July 15, 2025 Google Gemini Pro 2.5 Deep Research Web www.digitalbd.io

GT Biopharma (GTBP): A High-Risk, High-Reward Play on a Differentiated NK Cell Engager Platform

Executive Summary: Initiating Coverage with a Speculative Buy Rating

Investment Thesis: GT Biopharma, Inc. (NASDAQ: GTBP) represents a compelling, albeit exceptionally high-risk, investment opportunity for institutional investors with a high tolerance for volatility. The company's core value is rooted in its proprietary Tri-specific Killer Engager (TriKE®) platform, which possesses a key scientific differentiator: the simultaneous co-stimulation of Natural Killer (NK) cells via the CD16 activating receptor and an integrated Interleukin-15 (IL-15) moiety. This unique mechanism is designed to deliver superior efficacy and persistence compared to competing NK cell engager platforms. GTBP is currently trading at a micro-capitalization valuation that reflects extreme financial distress and significant dilution risk, creating a potential disconnect from the intrinsic value of its technology, as suggested by comparable M&A and licensing deals in the immuno-oncology (I-O) space.

The primary investment thesis hinges on the potential for a significant valuation re-rating driven by positive initial data from the lead asset, GTB-3650, in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndromes (MDS). A clear clinical signal of safety and efficacy could serve as a pivotal de-risking event, unlocking non-dilutive financing opportunities (e.g., strategic partnerships or licensing deals) and addressing the company's most significant overhang: its precarious capital position and the looming threat of massive shareholder dilution. The market appears to be pricing in a high probability of financial failure while ascribing near-zero value to the promising underlying science, the broader pipeline targeting solid tumors (GTB-5550), and a valuable, non-correlated call option in the multi-billion-dollar autoimmune disease market with GTB-7550.

Valuation and Price Target: We are initiating coverage on GTBP with a **Speculative Buy** rating and a risk-adjusted 12-month price target of **$15.00 per share**. This valuation is derived from a sum-of-the-parts, risk-adjusted Net Present Value (rNPV) model of the lead clinical and preclinical assets, supported by precedent transaction analysis of early-stage immuno-oncology platforms.

Key Catalysts (Next 12-18 Months):

- Initial Phase 1 safety and efficacy data readout for GTB-3650 in AML/MDS (H2 2025).
- Filing of an Investigational New Drug (IND) application for GTB-5550 (B7H3-TriKE®) in solid tumors (Q4 2025).
- Securing a strategic partnership for either a pipeline asset (e.g., GTB-5550) or the TriKE® platform.
- Resolution of Nasdaq listing compliance and stabilization of the company's capital structure.

Primary Risks:

- **Financial Risk:** The company faces significant "going concern" risk, as disclosed in SEC filings. Current cash reserves are insufficient to fund operations for the next 12 months without securing additional financing.[1]
- **Dilution Risk:** A recently filed S-1 shelf registration for up to 54.4 million shares—on a float of approximately 3.27 million shares—presents a massive potential dilution overhang from outstanding warrants, convertible preferred stock, and a committed equity facility.[1]
- **Clinical Risk:** Early-stage oncology development is characterized by a high probability of failure. Negative or ambiguous data for GTB-3650 would be catastrophic for the company's valuation and viability.
- **Competitive Risk:** The NK cell engager field is intensely competitive, with larger, better-funded companies such as Innate Pharma and partners of Dragonfly Therapeutics advancing their own platforms.

The TriKE® Platform: Engineering a Superior NK Cell "Serial Killer"

A. The Scientific Rationale for NK Cell Engagement

Natural Killer (NK) cells are cytotoxic lymphocytes of the innate immune system, serving as a first line of defense against malignant and virally infected cells. Their cancer-fighting ability is mediated, in part, through a mechanism known as Antibody-Dependent Cellular Cytotoxicity (ADCC). In ADCC, traditional monoclonal antibodies (mAbs) bind to a tumor-associated antigen (TAA) on a cancer cell, and the antibody's Fc region is then recognized by the CD16a receptor (FcγRIIIa) on the surface of an NK cell. This engagement triggers the NK cell to release cytotoxic granules, such as perforin and granzyme B, leading to the destruction of the tumor cell.[4]

However, this process has limitations. The interaction between the mAb's Fc region

and the CD16a receptor is often transient and of relatively low affinity, which can limit the potency and durability of the anti-tumor response. NK Cell Engagers (NKCEs) represent a next-generation immunotherapeutic approach designed to overcome these limitations. By engineering molecules that can simultaneously and stably bind to both an activating receptor on an NK cell and a TAA on a tumor cell, NKCEs create a more robust and efficient immunological synapse, significantly amplifying the NK cell's killing power.[4]

B. GTBP's Differentiated Mechanism: The Power of Co-Stimulating CD16 and IL-15

GT Biopharma's TriKE® platform is built upon a differentiated scientific architecture that distinguishes it from many competing NKCEs. The core of the platform is a tri-specific recombinant fusion protein composed of three key domains:

1. An **anti-CD16 binding domain** to engage and activate NK cells.
2. An **anti-TAA binding domain** to target the molecule to cancer cells.
3. A human **Interleukin-15 (IL-15) cross-linker** positioned between the two binding domains.[5]

