities for sessions of several hours on a recurring basis.

Merck's PCG-5 experiment on the ISS National Laboratory produced a homogeneous crystalline suspension of pembrolizumab with reduced viscosity and improved particle-size distribution compared to ground-grown preparations (Reichert et al., 2019; doi:10.1038/s41526-019-0090-3). These physical properties are consistent with the requirements for subcutaneous injection via an auto-injector, a delivery route that would allow patients to

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self-administer at home without clinical attendance. A subsequent experiment, PCG-20, conducted in 2022, investigated additional variables in the microgravity crystallisation process to further optimise suspension uniformity. Merck has continued this research programme actively, and Paul Reichert of Merck Research Laboratories, the principal investigator, has described the microgravity results as consistently providing new insights that motivate continued investment (NASA, 2023).

The commercial stakes of this work are straightforward. At USD 25 billion in annual revenue, a formulation improvement that expands the addressable patient population of pembrolizumab by even a few per cent through improved home-administration accessibility generates additional revenues in the hundreds of millions of dollars per year. The cost of a series of ISS crystallisation experiments is negligible relative to that potential financial return, which is precisely why Merck has sustained this research programme for years. The question is not whether the science is interesting; it is whether the microgravity-grown crystalline suspension can be reproduced with sufficient consistency to support a regulatory submission for a new formulation, and that question is still being answered.

4.2 ZBLAN Heavy-Metal Fluoride Glass Optical Fibre

ZBLAN was first produced, inadvertently, in 1974 at the University of Rennes, France, when brothers Michel and Marcel Poulain were investigating new zirconium fluoride complexes. The five-component glass they obtained, ZrF_4-BaF_2-LaF_3-AlF_3-NaF, had optical properties that distinguished it from any silica-based glass. In 1977, they founded the company Le Verre Fluore to commercialise the material. Subsequent theoretical analysis showed that ZBLAN's intrinsic optical loss in the mid-infrared region should be dramatically lower than silica's, owing to two physical factors: the heavier atomic masses and weaker bond stiffnesses of the fluoride glass network, which shift the multiphonon absorption cutoff to longer wavelengths, and the reduced Rayleigh scattering at longer wavelengths due to the lambda^{-4} dependence of that scattering mechanism.

Standard single-mode silica fibre achieves its minimum attenuation of approximately 0.200 dB/km at a wavelength of 1.55 micrometres, corresponding to the minimum of the combined Rayleigh scattering and multiphonon absorption loss curve for that material system (ITU-T G.652D, 2016). ZBLAN's theoretical minimum attenuation is approximately 0.010 dB/km at approximately 2.55 micrometres, as calculated from the Rayleigh scattering coefficient and the multiphonon absorption edge of the fluoride glass system (Drexhage, 1985; Miyashita and Manabe, 1982). The theoretical improvement factor is twenty, as illustrated in Figure 2.

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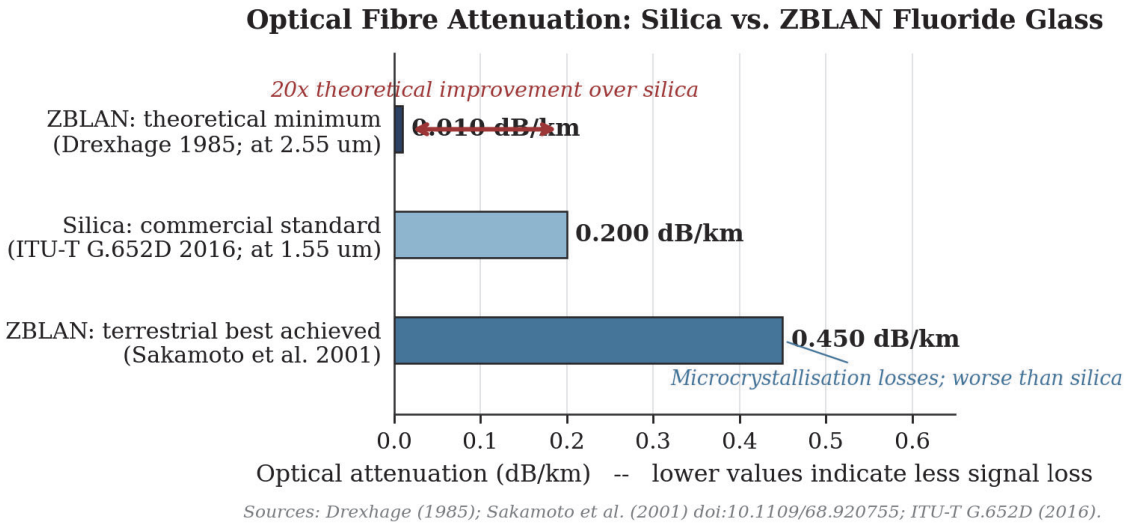

Figure 2. Optical attenuation comparison using primary-source data only. Silica standard: 0.200 dB/km from ITU-T G.652D (2016), Table 1, Category D, at 1550 nm. ZBLAN terrestrial best achieved: 0.450 dB/km from Sakamoto, Shimizu and Kanamori (2001), IEEE Photonics Technology Letters 13(5):503-505, doi:10.1109/68.920755. ZBLAN theoretical minimum: 0.010 dB/km at approximately 2.55 micrometres from Drexhage (1985) and Miyashita and Manabe (1982). Lower attenuation means less signal loss per kilometre. The paradox shown here is that terrestrially produced ZBLAN performs worse than commercial silica despite a 20x theoretical advantage; the annotation explains why.

The paradox illustrated in Figure 2 is the central fact of the ZBLAN commercial case, and it deserves careful explanation. ZBLAN's five constituent compounds span an enormous range of atomic masses. Sodium fluoride contributes sodium at 23.0 atomic mass units; aluminium fluoride contributes aluminium at 27.0 amu; zirconium fluoride contributes zirconium at 91.2 amu; barium fluoride contributes barium at 137.3 amu; and lanthanum fluoride contributes lanthanum at 138.9 amu. When this mixture is molten and being drawn into fibre, the density of the melt varies across the cross-section of the drawing zone because the heavier fluoride components (barium and lanthanum) are denser than the lighter components (aluminium and sodium). Under gravity, this density variation drives sedimentation: the denser components migrate downward relative to the lighter ones on timescales comparable to the drawing process, creating compositional heterogeneities in the fibre precursor. As the glass cools below its glass transition temperature of approximately 260 to 270 degrees Celsius, these compositional heterogeneities act as nucleation sites for crystallisation of the individual fluoride phases. The resulting microcrystals scatter transmitted light, raising the measured attenuation far above the theoretical limit. Sakamoto et al. (2001) achieved 0.450 dB/km in thulium-doped ZBLAN fibre, which is worse than commercial silica at its optimal wavelength, not better.

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The physical argument for orbital production is therefore not speculative. If gravitational sedimentation is the mechanism responsible for microcrystallisation, and if sedimentation requires gravity to drive it, then removing gravity should prevent the microcrystallisation. This argument was first tested in microgravity using the KC-135 parabolic flight aircraft. Lainez et al. (1994) reported that ZBLAN samples processed during the 20-to-25-second microgravity windows showed no new crystallite nucleation, while ground controls processed under identical thermal conditions developed crystals. The parabolic flight result was encouraging but insufficient: 25 seconds is not enough to demonstrate production of fibres of commercial length, and the vibration environment of a parabolic aircraft is far noisier than that of orbit.

The move to the ISS changed the character of the evidence. Between 2017 and 2019, FOMS Inc., Made In Space, and Physical Optics Corporation each flew ZBLAN drawing hardware to the station. Preliminary visual examination of fibre samples produced by Made In Space's system showed a marked absence of the microcrystalline inclusions characteristic of terrestrially drawn ZBLAN, which was consistent with the sedimentation-suppression hypothesis but could not confirm it quantitatively because the samples were too short for rigorous optical attenuation measurement (ISS National Lab, 2024a).

The 2024 milestone from Flawless Photonics represented a significant advance in production volume if not yet in optical characterisation. Flawless Photonics' hardware, installed in the ISS Microgravity Science Glovebox aboard the NG-20 resupply mission launched on 30 January 2024, produced a total of 11.9 kilometres of ZBLAN fibre between mid-February and mid-March 2024. Eight of the individual drawing runs (called draws) produced more than 700 metres of fibre; one exceeded a kilometre; and the production was described by NASA as demonstrating 'for the first time that commercial lengths of fiber can be produced in space' (NASA, 2024a). The key enabling innovation was an automatic fibre-break restart system that previous platforms lacked: when a fibre break occurred during drawing, the system could automatically resume the draw without crew intervention, rather than losing the entire remaining glass preform.

