

**Category**

Best Startup

**General Information****Company Name \***

Gatehouse Bio, Inc.

**Turnover and/or Funding**

Since its founding in 2017, Gatehouse Bio has raised over \$17 million in dilutive capital from top-tier investors including SOSV, IndieBio, Claritas Capital, Front Row Fund, and The Sharp Family.

In parallel, since 2020, the company has generated more than \$5 million in revenue through collaborations and partnerships with leading pharmaceutical companies such as AstraZeneca, AbbVie, and Sanofi, as well as with prominent disease foundations including the Alzheimer's Drug Discovery Foundation (ADDF) and the CHDI Foundation.

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**Sub-Category \***

Biotechnology

**Background**

**Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions)  
(please be as specific as possible in your description; limit 500 words)**

Gatehouse Bio was founded in 2017 with the mission to unlock the therapeutic and diagnostic potential of non-coding RNAs, focusing particularly on microRNAs and their isomiRs - small RNA variants that fine-tune gene expression and underlie diverse disease processes. Headquartered in Boston, Massachusetts, the company emerged from pioneering academic work on microRNA biology and has since evolved into a precision medicine company at the forefront of RNA biomarker discovery and oligonucleotide drug development.

At the heart of Gatehouse Bio's approach is its Code-Breaker™ Platform, which uses machine learning to identify disease-associated isomiRs for precise patient stratification, and artificial intelligence to biologically model their role in disease. Applied in drug-treated patients, this technology can predict drug response, toxicity, and placebo effect - paving the way for better patient selection and outcome prediction. Importantly, the platform also enables the design of precision oligonucleotide therapies from the ground up, creating a fully integrated pipeline for both therapeutic and companion diagnostic development.

Key milestones include:

2019: Development of the Code-Breaker™ Platform for high-resolution isomiR discovery and functional annotation, addressing a major blind spot in RNA biology.

2020: Launch of revenue-generating partnerships with major pharmaceutical companies, including AstraZeneca, AbbVie, and Sanofi, focused on identifying novel RNA biomarkers in pulmonary, cardiovascular, neurological, metabolic, and rare diseases.

2021: Strengthening collaborations with disease foundations, including the Alzheimer's Drug Discovery Foundation (ADDF) and the CHDI Foundation.

2023: Expansion into therapeutics, creating GHB1589, the first precision oligonucleotide therapeutic designed to treat idiopathic pulmonary fibrosis (IPF), supported by a Translational Research Grant from AnaBios.

To date, Gatehouse Bio has raised over \$17 million in dilutive capital from leading investors (SOSV, IndieBio, Claritas Capital, Front Row Fund, and The Sharp Family) and has generated over \$5 million in revenue from industry partnerships.

Gatehouse Bio's flagship program targets idiopathic pulmonary fibrosis (IPF), a devastating interstitial lung disease affecting approximately 3 million people worldwide and 130,000 in the United States. IPF causes progressive lung scarring that impairs gas exchange, leading to respiratory failure and death within 3-5 years of onset.

Current therapies (pirfenidone and nintedanib) offer modest benefit by slowing lung function decline but do not halt or reverse disease progression. Lung transplantation remains the only curative option but is available to few patients. There is a profound need for therapies that directly address the molecular drivers of fibrosis, improve survival, and enhance quality of life.

Beyond IPF, Gatehouse Bio's platform extends to diseases such as Alzheimer's disease, Huntington's disease, multiple sclerosis, and heart failure, where it collaborates with industry partners to identify dysregulated microRNAs in drug-treated patients and advance early discovery programs. By harnessing isomiR biology, Gatehouse Bio uncovers novel drug targets, develops first-in-class oligonucleotide therapies, and creates predictive biomarkers to stratify patients and monitor therapeutic response.

With its unique integration of machine learning, molecular biology, and therapeutic development, Gatehouse Bio aims to deliver transformative, precision-engineered solutions for patients lacking effective treatment options.

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**History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations) \***

**(please be as specific as possible in your description; 500 words)**

Gatehouse Bio's flagship therapeutic program, GHB1589, represents the first precision oligonucleotide therapy designed to treat idiopathic pulmonary fibrosis (IPF) by targeting disease-associated isomiRs, a novel class of microRNA sequence variants that regulate gene expression. The development of GHB1589 and the underlying Code-Breaker™ Platform emerged from proprietary intellectual property covering the discovery, characterization, and therapeutic targeting of isomiRs, a space largely invisible to conventional transcriptomic and bioinformatic approaches.