This design is unique in its ability to deliver two distinct and synergistic signals to the NK cell simultaneously. The CD16 engagement provides the potent "kill" signal, initiating ADCC. Concurrently, the integrated IL-15 domain provides a critical "proliferate and survive" signal by binding to the IL-15 receptor complex on the same NK cell.[6] IL-15 is a cytokine known to be essential for the development, proliferation, and survival of NK cells and memory CD8+ T cells.[9] Crucially, IL-15 does not stimulate regulatory T-cells (Tregs), an immunosuppressive cell type that is promoted by the related cytokine IL-2, giving it a superior profile for cancer immunotherapy.[10]
The hypothesis underpinning the TriKE® platform is that by tethering IL-15 directly to the cell-engaging molecule, its proliferative signal is localized specifically to the tumor microenvironment, promoting the *in vivo* expansion and persistence of only those NK cells that are actively engaged with tumor targets. This is designed to create a population of self-sustaining, tumor-directed NK "serial killers" without the need for *ex vivo* cell expansion and infusion, as required by cell therapies, and potentially avoiding the systemic toxicities associated with recombinant cytokine administration.[6]

The integrated cytokine adds a layer of complexity, and its safety is paramount. Systemic administration of cytokines like IL-15 has historically been plagued by significant toxicity. Therefore, the ability of the TriKE® platform to deliver this signal in a targeted, localized manner is central to its viability. The first-generation asset, GTB-3550, provided the first crucial human proof-of-concept for this approach. In its

Phase 1 trial, GTB-3550 was well-tolerated with minimal cytokine release syndrome (CRS) observed, providing the first clinical evidence that this integrated cytokine design could be safe in humans.[6] The ability of the second-generation platform to replicate and improve upon this safety profile is a key focus of the ongoing GTB-3650 trial.

C. The Camelid Nanobody Advantage: Upgrading to 2nd Generation TriKEs®

GT Biopharma has significantly upgraded its platform with its second-generation assets (GTB-3650, GTB-5550, GTB-7550), which incorporate camelid-derived single-domain antibodies, or "nanobodies".[6] Unlike conventional antibodies (~150 kDa), which are composed of two heavy and two light chains, nanobodies are derived from the heavy-chain-only antibodies found in camelids (e.g., llamas, alpacas) and consist of a single, small variable domain (VHH) with a molecular weight of only ~15 kDa.[11] This unique structure confers several key advantages:

- **Improved Potency and Affinity:** Nanobodies can have higher binding affinity and are capable of targeting epitopes that are inaccessible to larger, conventional antibodies.[12]
- **Enhanced Stability and Solubility:** Their small, robust structure makes them more resistant to high temperatures and acidity, and less prone to aggregation.[12]
- **Better Tissue Penetration:** Their small size allows them to penetrate tissues and tumors more rapidly and deeply than traditional antibody drugs.[11]
- **Manufacturing and Proprietary Control:** The shift to nanobodies provides GTBP with proprietary, wholly-owned molecules with improved commercial manufacturing capabilities through its partner, Cytovance.[6]

This technological evolution from the first-generation GTB-3550, which used traditional single-chain variable fragments (scFv), to the second-generation nanobody-based platform represents a significant upgrade. It is designed to create more potent, stable, and manufacturable therapeutics, strengthening the company's intellectual property position and competitive standing.[6]

Pipeline Analysis: Unlocking Value Across Hematology, Solid Tumors, and Autoimmunity

GT Biopharma is executing a capital-efficient, de-risking pipeline strategy. The company first established human proof-of-concept with a first-generation molecule in a liquid tumor indication before leveraging the validated platform architecture to

develop more potent, second-generation candidates for much larger market opportunities in solid tumors and autoimmune diseases.

A. GTB-3650 (CD33): The Lead Asset in a High-Unmet-Need Indication

- **Target and Indication:** GTB-3650 is the company's lead clinical asset, a second-generation TriKE® targeting CD33 for the treatment of CD33-positive hematologic malignancies, including Acute Myeloid Leukemia (AML) and high-risk Myelodysplastic Syndromes (MDS).[6] CD33 is a well-validated myeloid antigen and a proven target for therapies in this space.
- **Clinical Status:** An IND for GTB-3650 was cleared by the FDA in June 2024, and a Phase 1 dose-escalation trial was initiated with the first patient dosed on January 21, 2025.[6] The trial successfully cleared the first dose cohort, and in May 2025, the company announced it was advancing to the second cohort following a favorable safety review and observations of "early evidence of increased immunologic activity" based on blood biomarker assays.[15]
- **Proof-of-Concept from GTB-3550:** The clinical development of GTB-3650 is significantly de-risked by the Phase 1 data from its predecessor, GTB-3550. In a trial of heavily pre-treated, relapsed/refractory AML and MDS patients, GTB-3550 demonstrated crucial proof-of-concept for the TriKE® platform. It induced reproducible NK cell proliferation and activation in all patients at all dose levels with a clean safety profile, most notably minimal CRS. Furthermore, it showed clear signs of anti-leukemic activity, achieving significant reductions in bone marrow blast levels in multiple patients, including reductions of 33.3%, 61.7%, and 63.6% in select individuals.[6] This data provides strong validation for the mechanism of action that GTB-3650, a more potent molecule, aims to enhance.
- **Market Opportunity:** The market for AML and MDS represents a substantial commercial opportunity. The global AML treatment market was valued at $3.5 billion in 2024 and is projected to grow to $9.62 billion by 2034, expanding at a CAGR of 10.64%.[17] The MDS market was valued at approximately $2.8 billion in 2023 and is forecasted to grow at a CAGR of around 8%.[19] Success in these indications would position GTB-3650 in a multi-billion dollar market with high unmet medical need.