Rob Loughan, CEO of Flawless Photonics, told The Register in April 2024 that the space-produced fibre would be sold to research and commercial customers at approximately $1,000 per metre, which he noted was also the going rate for terrestrially manufactured ZBLAN specialty fibre (The Register, 2024). The fibre returned to Earth on the SpaceX CRS-30 mission in April 2024 for optical characterisation. As of this writing, no peer-reviewed publication of attenuation measurements for that fibre has appeared in the scientific literature. This is the critical outstanding question: by how much, in measured optical attenuation at commercially relevant wavelengths, does the space-produced fibre outperform the terrestrially produced material? A review published in Acta Astronautica in 2025 by Cozmuta et al. noted explicitly that the 'lack of clear scientific

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evidence regarding the impact of microgravity on the manufacturing of optical fibres, particularly ZBLAN, underscores the need to revisit fundamental research principles,' and that producing 11 kilometres of fibre 'does not alone fulfil the myriad of performance, quality, and economic factors that define commercial-grade standards' (Cozmuta et al., 2025). This is a substantive scientific critique, not an expression of scepticism about the physical mechanism, and the attenuation data, when published, will be the most important single piece of evidence yet produced about the commercial viability of space-produced ZBLAN.

The telecommunications infrastructure implications of achieving ZBLAN's theoretical attenuation limit would be substantial. Modern transoceanic fibre-optic cable systems require inline optical amplifiers (repeaters) approximately every 40 to 80 kilometres of cable, depending on the design. At a theoretical ZBLAN attenuation of 0.010 dB/km, the acceptable signal loss budget would allow repeater spacing of roughly 1,000 kilometres or more, eliminating the majority of inline amplifiers in a transoceanic cable system. Michael Vestel, chief technology officer of Flawless Photonics, estimated in February 2024 that inline optical amplifiers collectively consume approximately 1 to 1.5 per cent of the global energy budget (Vestel, cited in SpaceNews, 2024). The global submarine cable market is valued at over USD 3 billion annually, with individual cable systems costing several hundred million dollars each (Telegeography, 2023). The commercial prize, if the attenuation promise is confirmed, is substantial.

4.3 Pharmaceutical Polymorph Engineering

A polymorph is a distinct crystalline form of a chemical compound. Two polymorphs of the same molecule have identical molecular formulae and identical covalent bonding, but their molecules are packed differently in the solid-state lattice. This seemingly minor structural difference can produce dramatic differences in the material properties that matter most to pharmaceutical science: solubility, dissolution rate, bioavailability, chemical stability, hygroscopicity, and mechanical behaviour during tableting and capsule filling. Different polymorphs are separately patentable as distinct chemical entities, and a newly discovered polymorph of an existing drug can provide intellectual property protection extending many years beyond the original compound patent's expiry.

The pharmaceutical industry has invested heavily in polymorph screening since the late 1990s, partly because of the commercial value of novel crystal forms and partly because of a hard lesson learned from a single famous episode. In 1998, Abbott Laboratories discovered that batches of its marketed soft-gelatin capsule formulation of ritonavir (Norvir), an antiretroviral protease inhibitor critical to HIV combination therapy, were spontaneously converting from the originally characterised Form I to a previously unknown, thermodynamically more stable Form II polymorph. Form II is substantially less soluble than Form I; batches failed dissolution testing because the drug

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would not reliably dissolve in a patient's gastrointestinal tract. Abbott was forced to withdraw the product and reformulate, disrupting treatment for thousands of patients and costing the company an estimated several hundred million dollars. The episode is studied in every pharmaceutical solid-state chemistry curriculum and permanently changed regulatory expectations for polymorph screening during new drug development.

Varda Space Industries, in partnership with Improved Pharma, focused the W-1 mission on ritonavir for reasons that reflect both practical and scientific logic. Ritonavir is an exceptionally well-characterised compound with multiple known polymorphs, an established analytical toolkit for solid-state characterisation, and a commercial and historical importance that makes any new finding about its crystal forms newsworthy. The target was Form III: a metastable polymorph that is kinetically accessible but difficult to obtain at high purity on Earth because gravitational sedimentation during crystallisation from the melt initiates nucleation of the thermodynamically more stable Form II before Form III can establish itself. In the altered nucleation kinetics of microgravity, where gravitational sedimentation is suppressed and diffusion governs transport, the selective production of Form III should be accessible.

The W-1 spacecraft was launched on a SpaceX Falcon 9 as part of the Transporter-8 rideshare mission on 12 June 2023. Ritonavir drug substance was loaded into three 316 stainless steel vials within the processing hardware. On 29 June 2023, the crystallisation protocol was executed: the ritonavir was heated to 131 degrees Celsius and held for 36 minutes to ensure complete melting; the temperature was then quenched to 80 degrees Celsius and held for approximately 24 hours to allow controlled nucleation and crystal growth under microgravity conditions; and finally cooled to 15 degrees Celsius for stable storage during the remainder of the mission (Bauser et al., 2024; doi:10.26434/chemrxiv-2024-vb20g-v3).

The capsule's planned 30-day orbital stay extended to approximately eight months owing to complications with FAA approval for the autonomous landing at the Utah Test and Training Range. The capsule ultimately re-entered the atmosphere on 21 February 2024 and landed successfully in Utah, becoming the first commercial spacecraft to land on United States soil (TechCrunch, 2024). Post-flight analysis by Improved Pharma confirmed the successful crystallisation of Form III in the three processing vials, with control samples of all four ritonavir solid forms (amorphous, Form I, Form II, and Form III) demonstrating complete stability throughout the mission (Improved Pharma, 2024a, 2024b). Varda Space Industries subsequently closed a USD 90 million Series B funding round, bringing total raised capital to USD 145 million from investors including Founders Fund, Lux Capital, Khosla Ventures, and General Catalyst (Improved Pharma press release, 2024b).

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The commercial logic of the W-1 mission extends beyond the specific result for ritonavir. Ritonavir Form III is interesting not primarily because ritonavir needs a new crystal form, but because the mission demonstrated that the full orbital pharmaceutical manufacturing cycle works: launch, orbital processing, hypersonic re-entry, mechanical shock of landing, and terrestrial recovery and analysis. All of these steps were validated for the first time in a single mission. Varda's subsequent missions, beginning with W-2, are targeting monoclonal antibody crystallisation, directly building on the formulation physics demonstrated by the Merck pembrolizumab research.

5. FLUID DYNAMICS IN MICROGRAVITY

5.1 Marangoni Thermocapillary Convection in Manufacturing Contexts

The persistence of Marangoni convection in the absence of buoyancy has specific consequences for each of the three manufacturing domains discussed in Section 4. For protein crystallisation in aqueous solutions, Marangoni flows are generally weak and play a secondary role compared to the diffusion-dominated transport near the depletion zone. The Prandtl number of aqueous solutions is high, meaning that thermal diffusion is slow relative to momentum transport, and Marangoni flows in such systems tend to be confined to thin layers near the free surface rather than penetrating deeply into the bulk. For most protein crystallisation experiments in closed containers, there is no significant free surface during the crystallisation period, and Marangoni effects are genuinely negligible.

For ZBLAN fibre drawing, the situation is different. The drawing zone involves a free surface of molten glass with large thermal gradients along its axis, from the hot preform tip to the cooler drawn fibre below. These temperature gradients create surface-tension gradients that drive Marangoni flows within the molten zone. The Prandtl number of molten ZBLAN is relatively high compared to liquid metals but low compared to aqueous solutions, placing ZBLAN in an intermediate regime where Marangoni flows are significant but not dominant. Process design for orbital ZBLAN drawing must account for these flows, which affect the shape and stability of the molten zone and the compositional uniformity of the drawing region. Quantitative characterisation of Marangoni convection in ZBLAN drawing is an area that requires further research, particularly given the absence of published attenuation data for space-produced fibres that would confirm the net outcome.