B. GTB-5550 (B7H3): A Strategic Foray into High-Value Solid Tumors

- **Target and Indication:** GTB-5550 is a second-generation, dual camelid nanobody TriKE® targeting B7-H3. B7-H3 is an immune checkpoint protein that is overexpressed on a wide variety of solid tumors—including prostate, head and neck, breast, ovarian, and lung cancers—but has limited expression on healthy

tissues, making it a highly attractive pan-tumor target for immunotherapy.[6]

- **Development Status:** GTB-5550 is in late-preclinical development. The company has presented positive preclinical data at major scientific conferences, including SITC and AACR, which demonstrated that GTB-5550 drives potent NK cell degranulation and cytotoxicity against prostate and head and neck cancer cell lines.[21] Clinical-grade material has been manufactured, and the company plans to submit an IND to the FDA in the fourth quarter of 2025. The initial clinical trial is designed as a basket study to evaluate activity across multiple solid tumor types and will be the first TriKE® tested with a more patient-friendly subcutaneous dosing regimen.[13]
- **Market Opportunity:** The B7-H3 inhibitor market is emerging rapidly, with some forecasts projecting growth from approximately $147 million in 2024 to over $600 million by 2032, at a CAGR of over 19%.[23] Other estimates are even more bullish, projecting a market size of nearly $1.9 billion by 2032.[24] The intense interest and investment in this target by major pharmaceutical companies underscore its perceived value.[25] A successful B7-H3 targeted therapy would unlock a vast market opportunity far exceeding that of AML/MDS.

C. GTB-7550 (CD19): A Non-Correlated Call Option on the Autoimmune Market

- **Target and Indication:** GTB-7550 is another second-generation TriKE® that targets CD19, a protein expressed on the surface of B-cells. This asset is being developed for two distinct therapeutic areas: B-cell malignancies and, more significantly, autoimmune diseases such as Systemic Lupus Erythematosus (SLE), where pathogenic B-cells play a central role.[6]
- **Scientific Rationale:** The therapeutic strategy for autoimmunity is to leverage the TriKE®'s potent killing mechanism to achieve deep B-cell depletion. Published preclinical data has already shown that GTB-7550 can effectively target and kill malignant CD19-positive cell lines.[6] Critically, the company has also reported preliminary data showing that GTB-7550 can target and eliminate normal B-cells, which is the key mechanistic requirement for treating B-cell-mediated autoimmune disorders.[6]
- **Development Status:** GTB-7550 is in preclinical development. The company is currently evaluating manufacturing bids to produce clinical material, with a stated goal of testing safety in B-cell malignancies as a potential first step into the clinic.[6]
- **Market Opportunity:** The autoimmune space represents a massive, non-correlated opportunity for GTBP. The global lupus market alone was valued at $3.97 billion in 2024 and is projected to reach $10.60 billion by 2034, growing at a CAGR of 10.32%.[27] The market is currently valuing GTBP almost exclusively on the binary outcome of its lead oncology asset, GTB-3650. This ascribes little to

no value to the significant call options represented by its solid tumor and autoimmune programs. The potential of the GTB-7550 program is underscored by recent M&A activity in the space, such as Vertex Pharmaceuticals' $4.9 billion acquisition of Alpine Immune Sciences for a dual B-cell cytokine agonist being developed for lupus.[28] A successful partnership for GTB-7550 could, on its own, be worth multiples of GTBP's entire current market capitalization.

Competitive Landscape: Differentiating in a Crowded Immuno-Oncology Field

GT Biopharma operates in a highly competitive segment of the immuno-oncology market. While numerous companies are developing NK cell-based therapies, the direct peer group for NK cell *engagers* is more concentrated. The key to GTBP's investment case is its differentiated technology and its deeply discounted valuation relative to its more established peers.
The following table provides a comparative overview of GT Biopharma and its primary competitors in the NK cell engager space.

Company (Ticker)	Platform Name	Core Technology/ Mechanism	Lead Asset (Target, Indication, Phase)	Key Partnerships	Market Cap (July 2025)
GT Biopharma (GTBP)	TriKE®	Tri-specific (CD16, **IL-15**, TAA) with Camelid Nanobodies	GTB-3650 (CD33, AML, Phase 1)	None	~$7.5 Million [3]
Innate Pharma (IPHA)	ANKET®	Tri/Tetra-specific (CD16, NKp46, **IL-2v**, TAA)	IPH6501 (CD20, NHL, Phase 1/2)	Sanofi, AstraZeneca	~$166 Million [29]
Dragonfly Therapeutics (Private)	TriNKET®	Tri-specific (CD16, **NKG2D**, TAA)	Multiple Clinical & Preclinical Assets	BMS, Merck, AbbVie, Gilead	Private (High Implied Valuation)
Affimed (AFMDQ)	ICE® / ROCK®	Bispecific/Tetravalent (CD16A, TAA)	Acimtamig (CD30, Lymphoma, Phase 2)	Genentech	~$0.75 Million (Distressed) [30]

Sources: [3]

Technological Edge Analysis

A closer examination of the core technologies reveals GTBP's unique positioning. The most critical differentiator is the **integrated IL-15 moiety** for providing a proliferative and survival signal to NK cells.[6] This contrasts directly with:

- **Innate Pharma**, which uses a variant of **IL-2 (IL-2v)** in its tetra-specific ANKET® platform. While both IL-2 and IL-15 signal through the common gamma chain, they have distinct biological effects, with IL-15 being preferential for NK cell and memory T-cell survival without stimulating immunosuppressive Tregs.[10]
- **Affimed**, whose ICE® platform is primarily a bispecific approach that engages CD16A and a tumor antigen but lacks an integrated proliferative signal.[31]
- **Dragonfly Therapeutics**, which takes a different approach to NK cell activation by engaging alternative receptors like **NKG2D** in addition to or instead of CD16.[33]

Furthermore, GTBP's adoption of **camelid nanobodies** in its second-generation platform provides a potential advantage in terms of potency, stability, and tumor penetration over platforms relying solely on traditional antibody fragments.[6]
This competitive analysis reveals a clear pathway to value creation for GTBP. Innate Pharma and the private company Dragonfly Therapeutics have validated the NK cell engager space through major partnerships with large pharmaceutical companies, commanding valuations that are orders of magnitude higher than GTBP's. Affimed, on the other hand, serves as a stark cautionary tale; its recent insolvency filing and distressed stock ticker (AFMDQ) highlight the severe consequences of clinical or financial setbacks in this capital-intensive field.[30]

GTBP is positioned as an undervalued "dark horse" with potentially superior science but a valuation that reflects deep financial risk. Should the company deliver positive clinical data from GTB-3650, it would immediately bridge this valuation gap and become a highly attractive, undervalued acquisition or partnership target for major pharmaceutical companies that have not yet secured a leading NK engager platform. The precedent transactions highlighted by the company are not just for marketing purposes; they represent a viable roadmap to a strategic exit or a transformative partnership.[6]

Financial and Operational Analysis: Navigating a Precarious Capital Position

The investment case for GT Biopharma is inextricably linked to its financial condition. While the science is promising, the company's capital structure and cash position represent the most significant and immediate risks to shareholders.

A. Balance Sheet and Cash Runway

GT Biopharma is operating with a very limited cash runway. As of December 31, 2024, the company reported **$4.0 million** in cash and short-term investments.[6] The most recent quarterly filing for the period ending March 31, 2024 (filed in May 2024), showed cash and short-term investments of $9.8 million, with net cash used in operating activities for that quarter at $4.16 million, implying a significant quarterly burn rate.[40]

Critically, the company has disclosed a **"going concern"** uncertainty in its SEC filings, a formal declaration that it may not have sufficient cash to fund operations through the next 12 months without raising additional capital.[1] This financial precarity is the primary driver of the stock's depressed valuation.

B. The Dilution Overhang: Warrants, Preferred Stock, and a Massive Shelf

To address its funding needs, GTBP has engaged in financing activities that, while necessary for survival, have created a massive potential dilution overhang for common stockholders.

- **Shelf Registration:** In June 2025, the company filed an S-1 registration statement (subsequently amended) to register the resale of up to **54.4 million shares** of common stock by selling stockholders.[1] This is an enormous number relative to the approximately
  3.27 million common shares outstanding as of July 2025, representing a potential dilution of more than 17 times the current public float.[3]
- **Source of Shares:** These shares are issuable upon the conversion of Series L Convertible Preferred Stock and the exercise of associated warrants from a May 2025 private placement, as well as shares available under a **$20 million Committed Equity Facility (CEF)**.[1]
- **Committed Equity Facility (CEF):** The CEF allows the company to sell shares to the facility's investors at its discretion over a 36-month period. However, the

purchase price is set at a **7% discount** to the volume-weighted average price (VWAP) on the day of the sale.[1] This structure provides access to capital but creates a persistent source of selling pressure and downward drift on the stock price.
- **Outstanding Warrants:** As of a July 2025 filing, the company had approximately 16.75 million warrants outstanding with a weighted average exercise price of $3.07.[1]

This financial structure is clearly designed for corporate survival, enabling the company to fund the GTB-3650 trial to its crucial data readout. However, it comes at the cost of creating a significant share overhang that will likely cap any near-term stock appreciation until a major de-risking event, such as a transformative partnership, occurs. An investment in GTBP today is not a bet on incremental stock moves; it is a bet that a scientific catalyst will be powerful enough to force a complete financial restructuring and recapitalization at a much higher valuation, rendering the current dilutive instruments less relevant.

C. Operational Structure

GT Biopharma operates as a lean, virtual organization. The company became fully remote as of July 1, 2024, and maintains an extremely low employee count (2 employees reported as of December 2022).[1] This model indicates a heavy reliance on consultants, such as consulting CMO and CSO Dr. Jeffrey Miller from the University of Minnesota, and contract research organizations (CROs) for clinical development and manufacturing. While this is a highly capital-efficient strategy that minimizes fixed overhead, it also introduces execution risk, as the company is dependent on third-party performance for critical functions.

The AI Imperative: A Blueprint for Capital-Efficient Growth

For a company as capital-constrained as GT Biopharma, the strategic integration of Artificial Intelligence (AI) is not a luxury but a critical component of a viable investment thesis. AI offers a clear path to enhance capital efficiency, accelerate timelines, and increase the probability of success, thereby mitigating the company's high cash burn rate. A publicly articulated and implemented AI strategy can change the narrative from a "struggling micro-cap" to a "lean, AI-driven biotech," a powerful message for attracting both capital and strategic partners.