For compound semiconductor float-zone crystal growth, Marangoni convection is the dominant transport mechanism in microgravity. The low Prandtl numbers of semiconductor melts mean that thermal diffusion is fast relative to momentum transport, and Marangoni flows generated at the free surface of the molten zone can penetrate far into the bulk. The JAXA MEIS experiments

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measured Marangoni flow velocities in silicone oil liquid bridges as a model system with a variable Prandtl number, validating computational models for predicting Marangoni flow intensity as a function of temperature gradient and Prandtl number (Kawasaki et al., 2019). These models are directly applicable to the design of float-zone furnaces for semiconductor crystal growth in orbit.

5.2 Containerless Processing

Containerless processing, the ability to heat and manipulate a molten sample without any contact with vessel walls, becomes practically accessible in microgravity. On Earth, acoustic levitation or electrostatic suspension can support small samples against gravity, but the forces required limit practicable sample masses to milligrams. In microgravity, only the small residual accelerations need be overcome, making containerless processing of samples of substantially greater mass feasible. The advantage is the complete elimination of container-induced heterogeneous nucleation and contamination. Container walls are primary sources of unwanted nucleation in many high-purity and high-reactivity processing contexts; their elimination permits deeply undercooled liquid states that are inaccessible in any crucible-based process.

NASA's Electrostatic Levitation (ESL) facility on the ISS has used containerless processing to measure thermophysical properties of metallic and semiconducting materials in deeply undercooled states. Specific heat, viscosity, surface tension, and electrical resistivity have been measured for liquid semiconductors at temperatures 300 to 500 degrees below their equilibrium melting points, conditions that cannot be maintained in any container because the container surface would immediately trigger solidification. These measurements feed directly into models of semiconductor crystal growth that improve terrestrial manufacturing processes, demonstrating that the orbital environment generates value for materials science even when the ultimate manufacturing remains Earth-based.

5.3 Alloy Solidification and Phase Separation

The solidification of metallic alloys in microgravity has been studied since the first dedicated materials science experiments on the Space Shuttle. On Earth, compositional inhomogeneity in a solidifying alloy arises partly from diffusion in the solid-liquid interface region but also from bulk convective mixing in the remaining liquid. This convection, driven by the density differences between the solute-depleted liquid near the growing solid and the solute-rich bulk liquid, produces macro-scale compositional gradients and impurity striations that are persistent quality problems in large-diameter crystal growth for electronic applications.

Space Shuttle experiments using the Crystal Growth Furnace and the Advanced Automated Directional Solidification Furnace demonstrated reduced impurity striations and improved radial compositional homogeneity in gallium arsenide (GaAs) and indium phosphide (InP) crystals grown

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in microgravity compared to identically prepared ground controls (Witt et al., 1997). These results are consistent with the expected suppression of buoyancy-driven convective mixing in the III-V compound semiconductor melts. The commercial implications depend on whether the quality improvement is sufficient to justify orbital production costs, a question examined in Section 8.

6. ORBITAL MANUFACTURING PLATFORMS: CURRENT LANDSCAPE

The commercial infrastructure for orbital manufacturing has changed substantially since 2017. The most important change is qualitative rather than quantitative: before that year, in-space manufacturing was almost exclusively a national space agency activity, conducted on the ISS as a research rather than commercial endeavour. Since then, a cohort of purpose-built commercial platforms and services has emerged, each designed around specific product categories and commercial requirements rather than general research flexibility. Understanding what these platforms are, who operates them, and what they have actually demonstrated is essential for evaluating where the field stands.

The International Space Station remains the primary operational platform for all commercial manufacturing activity as of early 2026. Operated in partnership by NASA, ESA, JAXA, CSA, and Roscosmos, the ISS has been continuously crewed since November 2000. The Center for the Advancement of Science in Space (CASIS) manages the U.S. National Laboratory segment under a cooperative agreement with NASA, and the In Space Production Applications (InSPA) programme within CASIS specifically supports the transition from research to commercial production. The ISS carries real limitations as a permanent manufacturing facility: it is crewed, generating g-jitter; its power, volume, and crew time are competed resources; and NASA has announced a deorbit plan for no earlier than January 2030. The transition away from ISS dependence is a live infrastructure planning issue for every company currently operating there.

Varda Space Industries, founded in 2020 and based in El Segundo, California, has built the only architecture in commercial operation today that integrates orbital manufacturing with autonomous re-entry and terrestrial product recovery. Each W-series mission pairs a Rocket Lab Photon satellite bus, which provides power, communications, attitude control, and orbital manoeuvring, with a Varda-designed pharmaceutical processing capsule that functions as both the manufacturing vessel and the re-entry vehicle. The entire system is uncrewed and operates autonomously during the manufacturing phase. The product is never transferred between spacecraft: it is processed in orbit within the same physical container that subsequently re-enters and lands, eliminating the contamination and physical disruption that would accompany any in-orbit product transfer operation.

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Flawless Photonics, based in Reno, Nevada, and co-funded by the European Space Agency and the Luxembourg Space Agency, operates ZBLAN drawing hardware installed in the ISS Microgravity Science Glovebox. The company operates a fourteen-person engineering team in Luxembourg dedicated to machine building, working with NASA, ESA, and the University of Adelaide. Flawless Photonics' automatic fibre-break restart system is its principal technical differentiator, enabling the production run lengths that previous hardware could not achieve. The next phase of development involves in-space preform manufacturing; a NASA InSPA-funded collaboration with the University of Adelaide, Axiom Space, and Visioneering Space aims to produce ZBLAN preforms in orbit rather than launching them from Earth, which would eliminate the last remaining terrestrial step in the production process.

Redwire Space, which acquired Made In Space in 2020, has the longest commercial operational track record on the ISS. Its BioFabrication Facility produced the first human tissue samples ever bioprinted in orbit, using a process that exploits microgravity to construct three-dimensional tissue structures that would collapse under their own weight on Earth. FOMS Inc. holds patents on aspects of in-orbit ZBLAN drawing and has demonstrated incorporation of rare-earth dopants such as erbium at concentrations not achievable in terrestrial production without dopant clustering and associated quenching of optical gain. This concentration advantage is directly relevant to the optical amplifier fibre market, where higher dopant concentrations enable shorter, higher-gain amplifier sections.

Space Forge, based in Cardiff and backed by Airbus Ventures, is developing the ForgeStar platform for compound semiconductor and specialty alloy manufacturing in orbit. Unlike Varda's pharmaceutical focus, Space Forge targets inorganic materials that require the further launch cost reductions projected for Starship before orbital production is commercially viable. The ForgeStar platform is designed as a returnable, refurbishable spacecraft, intended for multiple production missions on the same hardware to reduce per-mission amortised capital cost. ForgeStar-0, the company's technology demonstrator, was lost in a Rocket Lab Electron launch failure in January 2023; ForgeStar-1 development continues.

Company	Platform	Product focus	Status (early 2026)
Varda Space Industries	W-series uncrewed capsule and Rocket Lab Photon bus	Pharma polymorph engineering; biologics	W-1 success Feb. 2024; $145M raised total; W-2 and W-3 in development
Flawless Photonics	ISS Microgravity Science Glovebox hardware	ZBLAN optical fibre	11.9 km drawn Mar. 2024; attenuation testing pending publication; preform programme planned

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Company	Platform	Product focus	Status (early 2026)
Redwire Space (fmr. Made In Space)	ISS modules; BioFabrication Facility	ZBLAN; in-orbit bioprinting; structural manufacturing	First in-orbit human tissue bioprinted; ongoing ZBLAN production since 2019
FOMS Inc.	SpaceFORM system (ISS National Lab)	ZBLAN; rare-earth-doped amplifier fibre	Patents on in-orbit ZBLAN draw process; high-concentration Er doping demonstrated
Space Forge	ForgeStar returnable free-flyer (in development)	Compound semiconductors; specialty alloys	ForgeStar-0 lost in launch failure Jan. 2023; ForgeStar-1 in development
Axiom Space	ISS commercial module; future standalone station	General platform; pharma and materials R and D	Module integration planned; multiple research partnership agreements active
JAXA (PCG programme)	ISS Kibo module (counter-diffusion crystallisation)	Protein crystal growth for drug discovery (fee-for-service)	Over 20 yr. continuous operation; 3 to 4 campaigns per year; TAS-205 Phase 3 trial concluded

Table 1. Commercial in-space manufacturing companies and programmes, early 2026. Compiled from company disclosures, NASA ISS National Laboratory programme records, and verified press coverage. Note: TAS-205 Phase 3 (REACH-DMD) did not meet its primary endpoint (AJMC, 2025), which is distinct from the scientific value of the underlying structural data obtained from JAXA space-grown crystals.