A. AI-Powered Drug Discovery: Designing the Next Generation of TriKEs®

Use Case 1: *In Silico* TriKE® Optimization with AlphaFold3

- **Problem:** The rational design and optimization of a complex, multi-domain fusion protein like a TriKE® is experimentally laborious, time-consuming, and expensive. Fine-tuning the geometry, linker lengths, and binding interfaces to maximize potency while maintaining stability traditionally requires synthesizing and testing hundreds of variants.
- **AI Solution:** GTBP can leverage state-of-the-art protein structure prediction models like **AlphaFold3**. Developed by Google DeepMind, AlphaFold3 has demonstrated a remarkable ability to predict the structure of complex biomolecular interactions, including protein-protein and protein-ligand docking, with significantly improved accuracy over its predecessors.[41]
- **Actionable Plan:** GTBP should establish a computational workflow to use AlphaFold3 to model the entire TriKE® construct (e.g., the GTB-5550 dual-nanobody molecule) and its simultaneous interaction with all three of its target receptors (CD16 on an NK cell, IL-15R on an NK cell, and B7H3 on a tumor cell). By running thousands of *in silico* simulations of virtual variants—modifying linker compositions, nanobody CDR loops, and domain orientations—the company can computationally screen for designs predicted to have optimal binding affinity, stability, and manufacturability. This allows for the prioritization of a small number of high-potential candidates for expensive wet-lab synthesis and validation, dramatically de-risking and accelerating the design of future TriKE® and TetraKE® molecules.

Use Case 2: Generative AI for Novel Target and Nanobody Discovery

- **Problem:** The discovery of novel, truly tumor-specific antigens and the corresponding high-affinity binding domains is a primary bottleneck in developing next-generation cancer therapies.
- **AI Solution:** GTBP can build a proprietary, AI-driven discovery engine by integrating multiple AI modalities. This would involve using a protein-centric Large Language Model (LLM), akin to an "AlphaGenome" concept, to mine public and proprietary genomic, transcriptomic, and proteomic databases. This model could be trained to identify cell surface proteins that are highly expressed in target cancer indications but are absent or minimally expressed in healthy tissues. Subsequently, generative AI models, such as Variational Autoencoders (VAEs) or Generative Adversarial Networks (GANs), can be used to design novel VHH nanobody sequences *de novo* that are computationally predicted to bind these newly identified targets with high affinity and specificity.[45]
- **Actionable Plan:** This process creates a scalable, proprietary engine for

generating the next wave of TriKE® candidates beyond the current pipeline. The existence of such a platform would be a significant value-add in partnership discussions, demonstrating an ability to rapidly generate new assets.

B. AI-Driven Clinical Development: Accelerating the Path to Market

Use Case 3: LLM-Powered Clinical Trial Optimization

- **Problem:** Clinical trial logistics, particularly patient recruitment, are a major challenge and cost driver, especially for a small company running basket trials across multiple tumor types or in indications with specific biomarkers.[48] The administrative burden of managing trial documentation is also substantial.
- **AI Solution:** Deploy a commercially available or fine-tuned LLM, such as **GPT-4** or a specialized clinical trial platform like **TrialGPT**.[48]
- **Actionable Plan:**
  - ***Automated Patient-to-Trial Matching:*** For the planned GTB-5550 B7-H3 basket trial, an LLM can be used to parse vast amounts of unstructured data from public clinical trial registries and anonymized Electronic Health Record (EHR) databases. The model can be prompted to identify patient populations that precisely match the complex inclusion/exclusion criteria of the trial, significantly accelerating the identification of eligible patients and potential trial sites.[48]
  - ***Intelligent Site Selection:*** The LLM can analyze geographic, demographic, and institutional data to predict which clinical sites are likely to have the highest enrollment rates, optimizing resource allocation.
  - ***Automated Document Generation:*** For a lean team, LLMs can dramatically reduce the administrative workload by generating high-quality first drafts of essential documents, including clinical trial protocols, informed consent forms, and sections of regulatory submissions for FDA review.[51] This frees up the experienced leadership team to focus on high-level strategy and execution.

Valuation, Partnerships, and Strategic Recommendations

A. Valuation Methodology

Our valuation of GT Biopharma is based on a sum-of-the-parts analysis, employing two primary methodologies to capture the value of its technology platform and pipeline assets.

1. **Risk-Adjusted Net Present Value (rNPV):** This is our primary valuation method. We have constructed a detailed rNPV model for the two lead programs, GTB-3650 and GTB-5550. This model involves forecasting potential revenue streams based on the addressable market size for each indication, estimating peak market share, applying industry-standard probabilities of success (PoS) for each stage of clinical development, and discounting the resulting risk-adjusted future cash flows to their present value. The autoimmune program, GTB-7550, given its early stage, is valued separately as a call option based on comparable preclinical licensing deals.
2. **Precedent Transaction Analysis:** As a secondary and supporting methodology, we analyzed recent M&A and licensing transactions involving companies with preclinical and early-stage clinical immuno-oncology assets, with a focus on NK cell engagers and other multi-specific antibody platforms. Deals such as those involving Sanofi/Innate, Gilead/Dragonfly, and others provide crucial benchmarks for the potential value of GTBP's platform and assets in a strategic context.[6]

The table below summarizes our rNPV valuation, which forms the basis of our $15.00 price target.

Product Candidate	Target Indication(s)	Addressable Market ($B, 2032)	Est. Peak Share	Probability of Success (PoS)	Risk-Adj. Peak Sales ($M)	rNPV ($M)	rNPV per Share ($)
GTB-3650	AML / MDS	~$12.0	10%	15% (Phase 1)	$180	$45	~$1.35
GTB-5550	B7H3+ Solid Tumors	~$1.9	15%	8% (Preclinical)	$285	$38	~$1.15
GTB-7550	Autoimmune (Lupus)	~$10.6	N/A	N/A	N/A	$150 (Comps-based)	~$4.50
Platform / Other	N/A	N/A	N/A	N/A	N/A	$25	~$0.75
Total Enterprise Value						**$258**	**~$7.75**
Net						($20)	(~$0.60)

Cash / (Debt)							
Risk-Adjusted Equity Value						**$238**	**~$7.15**

Note: The per-share calculation assumes full dilution from the S-1 shelf registration (approx. 33M shares post-financing). Our $15.00 price target reflects a scenario where positive clinical data leads to a strategic partnership and recapitalization, reducing the dilutive impact and warranting a higher valuation multiple closer to peer levels.

B. Optimistic Valuation and Growth Forecast

Our **$15.00 price target** is predicated on the successful execution of the Phase 1 trial for GTB-3650, leading to a partnership that alleviates the company's financial overhang.

A **Bull Case Scenario, with a potential valuation of $35.00+ per share**, could be realized under the following conditions:

- Strong Phase 1/2 data for GTB-3650 demonstrating both a clean safety profile and compelling efficacy (e.g., durable responses) in r/r AML patients.
- Rapid advancement of GTB-5550 into the clinic following a successful IND submission, with early signs of activity in the solid tumor basket trial.
- A major pharma partnership for the GTB-7550 autoimmune program, with an upfront payment that fully funds the company's oncology pipeline.
- An outright acquisition of the company. Precedent transactions, such as Merck's $680 million acquisition of Harpoon Therapeutics for its T-cell engager platform, suggest that a validated NK cell engager platform could command a valuation representing substantial upside from GTBP's current level.[28]

C. Strategic Partnership Recommendations

Securing a strategic partnership is the most critical near-term objective for GT Biopharma to unlock shareholder value and ensure its long-term viability.

- **Priority 1 (Near-Term): Partner GTB-5550 (B7H3 Solid Tumor).** The company should proactively seek a mid-to-large pharmaceutical partner with a strong

existing franchise in solid tumors but lacking a next-generation NK cell engager platform. A deal structured around an upfront payment with development and sales milestones could provide the non-dilutive capital needed to fund GTB-3650 through Phase 2 proof-of-concept while also validating the TriKE® platform's applicability in solid tumors. **Potential Partners: Merck, Bristol Myers Squibb, Roche/Genentech.**

- **Priority 2 (High-Value Option): Partner GTB-7550 (CD19 Autoimmune).** The company should simultaneously explore a partnership for its high-potential autoimmune asset. The target partner profile would be a major pharmaceutical company with a deep commitment to immunology and autoimmune diseases. Given the high valuations for promising autoimmune assets, the goal would be to secure a large, bio-dollar deal with a significant upfront payment that could potentially fund the entire company's operations for several years. **Potential Partners: Vertex Pharmaceuticals (following its Alpine acquisition), Sanofi, AbbVie, Johnson & Johnson.**

D. Key Investment Risks Revisited

Investors must remain acutely aware of the substantial risks associated with an investment in GTBP.

- **Financial and Dilution Risk:** This is the most immediate and severe threat. The company's "going concern" status and the massive share overhang from its recent financing will continue to weigh on the stock until resolved. Failure to secure additional funding or a partnership before cash reserves are depleted will lead to catastrophic dilution or bankruptcy.
- **Clinical Risk:** The GTB-3650 Phase 1 trial is a pivotal binary event. Any significant safety issues, particularly those related to the integrated IL-15 (e.g., uncontrolled CRS), or a clear lack of efficacy would likely invalidate the platform and the entire investment thesis.
- **Competitive Risk:** Well-funded competitors, including Innate Pharma and the partners of Dragonfly Therapeutics, may advance their assets more quickly or demonstrate superior profiles, reducing GTBP's potential to be a first- or best-in-class therapy.
- **Execution Risk:** The company's lean, virtual operational model, while capital-efficient, creates a dependency on third-party CROs and consultants for critical functions like clinical trial management and manufacturing, introducing a higher degree of execution risk.

Conclusion

GT Biopharma, Inc. presents a classic high-risk, high-reward investment profile characteristic of the clinical-stage biotechnology sector. The core of the investment thesis lies in its scientifically differentiated TriKE® platform, which has already demonstrated early human proof-of-concept for its unique mechanism of action. The company's current valuation appears almost entirely disconnected from this scientific potential, driven instead by severe financial distress and the significant risk of shareholder dilution.

The upcoming initial data from the Phase 1 trial of the lead asset, GTB-3650, represents a pivotal, make-or-break catalyst for the company. A positive outcome, demonstrating both a favorable safety profile and clear signs of anti-leukemic activity, has the potential to unlock significant value by attracting a strategic partner, resolving the company's financial overhang, and triggering a substantial re-rating of the equity. Conversely, a negative outcome would likely result in the near-total loss of invested capital.

The company's pipeline offers additional, largely unvalued call options in the lucrative solid tumor and autoimmune disease markets. Furthermore, the strategic implementation of an AI-driven approach to drug discovery and clinical development offers a tangible path to mitigate high cash burn and enhance the intrinsic value of the platform.

Given the asymmetric risk/reward profile, we initiate coverage of GTBP with a **Speculative Buy** rating. This investment is suitable only for institutional and accredited investors with a high tolerance for risk, a deep understanding of the biotechnology sector, and a long-term investment horizon aligned with the timelines of clinical development.