7. PHARMACEUTICAL APPLICATIONS AND COMMERCIAL ECONOMICS

Pharmaceutical biologics are the commercial anchor of in-space manufacturing, and for a reason that can be stated with numerical precision. Monoclonal antibody therapeutics are priced in the range of USD 50,000 to several hundred thousand dollars per kilogram of active pharmaceutical ingredient at typical clinical-grade specifications, based on broad industry estimates (Grand View Research, 2023). The total round-trip transportation cost of orbital processing, using a Falcon 9 Transporter rideshare at $5,950/kg outbound plus an estimated $8,000 to $12,000/kg return, is approximately $14,000 to $18,000 per kilogram. At a monoclonal antibody API value of $100,000/kg, the transportation overhead represents 14 to 18 per cent of the product's raw value. This is commercially acceptable for a product that may command a formulation premium for improved deliverability; it is not an insuperable obstacle in the way that $54,500/kg Shuttle launch costs were. The economics work, which is why pharmaceutical biologics are the near-term commercial focus of every serious in-space manufacturing company.

Three distinct value channels exist through which microgravity processing can create pharmaceutical value, and they differ in their commercial timelines, regulatory requirements, and interactions with existing pharmaceutical company workflows.

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The first channel is structural biology for drug discovery. Space-grown protein crystal structures, resolved at sub-angstrom precision, enable structure-based drug design programmes of a quality that ground-grown crystals cannot support for certain proteins. JAXA's PCG programme is the established commercial service in this space, with over twenty years of operation and hundreds of structures produced. The accurate assessment of this channel's pharmaceutical output requires noting, as discussed in Section 4.1, that while the structural work underpinning TAS-205 was enabled by space-grown crystals, the drug itself did not demonstrate clinical efficacy in its Phase 3 trial. The structural contribution remains valid; the therapeutic outcome was unsuccessful.

The second channel is biologic reformulation. Crystalline suspensions of monoclonal antibodies produced in microgravity may have physical properties, specifically particle-size homogeneity and reduced viscosity, that make them suitable for subcutaneous injection rather than intravenous infusion. The global monoclonal antibody therapeutics market exceeded USD 200 billion in 2023 and is projected to approach USD 400 billion by 2030 (Grand View Research, 2023). Subcutaneous formulations command significant premium pricing in markets where home administration is valued by patients and payers, and they expand access in settings where clinical infusion infrastructure is limited. Merck's sustained investment in the pembrolizumab microgravity crystallisation programme reflects a considered assessment that the potential return, at $25 billion in current annual revenues, justifies the cost of the orbital experiments.

The third channel is polymorph engineering, demonstrated by the Varda W-1 mission. Selectively accessible metastable polymorphs may have superior bioavailability, improved stability profiles, or patentable novelty relative to existing marketed forms. The commercial interest for pharmaceutical companies centres on lifecycle management: a patentable new crystalline form of a drug approaching patent expiry can extend commercial exclusivity and preserve revenue streams that would otherwise be eroded by generic competition. The regulatory environment for new polymorphs, relative to new chemical entities, is more established, which somewhat reduces development risk and timeline.

The regulatory pathway for orbital pharmaceutical manufacturing remains unmapped. No product manufactured in space has received regulatory approval from the FDA or any major national regulatory authority for commercial sale on that basis. The FDA's cGMP framework was built for terrestrial facilities; it does not address the specific variables of orbital processing, including radiation exposure, the impossibility of human intervention during manufacturing, and the mechanical and thermal stresses of atmospheric re-entry. These gaps are real. The FDA has indicated willingness to engage constructively with companies developing orbital manufacturing processes, and the empirical foundation for regulatory submissions is being built through the W-series mission programme, but the timelines for formal regulatory guidance are measured in

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years rather than months.

Product category	Estimated API value (USD/kg)	Representative products	Microgravity mechanism
Monoclonal antibody therapeutics	~$100K to $500K (order of magnitude)	Pembrolizumab (Keytruda); Adalimumab (Humira); Ocrelizumab (Ocrevus)	Crystal suspension optimisation for subcutaneous delivery formulation
Small-molecule antiretrovirals	~$5K to $50K	Ritonavir; Atazanavir; Cobicistat	Selective metastable polymorph production; novel crystalline form IP
Oncology small molecules	~$10K to $100K	Ibrutinib; Venetoclax; Palbociclib	Polymorph engineering; bioavailability enhancement; lifecycle extension
Interferon biologics	~$20K to $200K	Interferon beta-1a; Peginterferon alfa-2a	Crystalline formulation stability; reduction of cold-chain requirements
Insulin analogues	~$5K to $40K	Insulin glargine; Insulin degludec; Insulin lispro	Crystal particle-size uniformity for long-acting pharmacokinetic profiles

Table 2. Pharmaceutical product categories of interest for orbital manufacturing. Per-kilogram API values are conservative, order-of-magnitude estimates based on industry sources; actual values vary by product, purity level, and market context. The relevant commercial figure is the value premium of the space-processed formulation over its best available terrestrial equivalent, which varies by product and is not yet quantifiable for most categories before space-processed formulations reach the market.

8. SEMICONDUCTOR AND PHOTONICS APPLICATIONS

The semiconductor materials case for orbital manufacturing differs structurally from the pharmaceutical case in one commercially critical respect: the per-kilogram values of most semiconductor materials are lower, and at current launch prices, the break-even condition is not satisfied for most semiconductor product categories. This is a statement about current economics, not about the scientific or technical merit of the work.

ZBLAN specialty photonic fibre is the clear near-term exception. As noted in Section 4.2, Rob Loughan of Flawless Photonics confirmed in April 2024 that space-produced ZBLAN fibre was being sold to research and commercial customers at approximately $1,000 per metre (The Register, 2024). Given a ZBLAN fibre outer diameter of 125 micrometres and a glass density of approximately 4.5 g/cm^3, one metre of fibre has a mass of approximately 55 milligrams, corresponding to approximately 18,000 metres per kilogram. At $1,000 per metre, one kilogram of

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specialty photonic ZBLAN fibre has a raw value of approximately $18 million. Even allowing for substantial processing cost and using the most conservative round-trip transport estimate of $15,000 to $18,000/kg, the commercial logic is straightforwardly favourable. The remaining question is not whether the economics work but whether the fibre actually performs better than terrestrial alternatives, which requires the publication of attenuation data.

For longer wavelength telecommunications ZBLAN applications, the per-metre price may be lower than specialty photonic grade, but the volume required is much larger. The economics of producing telecommunications-grade ZBLAN in orbit depend on achieving both the quality improvement (confirmed by attenuation measurements) and the cost reduction required to compete with silica infrastructure. Both conditions are necessary; neither has been demonstrated.

Float-zone silicon, the highest-purity commercially available silicon, commands approximately $1,000 to $2,000 per kilogram compared to $50 to $200 per kilogram for standard Czochralski silicon (SEMI, 2023). The terrestrial float-zone process is gravity-limited: the diameter of ingots is constrained to approximately 200 mm because the molten zone becomes unstable under gravity at larger dimensions. Microgravity removes this constraint, opening the possibility of larger-diameter float-zone silicon with improved yield. However, at $1,500/kg for FZ silicon, the break-even condition requires round-trip transport costs well below current Falcon 9 pricing, placing this application firmly in the Starship-era category.

Gallium arsenide and indium phosphide compound semiconductor substrates command higher prices per wafer but are most accurately valued per kilogram of bulk crystal material in the range of $2,000 to $4,000/kg. Space Shuttle experiments demonstrated the quality improvement potential (Witt et al., 1997), but the commercial viability question depends on launch economics that are not yet available. Space Forge's ForgeStar platform is designed specifically for this application category, on the explicit assumption that Starship-era economics will materialise on a commercially relevant timescale.

9. FINANCIAL ANALYSIS AND MARKET SIZING

9.1 The Break-Even Condition

The commercial logic of in-space manufacturing reduces to a specific and calculable inequality. The break-even framework is presented formally in the box below.