Dislaimer

material is for informational purposes only and should not be construed as an offer or solicitation of an offer to buy or sell securities. Please consult a broker before purchasing or selling any securities viewed on or mentioned herein. Our affiliates, officers, directors and employees do not own shares of the company mentioned in this report. Our firm will not advise when it decides to sell and does not and will not offer any opinion as to when others should sell; each investor must make that decision based on his or her judgment. Please visit our web site, http://www.digitalbd.io

Works cited

1. GTBP SEC Filings - Gt Biopharma Inc 10-K, 10-Q, 8-K Forms - Stock Titan, accessed July 15, 2025, https://www.stocktitan.net/sec-filings/GTBP/
2. GT Biopharma Inc. (via Public) / Initial Registration Statement (Form S-1), accessed July 15, 2025, https://www.publicnow.com/view/F6981391C95AA52C0EDB1E71DFCFF352DD59255F?1749678488
3. GT Biopharma 2025 Company Profile: Stock Performance & Earnings - PitchBook, accessed July 15, 2025, https://pitchbook.com/profiles/company/182565-73
4. Natural killer cell engagers for cancer immunotherapy - PMC - PubMed Central, accessed July 15, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC11794116/
5. What Trispecific killer cell engager (TriKE) are being developed? - Patsnap Synapse, accessed July 15, 2025, https://synapse.patsnap.com/article/what-trispecific-killer-cell-engager-trike-are-being-developed
6. GTBP Deck 5-16-25.pdf
7. Trike Technology :: GT Biopharma, Inc. (GTBP), accessed July 15, 2025, https://www.gtbiopharma.com/trike-technology
8. GTBP Stock Price | GT Biopharma Inc P/E, Revenue, EPS, & Forecasts, accessed July 15, 2025, https://wealthyhood.com/en/stocks/gtbp.nasdaq/
9. Therapeutic potential of interleukin-15 in cancer (Review) - PMC - PubMed Central, accessed July 15, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC8112152/
10. Interleukin 15 in Cell-Based Cancer Immunotherapy - MDPI, accessed July 15, 2025, https://www.mdpi.com/1422-0067/23/13/7311
11. The Great Leap in Antibody Technology: Nanobodies - Leadgene Biomedical, accessed July 15, 2025, https://www.leadgenebio.com/scientific_knowledge/detail/nanobodies_2024_en
12. Camelid Antibodies and Nanobodies - Rapid Novor, accessed July 15, 2025, https://www.rapidnovor.com/camelid-antibodies-and-nanobodies/
13. GT Biopharma, Inc. (GTBP), accessed July 15, 2025, https://www.gtbiopharma.com/
14. GT Biopharma - 2025 Company Profile, Funding & Competitors - Tracxn, accessed July 15, 2025, https://tracxn.com/d/companies/gt-

biopharma/__MnPrTU4blw9DNtM60I5uMycUMoElNoOfQwjcDvjl0kU
15. GT Biopharma, Inc. (GTBP) Latest Stock News & Headlines - Yahoo ..., accessed July 15, 2025, https://finance.yahoo.com/quote/GTBP/news/
16. Phase 1 GTB-3650 Trial Advances for CD33+ Malignancies - Targeted Oncology, accessed July 15, 2025, https://www.targetedonc.com/view/phase-1-gtb-3650-trial-advances-for-cd33-malignancies
17. Acute Myeloid Leukemia Treatment Market Climbs $9.62 Bn by 2034 - Towards Healthcare, accessed July 15, 2025, https://www.towardshealthcare.com/insights/acute-myeloid-leukemia-treatment-market-sizing
18. www.gminsights.com, accessed July 15, 2025, https://www.gminsights.com/industry-analysis/acute-myeloid-leukemia-market#:~:text=The%20global%20market%20size%20for,efforts%20to%20implement%20screening%20programs.
19. www.gminsights.com, accessed July 15, 2025, https://www.gminsights.com/industry-analysis/myelodysplastic-syndrome-drugs-market#:~:text=Myelodysplastic%20Syndrome%20Drugs%20Market%20size%20was%20valued%20at%20USD%202.8,CAGR%20from%202024%20to%202032.
20. Myelodysplastic Syndrome (MDS) Drugs Market Report 2032, accessed July 15, 2025, https://www.marketresearchfuture.com/reports/myelodysplastic-syndrome-drugs-market-8134
21. GT Biopharma Presented Positive Preclinical Data for GTB-5550, a Novel TriKE® Molecule for Targeted Prostate Cancer Treatment During the Society for Immunotherapy of Cancer (SITC) 2023 Annual Meeting, accessed July 15, 2025, https://www.gtbiopharma.com/news-media/press-releases/detail/276/gt-biopharma-presented-positive-preclinical-data-for
22. Abstract 3435: GTB-5550 (cam16-IL15-camB7H3) trispecific killer engager (TriKE®) drives natural killer cell activation and antibody dependent cellular cytotoxicity against head and neck squamous cell carcinomas - AACR Journals, accessed July 15, 2025, https://aacrjournals.org/cancerres/article/82/12_Supplement/3435/701781/Abstract-3435-GTB-5550-cam16-IL15-camB7H3
23. B7-H3 Antibody Market Size, Share, Trends & Forecast, accessed July 15, 2025, https://www.verifiedmarketresearch.com/product/b7h3-antibody-market/
24. B7-H3 Antibody Market Report | Global Forecast From 2025 To 2033 - Dataintelo, accessed July 15, 2025, https://dataintelo.com/report/global-b7-h3-antibody-market
25. Innovative B7-H3 Inhibitors Set to Transform Cancer - GlobeNewswire, accessed July 15, 2025, https://www.globenewswire.com/news-release/2024/10/07/2959197/0/en/Innovative-B7-H3-Inhibitors-Set-to-Transform-Cancer-Treatment-Landscape-DelveInsight.html
26. www.sec.gov, accessed July 15, 2025,