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The Commercial Viability Condition:

$$V_{premium} > C_{launch} + C_{process} + C_{return}$$

$\mathbf{V_{premium}}$: value premium of the space-processed product over the best achievable terrestrial equivalent, per kilogram (USD/kg)

$\mathbf{C_{launch}}$: outbound launch cost per unit product mass, comprising rideshare fees and amortised spacecraft hardware (USD/kg)

$\mathbf{C_{process}}$: in-orbit manufacturing, monitoring, and quality-assurance cost per unit mass (USD/kg)

$\mathbf{C_{return}}$: re-entry vehicle operation, recovery, and post-processing cost per unit mass (USD/kg)

At Falcon 9 Transporter rideshare pricing ($5,950/kg outbound; SpaceX, 2024), a small dedicated re-entry capsule contributes an estimated additional $8,000 to $12,000/kg on return, giving a combined round-trip transport cost in the region of $14,000 to $18,000/kg. This condition is satisfied comfortably for pharmaceutical biologics ($V_{premium}$ potentially exceeding $50,000/kg for monoclonal antibodies), and for specialty ZBLAN photonic fibre (priced at approximately $1,000/m by Flawless Photonics, CEO Rob Loughan, April 2024). For compound semiconductor wafer substrates ($V_{premium}$ roughly $1,500 to $4,000/kg; SEMI, 2023), the condition is not satisfied until $C_{launch} + C_{return}$ approaches the level SpaceX projects for Starship.

Figure 5 illustrates the break-even framework graphically, comparing estimated product values per kilogram to current and projected round-trip transport costs across the five principal near-term product categories.

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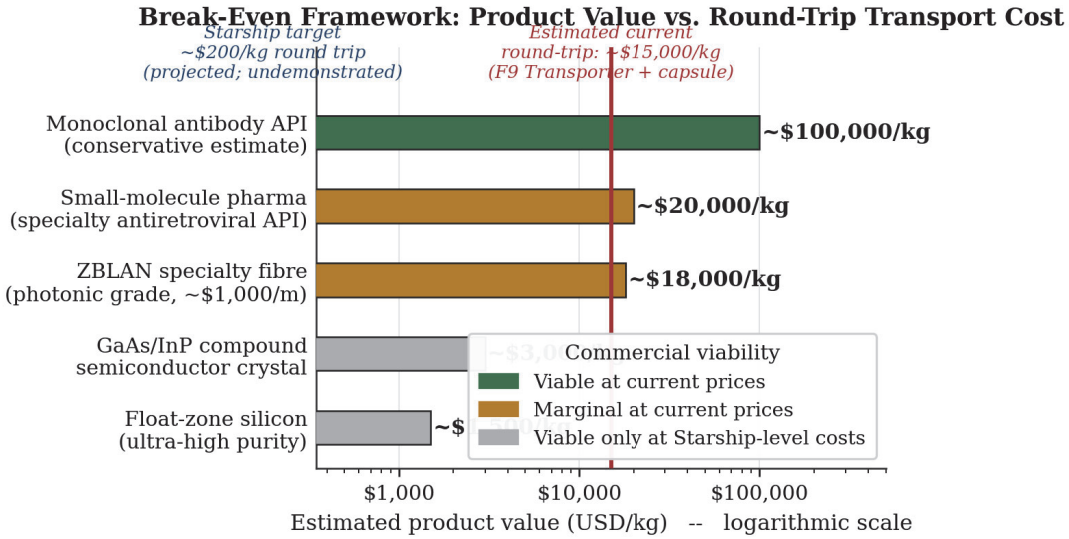

Product values are order-of-magnitude estimates. ZBLAN from The Register / Flawless Photonics CEO (April 2024). mAb: Grand View Research (2023). FZ-Si: SEMI (2023). Transport: SpaceX (2024) + indicative capsule return cost.

Figure 5. Break-even economics for in-space manufacturing. Horizontal bars show conservative, order-of-magnitude estimates of product value per kilogram; vertical lines show two transport cost scenarios. Current F9 round-trip approximately $15,000/kg: Falcon 9 Transporter outbound at $5,950/kg (SpaceX, 2024) plus estimated small reentry capsule return ($8,000 to $12,000/kg; indicative figure, varies by payload mass and vehicle). Starship target approximately $200/kg round trip: SpaceX stated goal of below $100/kg each way (Euroconsult, 2024), not yet demonstrated commercially. Green bars: commercially viable at current prices (value substantially exceeds current transport cost). Amber: marginal at current prices. Grey: viable only at Starship-level costs. ZBLAN price from The Register / Flawless Photonics CEO Rob Loughan (April 2024): ~$1,000/m, implying approximately $18,000/kg at a 125-micrometre outer diameter. All other values are order-of-magnitude estimates from cited industry sources.

9.2 Market Projections

Two independent research organisations have published detailed market projections for in-space manufacturing that provide useful, if imperfect, guidance on the sector's growth trajectory. Their methodologies and market definitions differ significantly; they should be read in conjunction rather than aggregated.

MarketsandMarkets published a report in November 2023 projecting the in-space manufacturing market at USD 4.6 billion in 2030, growing to USD 62.8 billion by 2040 at a compound annual growth rate of 29.7 per cent (MarketsandMarkets, 2023). The stated CAGR can be independently verified: (62.8 / 4.6)^(1/10) minus 1 equals 29.9 per cent, which is consistent with the stated 29.7 per cent. This projection covers a specific, relatively narrowly defined segment of active commercial in-space production.

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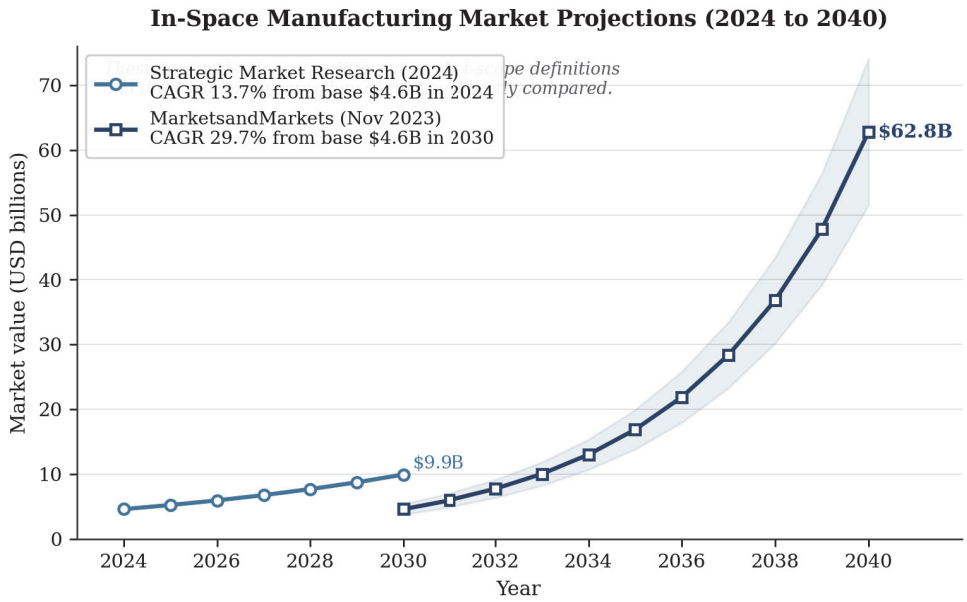
Strategic Market Research published a separate projection in 2024, placing the market at USD 4.6 billion in 2024 growing at a CAGR of 13.7 per cent (Strategic Market Research, 2024). At 13.7 per cent over six years from a 2024 base, the implied 2030 value is $4.6 times 1.137 to the sixth power, which equals approximately $9.94 billion. The firm's published headline of $11.2 billion by 2030 appears to use a base year of approximately 2022 rather than 2024, which reconciles the discrepancy. This projection uses a different market scope and different base year than MarketsandMarkets.

Allied Market Research, using the broadest scope definition that includes in-space servicing and transportation alongside manufacturing, projects USD 21.3 billion by 2030 and USD 135.3 billion by 2040 (Allied Market Research, 2024). McKinsey and the World Economic Forum identify in-space manufacturing as one of four primary growth drivers within a total space economy projected at USD 1.8 trillion by 2035 (McKinsey and Company, 2024).



Sources: MarketsandMarkets PRNewswire (9 Nov 2023); Strategic Market Research (2024). Shaded band: +/-18% uncertainty around MaM forecast.