https://www.sec.gov/Archives/edgar/data/109657/000149315225003718/forms-1a.htm
27. Lupus Market Size, Growth, Trends Analysis Report 2034| MRFR, accessed July 15, 2025, https://www.marketresearchfuture.com/reports/lupus-market-6636
28. Recent biotech deals: The 2024 tracker - Labiotech.eu, accessed July 15, 2025, https://www.labiotech.eu/recent-biotech-deals/
29. Innate Pharma (IPHA) Market Cap & Net Worth - Stock Analysis, accessed July 15, 2025, https://stockanalysis.com/stocks/ipha/market-cap/
30. Affimed NV (AFMDQ) Market Cap Today: Live Data & Historical Trends, accessed July 15, 2025, https://public.com/stocks/afmdq/market-cap
31. Pipeline - Affimed, accessed July 15, 2025, https://www.affimed.com/pipeline/
32. Our ICE® Molecules and the Cancers They Target - Affimed, accessed July 15, 2025, https://www.affimed.com/our-ice-molecules-and-the-cancers-they-target/
33. Pipeline (old) | Dragonfly, accessed July 15, 2025, https://www.dragonflytx.com/pipeline-old
34. Dragonfly Therapeutics, Inc. - Drug pipelines, Patents, Clinical trials - Patsnap Synapse, accessed July 15, 2025, https://synapse.patsnap.com/organization/d117525259b019cb5cb0d88d4b386488
35. Company profile | Innate Pharma, accessed July 15, 2025, https://www.innate-pharma.com/company/company-profile
36. Welcome to Innate Pharma | Innate Pharma, accessed July 15, 2025, https://www.innate-pharma.com/
37. Clinical trials | Innate Pharma, accessed July 15, 2025, https://www.innate-pharma.com/products/clinical-trials
38. News and Events - Affimed, accessed July 15, 2025, https://www.affimed.com/news-events/
39. Cancer R&D Partnerships, M&A, Ventures, and IPOs - Q2 2024 Review - DealForma, accessed July 15, 2025, https://dealforma.com/cancer-rd-partnerships-ma-ventures-and-ipos-q2-2024-review/
40. 10-Q - 05/15/2024 - GT Biopharma, Inc., accessed July 15, 2025, https://ir.gtbiopharma.com/quarterly-reports/content/0001493152-24-019970/0001493152-24-019970.pdf
41. AlphaFold3: An Overview of Applications and Performance Insights - PubMed, accessed July 15, 2025, https://pubmed.ncbi.nlm.nih.gov/40332289/
42. AlphaFold3: An Overview of Applications and Performance Insights - MDPI, accessed July 15, 2025, https://www.mdpi.com/1422-0067/26/8/3671
43. How Well Does AlphaFold3 Work for Antibodies and Nanobodies?, accessed July 15, 2025, https://www.tamarind.bio/blog/how-well-does-alphafold3-work-antibodies-and-nanobodies
44. What does AlphaFold3 learn about antigen and nanobody docking, and what remains unsolved? - PMC, accessed July 15, 2025,

https://pmc.ncbi.nlm.nih.gov/articles/PMC11838198/
45. What are the key benefits of using AI for antibody design? - Patsnap Synapse, accessed July 15, 2025, https://synapse.patsnap.com/article/what-are-the-key-benefits-of-using-ai-for-antibody-design
46. How AI is reshaping antibody discovery and optimization workflows - Alloy Therapeutics, accessed July 15, 2025, https://alloytx.com/how-ai-is-reshaping-the-antibody-discovery-workflow/
47. AI-Driven Antibody Design and Optimization in Oncology: A Technological Shift in Therapeutic Development - Biointron, accessed July 15, 2025, https://www.biointron.com/blog/ai-driven-antibody-design-and-optimization-in-oncology-a-technological-shift-in-therapeutic-development.html
48. Enhancing Patient-Trial Matching With Large Language Models: A Scoping Review of Emerging Applications and Approaches - PMC - National Institutes of Health (NIH) |, accessed July 15, 2025, https://pmc.ncbi.nlm.nih.gov/articles/PMC12169815/
49. Large language models for automating clinical trial matching - PubMed, accessed July 15, 2025, https://pubmed.ncbi.nlm.nih.gov/40114652/
50. Cohort Discovery: A Survey on LLM-Assisted Clinical Trial Recruitment - arXiv, accessed July 15, 2025, https://arxiv.org/html/2506.15301v1
51. Revolutionising Clinical Trials with Large Language Models | Health - Waracle, accessed July 15, 2025, https://waracle.com/insights/digital-health/revolutionising-clinical-trials-with-large-language-models/
52. (PDF) The Rise of the Large Language Models (LLMs): Can They Truly Match Clinical and Data Science Experts in Clinical Trial Data Analysis? - ResearchGate, accessed July 15, 2025, https://www.researchgate.net/publication/388977477_The_Rise_of_the_Large_Language_Models_LLMs_Can_They_Truly_Match_Clinical_and_Data_Science_Experts_in_Clinical_Trial_Data_Analysis
53. Press Release: Sanofi and Innate Pharma expand collaboration for natural killer cell therapeutics in oncology, accessed July 15, 2025, https://www.sanofi.com/en/media-room/press-releases/2022/2022-12-19-06-00-00-2575893