Figure 4. In-space manufacturing market projections, 2024 to 2040, from two independent research organisations with different market-scope definitions and base years. Light blue line: Strategic Market Research (2024), CAGR 13.7% from base $4.6B in 2024. At this CAGR over 6 years, the implied 2030 value is $9.94B; the firm's headline figure of $11.2B by 2030 implies a 2022 to 2023 base year. Dark blue line: MarketsandMarkets (Nov 2023), CAGR 29.7% from base $4.6B in 2030, reaching $62.8B by 2040 (independently verified as 29.9%, consistent with stated rate). Shaded band around the MarketsandMarkets line represents plus or minus 18% forecast uncertainty. These two series use different scope definitions and cannot be directly compared.

9.3 Launch Cost Trajectory

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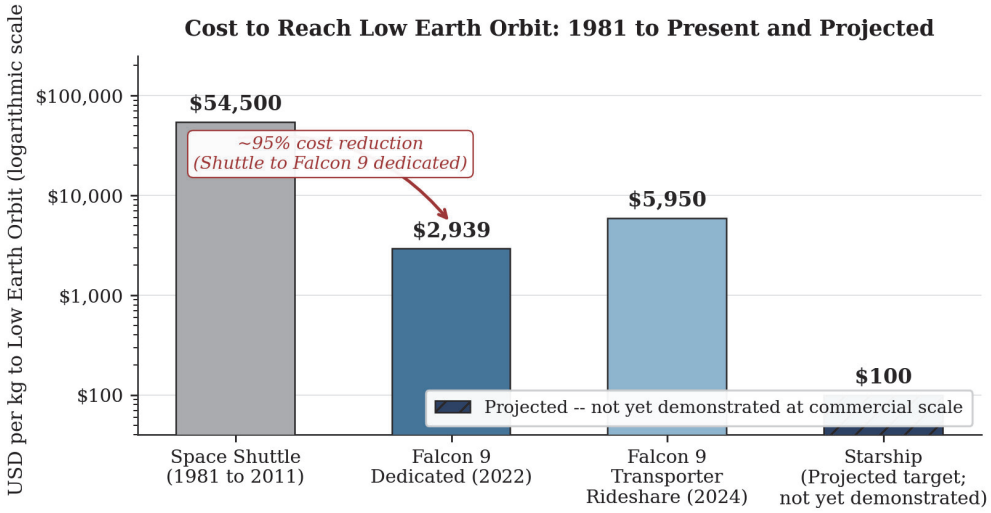

Sources: Pielke & Byerly (2011) doi:10.1038/472038a; SpaceX Falcon 9 User Guide rev 2 (2022); SpaceX Transporter pricing (2024); Euroconsult (2024).

Figure 3. Cost per kilogram to low Earth orbit across four vehicle generations, logarithmic scale. All values from verified primary sources. Space Shuttle: ~$54,500/kg programme-averaged in 2010 USD (Pielke and Byerly, 2011; doi:10.1038/472038a). Falcon 9 dedicated: ~$2,939/kg calculated from SpaceX published list price of $67M per launch (SpaceX, 2022) divided by maximum LEO payload of 22,800 kg. Falcon 9 Transporter rideshare: $5,950/kg to sun-synchronous orbit (SpaceX, 2024). Starship: SpaceX stated target of below $100/kg; hatched bar indicates this has not been demonstrated at commercial scale (Euroconsult, 2024). The annotation shows the approximately 95% reduction from Shuttle to Falcon 9 dedicated pricing.

9.4 Private Capital as a Market Signal

The investment trajectories of leading companies provide an independent signal of institutional confidence in the commercial case. Varda Space Industries disclosed in its March 2024 press release that it had raised over $53 million from investors including Founders Fund, Lux Capital, Khosla Ventures, and General Catalyst (Improved Pharma, 2024b). Following the W-1 mission's success, a USD 90 million Series B was closed, bringing total raised capital to USD 145 million. Space Forge attracted Airbus Ventures as a backer. Flawless Photonics received co-funding from ESA and the Luxembourg Space Agency, both of which conducted due diligence before committing public funds. Combined investment in in-space manufacturing startups globally exceeded USD 500 million between 2020 and 2024 (PwC, 2025). These figures are modest by the standards of, say, the commercial satellite communications industry, but they represent a level of informed institutional commitment that was entirely absent a decade ago.

10. REGULATORY AND POLICY LANDSCAPE

The regulatory environment for orbital pharmaceutical manufacturing is genuinely underdeveloped relative to the pace of technological progress. No pharmaceutical product

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manufactured in space has received regulatory approval for commercial sale on that basis from any major national authority. The gap is not one of regulatory hostility; it is a gap in the availability of applicable guidance.

The FDA's Current Good Manufacturing Practice (cGMP) framework was designed for terrestrial facilities with human operators who can monitor, adjust, and if necessary halt manufacturing processes in real time. An uncrewed orbital capsule on a limited-bandwidth communications link does not allow real-time human intervention during manufacturing. A process deviation that would be caught and corrected within minutes in a cGMP-compliant terrestrial cleanroom may go undetected until the batch is returned and tested weeks or months later. Process validation in a cGMP context requires documented batch-to-batch reproducibility across multiple production runs, and that documentation does not yet exist for any orbital pharmaceutical manufacturing process.

The FDA has acknowledged the existence of this gap and indicated willingness to engage constructively with companies developing orbital manufacturing processes. The Varda W-series programme is generating the empirical data that any future regulatory submission will require: batch characterisation, stability data from extended orbital stays, and documentation of the effects of re-entry on product physical properties. The process of building the regulatory science foundation is underway, but it will take several years to mature into the kind of formal guidance documents that pharmaceutical companies require before committing to orbital supply chains for approved products.

International regulatory considerations add complexity. Products manufactured in orbit aboard a U.S.-registered spacecraft are subject to U.S. jurisdiction during manufacturing under the framework of the Outer Space Treaty of 1967, which establishes national responsibility for space activities. Global commercial sales of space-manufactured pharmaceuticals would also require regulatory approval from the European Medicines Agency, Japan's PMDA, and other national authorities. Coordinated multi-agency regulatory guidance for orbital manufacturing does not exist and will require concerted international effort to develop. These are not novel problems in principle; the pharmaceutical industry navigates multi-jurisdictional regulatory requirements routinely. But the combination of a novel manufacturing environment with multiple national jurisdictions creates a regulatory complexity that will take time and sustained engagement to resolve.

11. CHALLENGES AND HONEST LIMITATIONS

A competition paper that presents only the affirmative case for in-space manufacturing would be intellectually dishonest. The obstacles are real, several are non-trivial, and the most important

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one, the ZBLAN attenuation verification gap, is currently the field's single most urgent unresolved scientific question. Each challenge is examined here without minimisation.

11.1 The ZBLAN Attenuation Verification Gap

The commercial case for orbital ZBLAN production rests on the premise that space-drawn fibre performs better optically than the best terrestrially drawn equivalent. Eleven kilometres of fibre produced in space does not, by itself, constitute evidence that this premise is correct. Cozmuta et al. (2025) made this point explicitly in Acta Astronautica, stating that 'the lack of clear scientific evidence regarding the impact of microgravity on the manufacturing of optical fibres, particularly ZBLAN, underscores the need to revisit fundamental research principles,' and that production volume alone does not fulfil the quality and economic standards required for commercial-grade optical fibre. The physical mechanism that should produce the improvement is well understood. The experimental confirmation that the improvement actually manifests in deployable fibre, measured by attenuation spectroscopy across the relevant wavelength range, has not been published. Until it is, the ZBLAN commercial case remains physically motivated but not empirically demonstrated.

11.2 The TAS-205 Clinical Outcome

Previous accounts of the JAXA PCG programme's pharmaceutical output have consistently cited TAS-205 as an example of direct clinical benefit from space-grown protein crystal structures. This framing is now inaccurate. In 2025, Taiho Pharmaceutical announced that TAS-205 failed to meet its primary endpoint in the Phase 3 REACH-DMD trial (NCT04587908): ambulatory patients showed no statistically significant improvement in the primary motor function measure compared to placebo at 52 weeks (AJMC, 2025). This outcome does not invalidate the structural science enabled by space-grown crystals; a drug's failure in Phase 3 is usually attributable to biological complexity, patient selection, or trial design issues rather than to the quality of the structural data used early in development. But accurate citation of what the JAXA programme has and has not achieved requires reporting this outcome honestly.

11.3 Mission Cadence and Return Vehicle Availability

The W-1 mission's eight-month orbital stay, extended from a planned 30 days by FAA landing-approval delays, illustrates a systemic constraint that affects all in-space manufacturing: re-entry cadence is measured in months rather than days or hours. Until multiple commercial re-entry vehicle providers create genuine competition and redundancy, and until regulatory approval timelines for autonomous landings are better established, in-space manufacturing cannot support the just-in-time delivery schedules that pharmaceutical manufacturers require. This is a transitional constraint, not a permanent physical limitation, but it imposes real restrictions on near-term commercial planning.

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11.4 Autonomous Process Control and Regulatory Reproducibility

Pharmaceutical cGMP compliance requires documented batch-to-batch reproducibility across multiple validated manufacturing runs. Varda's W-1 mission produced one experimental batch of ritonavir Form III. One batch does not satisfy cGMP reproducibility requirements. Building the validation dossier necessary for a regulatory submission requires multiple missions, consistent results, and thorough process characterisation documentation. This is achievable but requires sustained investment in a series of orbital campaigns. The W-2 and subsequent missions are building toward this goal, but the timeline from first mission to approved commercial product is measured in years rather than months.

11.5 ISS Succession Risk

NASA has announced a deorbit plan for the ISS no earlier than January 2030. The commercial stations intended to succeed it, including Axiom Space's planned independent station and the Blue Origin Orbital Reef concept, have received NASA Commercial LEO Destinations programme funding but have not been launched. The gap between ISS deorbit and commercial station availability is a genuine near-term infrastructure risk for companies that currently depend on ISS access. Varda's architecture, using independent free-flying capsules rather than an occupied station, is specifically insulated from this risk, which may be a significant architectural advantage over the next five to ten years.

11.6 Long-Term Semiconductor Case Uncertainty

The semiconductor case for orbital manufacturing ultimately depends on Starship or a comparable vehicle delivering launch costs in the range of $100 per kilogram at commercial scale. SpaceX has conducted multiple test flights of Starship and demonstrated impressive capabilities, but sustained commercial operation at the projected cost level has not been established as of this writing. The Starship programme has experienced delays relative to initial projections, and some independent engineers consider the stated cost targets optimistic under realistic commercial conditions. The semiconductor orbital manufacturing case is real at $100/kg but may remain aspirational longer than current projections suggest.

12. FUTURE OUTLOOK

The trajectory of in-space manufacturing over the next fifteen years will be determined by the interaction of three developments, each of which can advance or stall somewhat independently: launch cost reduction, platform maturation and regulatory framework development, and the accumulation of published scientific evidence confirming specific performance improvements in space-processed materials.

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The near-term window, from approximately 2026 to 2032, is defined by pharmaceutical crystallisation and ZBLAN photonic fibre. These are the two applications where the commercial case is strongest at current launch prices, and where the commercial ecosystem, including companies, investors, regulatory engagement, and pharmaceutical partnerships, is furthest developed. The key milestones to watch are the publication of rigorous attenuation data for space-produced ZBLAN; the results of Varda's W-2 and subsequent biologics missions; the commercial activation of Axiom Space's ISS-attached module; and the beginning of formal FDA regulatory guidance on orbital cGMP requirements. If all four resolve favourably within this window, the field will likely see a substantial acceleration of institutional investment and pharmaceutical company partnering.

The medium-term window, roughly 2032 to 2040, is where compound semiconductor applications become commercially accessible, contingent on Starship achieving commercial operation at projected costs. The same cost trajectory opens the possibility of producing substantially larger volumes of pharmaceutical biologics in orbit, not just batch-scale R and D demonstrations but production quantities sufficient to supply a meaningful fraction of a drug's commercial demand. If 0.1 per cent of the projected USD 400 billion global biologics market were produced in orbit by 2040, that would represent USD 400 million in annual orbital pharmaceutical manufacturing revenue, at margins likely to exceed those achievable in any terrestrial equivalent process.

Beyond 2040, the outlook depends on infrastructure transitions whose timelines are genuinely difficult to forecast: commercial space stations with dedicated manufacturing volumes and reliable crew access for maintenance; advanced robotic systems for complex in-orbit operations; and AI-based process control systems capable of autonomous quality management without human oversight. What can be stated with confidence is that the fundamental physical opportunities do not change. Gravity will continue to constrain protein crystallisation, ZBLAN fibre drawing, and pharmaceutical polymorph formation on Earth. The question is only when the cost of accessing orbit falls far enough, and the regulatory and logistical infrastructure matures sufficiently, for those opportunities to be exploited at commercial scale.

13. CONCLUSION

The argument of this paper has been specific and, where possible, quantitative. There is a class of manufacturing processes whose quality is limited not by chemistry or engineering skill but by the presence of gravitational body forces at Earth's surface. There is a body of experimental evidence, now including complete orbital manufacturing cycles demonstrated commercially in 2024, confirming that those limitations can be overcome in orbit. There is a break-even condition,

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CONCLUSION

The research question posed in Section 1 asked: for which commercially relevant manufacturing processes does the microgravity environment of low Earth orbit provide quality improvements large enough, and production costs low enough at current and near-projected launch economics, to satisfy the commercial viability condition? The evidence reviewed in this paper provides a specific and differentiated answer.

The answer is affirmative for two product categories at current Falcon 9 rideshare pricing. For pharmaceutical biologics, including monoclonal antibody crystalline suspensions and polymorph-engineered small molecules, the per-kilogram value of the space-processed material substantially exceeds the round-trip transportation and processing cost. The quality improvement mechanism, suppression of buoyancy-driven convection and gravitational sedimentation, is mechanistically established and experimentally confirmed across hundreds of experiments over four decades. The Varda W-1 mission demonstrated in February 2024 that the complete commercial orbital manufacturing cycle is operationally feasible for a private company without government infrastructure support beyond launch services. For specialty ZBLAN photonic fibre, the current market price of approximately $1,000 per metre implies a per-kilogram value of approximately $18 million, which satisfies the commercial viability condition overwhelmingly. The remaining uncertainty is whether the optical quality of space-produced fibre, confirmed by attenuation spectroscopy, will justify that premium.

The answer is conditional and currently negative for compound semiconductor substrates and float-zone silicon. The quality improvement potential is established from Space Shuttle experiments, but per-kilogram values of $1,500 to $4,000 do not satisfy the viability condition at current Falcon 9 pricing. The condition will be satisfied if and when Starship achieves its stated cost target of below $100 per kilogram, but that target has not been demonstrated at commercial scale and should be treated as aspirational.

Three milestones will determine the trajectory of the field with greater precision than any market projection. The publication of peer-reviewed optical attenuation data for space-produced ZBLAN fibre will either confirm or substantially revise the twenty-year-old commercial thesis for that material. The results of Varda's W-2 and subsequent biologics missions will determine whether the ritonavir Form III result generalises to the monoclonal antibody formulation market that represents the largest near-term pharmaceutical revenue opportunity. And FDA regulatory engagement on orbital cGMP requirements will determine whether pharmaceutical companies can responsibly commit to orbital supply chains for approved products within a commercially relevant timeframe.

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The original hypothesis of this paper was that microgravity provides measurably superior conditions for the three manufacturing domains examined, and that this advantage satisfies the commercial viability condition for pharmaceutical biologics and specialty photonic fibre at current economics. The evidence reviewed supports that hypothesis for the pharmaceutical domain with high confidence and for ZBLAN photonic fibre with strong physical motivation pending attenuation confirmation. In-space manufacturing has transitioned from laboratory hypothesis to operational commercial practice. The scientific foundations are real, the economics are improving, the commercial infrastructure is building, and the trajectory is clear. The pace of development will be determined by the three milestones identified above. This paper has provided the analytical framework for evaluating that progress as it occurs.

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DISCUSSION

The evidence reviewed in this paper supports a differentiated interpretation of the commercial case for in-space manufacturing. The case is strong, mechanistically coherent, and partially demonstrated in practice for pharmaceutical biologics and specialty photonic fibre. It is physically motivated but empirically incomplete for ZBLAN telecommunications applications. It is real but economically premature for compound semiconductor substrates at current launch costs. These distinctions are important and should not be collapsed into a single narrative of either unbounded promise or systematic overhype.

Significance of the Varda W-1 Mission

The most consequential single development in the field since the earliest Space Shuttle materials science flights is not the specific chemical result of the Varda W-1 mission, but the logistical demonstration it provided. The successful autonomous re-entry, recovery, and post-flight product characterisation of ritonavir Form III established that the complete orbital pharmaceutical manufacturing cycle is executable by a commercial operator without government infrastructure beyond launch services and landing rights. This is a qualitative change in the risk profile of the sector: before W-1, the operational feasibility of end-to-end orbital pharmaceutical manufacturing by a commercial entity was unproven. After W-1, it is demonstrated fact. The remaining questions are scientific (polymorph selectivity for other molecules), regulatory (cGMP compliance for autonomous orbital processes), and economic (batch-to-batch reproducibility across multiple missions).

The ZBLAN Attenuation Question

The most significant unresolved question in the field is whether space-produced ZBLAN fibre achieves measured optical attenuation substantially below the 0.200 dB/km commercial silica standard. The physical mechanism by which microgravity should prevent the microcrystallisation that limits terrestrial ZBLAN is well understood and has been confirmed in parabolic flight experiments. Eleven kilometres of orbital production by Flawless Photonics demonstrates scale, not quality. Until peer-reviewed attenuation spectroscopy data are published for space-drawn ZBLAN, the commercial thesis for that material system rests on strong physical reasoning and supportive but not conclusive qualitative evidence. This is precisely the uncertainty identified by Cozmuta et al. (2025) in Acta Astronautica, and it is the field's most important near-term empirical priority.

Protein Crystallography and Drug Discovery

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The JAXA PCG programme's twenty-year operational record provides the most extensive evidence base for any single in-space manufacturing application. The Ng et al. (2002) ValRS result, with a 0.8-Angstrom improvement in diffraction resolution from 2.9 to 2.1 Angstroms, is the most precisely documented single comparison in the peer-reviewed literature, and its mechanistic explanation in terms of depletion-zone stabilisation is well-established. The TAS-205 Phase 3 failure does not diminish this scientific record; drug development failures in Phase 3 are common and are far more frequently attributable to biological target complexity or trial design issues than to the quality of structural data used in early-stage design. The Merck pembrolizumab formulation programme represents a more direct commercial application, because its goal is not drug discovery but formulation optimisation for an approved commercial product, and the financial incentive at USD 25 billion in annual revenue is unambiguous.

Launch Economics and Structural Change

The approximately 95 per cent reduction in launch cost from the Shuttle era to Falcon 9 is the single most important enabling factor in the commercialisation of in-space manufacturing. It transformed the economics of orbital production from obviously impossible to conditionally viable for high-value pharmaceutical and photonic products. The projected further reduction to below $100 per kilogram with Starship would extend viability to compound semiconductors and substantially expand the addressable market for pharmaceutical biologics. However, the Starship cost target has not been demonstrated at commercial scale, and the timeline to commercial operation at projected costs remains uncertain. The semiconductor orbital manufacturing case should be evaluated against this uncertainty rather than against the stated target as though it were a current price.

Regulatory and Infrastructure Readiness

The regulatory gap is the most structurally limiting near-term constraint on the pharmaceutical applications of in-space manufacturing. The FDA's cGMP framework does not accommodate autonomous orbital manufacturing, and no product manufactured in orbit has received regulatory approval from any major national authority. The empirical data being generated by the Varda W-series programme, including batch characterisation, stability data from extended orbital stays, and documentation of re-entry effects, are the necessary precursor to any regulatory submission. The timeline for formal FDA guidance on orbital cGMP requirements is measured in years. This gap is real and material, but it is not fundamentally different in kind from the regulatory gaps that have preceded every other novel pharmaceutical manufacturing technology, from aseptic fill-finish to continuous manufacturing. It will be closed by the combination of accumulating empirical data and regulatory engagement that is already underway.

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LIMITATIONS AND FUTURE RESEARCH

This section synthesises the principal limitations identified throughout the paper and specifies the future research priorities that follow from them. The limitations are not peripheral qualifications; they are the substantive empirical gaps that separate the current state of commercial in-space manufacturing from a fully validated industrial practice.

ZBLAN Optical Attenuation Data

The most significant limitation is the absence of published peer-reviewed attenuation measurements for space-produced ZBLAN optical fibre. The commercial thesis for orbital ZBLAN production rests on the physical argument that microgravity suppresses the sedimentation-driven microcrystallisation that prevents terrestrially drawn ZBLAN from approaching its theoretical 0.010 dB/km attenuation minimum. That argument is physically sound and supported by parabolic flight data. It is not yet confirmed by rigorous spectroscopic characterisation of fibres drawn in orbit at commercial lengths. Future research must prioritise the publication of attenuation spectroscopy data across the relevant wavelength range for the Flawless Photonics CRS-30-returned fibre, followed by peer review. Until that data is published, the ZBLAN commercial case is physically motivated but empirically unconfirmed.

Pharmaceutical Batch Reproducibility

The Varda W-1 mission produced a single batch of ritonavir Form III. One batch does not satisfy the batch-to-batch reproducibility requirements of pharmaceutical cGMP validation. Future research must extend the W-series programme across multiple missions targeting the same and related molecular systems, with rigorous documentation of process parameters and solid-state characterisation data sufficient to support a regulatory dossier. The W-2 and subsequent missions targeting monoclonal antibody crystallisation are the necessary next step. The timeline from first orbital mission to regulatory approval for a space-manufactured pharmaceutical ingredient is estimated at a minimum of five to ten years under current regulatory frameworks.

Clinical Translation of Structural Data

The Phase 3 failure of TAS-205 (REACH-DMD, NCT04587908) in July 2025 requires an honest reassessment of claims regarding the direct clinical benefit of space-grown protein crystal structural data. The structural science enabled by JAXA PCG programme data remains valid. The inference that structural quality improvements translate directly into clinical efficacy is not supported by this outcome. Future research should distinguish carefully between the scientific value of improved structural resolution, which is demonstrated, and the clinical value of structure-based drug design programmes based on that data, which depends on factors well beyond structural quality.

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ISS Succession Risk and Platform Continuity

NASA's planned ISS deorbit no earlier than January 2030 creates a near-term platform continuity risk for companies operating ISS-based manufacturing hardware. Commercial station programmes (Axiom Space, Blue Origin Orbital Reef) have received NASA funding but have not launched. Future research should include contingency infrastructure planning for the ISS-to-commercial-station transition period. The architectural advantage of Varda's independent free-flying capsule model over ISS-dependent platforms is most pronounced during this transitional window.

Future Research Priorities

The three most important empirical priorities for the field are: first, publication of peer-reviewed attenuation spectroscopy for space-produced ZBLAN fibre (ZBLAN attenuation verification); second, demonstration of batch-to-batch reproducibility across multiple Varda W-series biologics missions (pharmaceutical cGMP foundation); and third, engagement with the FDA and international regulatory authorities to develop orbital manufacturing guidance documents that specify acceptable process validation approaches for autonomous spacecraft manufacturing environments. Beyond these immediate priorities, longer-term research should develop in-orbit ZBLAN preform manufacturing capability to eliminate the last terrestrial step in the fibre production chain, and should characterise Marangoni convection in ZBLAN melt drawing quantitatively to enable process design optimisation. The Starship cost reduction trajectory should be tracked against independent engineering assessments rather than accepted at face value, since the compound semiconductor commercial case is contingent on those projections materialising.

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The author acknowledges NASA's In Space Production Applications (InSPA) programme, which has consistently bridged the gap between research demonstration and commercial hardware development, and the JAXA Marangoni Experiment in Space (MEIS) programme for its systematic quantitative characterisation of thermocapillary flows that is directly relevant to process design for orbital manufacturing. The transparency with which Varda Space Industries, Flawless Photonics, Redwire Space, and FOMS Inc. have communicated their mission results, including both successes and unresolved questions, has made it possible to construct the evidence-based analysis presented here.

Finally, the author acknowledges the work of Cozmuta et al. (2025) in Acta Astronautica for providing an independent and rigorous critique of the ZBLAN commercial thesis that has informed the balanced treatment of that subject in this paper. Honest assessment of what remains empirically unconfirmed serves the long-term credibility of the field far better than uncritical optimism.

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