The Code-Breaker™ Platform integrates machine learning algorithms trained on large-scale patient datasets to identify dysregulated isomiRs, stratify patient subpopulations, and model their functional role in disease pathways. Using these insights, Gatehouse Bio has advanced multiple therapeutic programs, with GHB1589 being the most advanced. Preclinical development has been supported by funding from partners including AstraZeneca, AbbVie, and Sanofi, as well as grants from AnaBios, the ADDF, and CHDI. Collectively these partnerships have fueled Gatehouse with over 30,000 proprietary patient samples for analysis.

In preclinical studies, GHB1589 demonstrated the ability to reverse established fibrotic gene expression signatures in animal and human lung slice models, with marked reductions in collagen deposition,  $\alpha$ -SMA expression, and profibrotic cytokines such as TGF $\beta$ . Importantly, these effects were observed at nanomolar concentrations, suggesting potent target engagement and therapeutic potential. Gatehouse Bio has also developed pharmacokinetic and pharmacodynamic models supporting dose selection and translational alignment with planned clinical trials.

The intellectual property portfolio includes issued and pending patents covering:

- Identification and annotation of isomiRs as disease biomarkers;
- Use of isomiRs in patient stratification, companion diagnostics, and drug response prediction;
- Design and application of isomiR-targeted oligonucleotide therapeutics.

Gatehouse Bio has expanded its development collaborations beyond IPF into neurology and cardiovascular diseases, working with pharmaceutical companies and disease foundations to uncover novel RNA-based biomarkers of disease activity, treatment response, and toxicity. Notable collaborations include projects with the Alzheimer's Drug Discovery Foundation (ADDF) to identify microRNA signatures in Alzheimer's disease and the CHDI Foundation for Huntington's disease, where early discovery work has revealed novel RNA-based targets for therapeutic exploration.

The company's preclinical platform integrates molecular biology, bioinformatics, and drug discovery capabilities, enabling an end-to-end pipeline from target identification to lead optimization. This includes in vitro screening, ex vivo human tissue models, in vivo efficacy and toxicology studies, and preparation for IND-enabling studies. Gatehouse Bio is currently advancing GHB1589 toward IND submission, with toxicology studies, CMC development, and regulatory engagement planned for the next phase.

By pioneering the integration of isomiR biology into precision medicine, Gatehouse Bio aims to deliver a first-in-class therapeutic approach that not only addresses the unmet needs in IPF but establishes a scalable platform for RNA-targeted drug discovery across a range of complex diseases.

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**Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition \***

Gatehouse Bio's Code-Breaker™ Platform represents a groundbreaking advance in precision medicine by unlocking the diagnostic and therapeutic potential of isomiRs, a largely unexplored class of microRNA sequence variants that fine-tune gene expression. While traditional RNA analyses overlook isomiRs, dismissing them as technical artifacts or noise, Gatehouse Bio has demonstrated that these variants carry critical regulatory functions that underlie disease pathogenesis, patient heterogeneity, and therapeutic response.

The Code-Breaker™ Platform integrates advanced machine learning and artificial intelligence algorithms with proprietary molecular datasets to systematically identify disease-associated isomiRs, stratify patient populations, and predict their contribution to disease biology. This approach enables two transformative applications: (1) identifying RNA biomarkers for patient selection, response prediction, and toxicity monitoring, and (2) designing first-in-class oligonucleotide therapeutics that directly target pathogenic isomiRs and their downstream pathways.

The platform's innovation lies not only in its novel biology but in its integration of computational and experimental methods. By combining in silico prediction, in vitro validation, ex vivo modeling in human tissues, and in vivo preclinical testing, Code-Breaker™ creates a scalable framework for rapid target discovery, drug development, and companion diagnostic design - a major advance over traditional drug discovery pipelines that often rely on limited genomic markers or single-modality approaches.

The most advanced therapeutic to emerge from this platform is GHB1589, the first precision oligonucleotide therapy targeting isomiRs implicated in idiopathic pulmonary fibrosis (IPF). IPF is a devastating lung disease characterized by relentless scarring and progressive respiratory failure, with median survival of just 3-5 years after diagnosis. Current therapies offer only modest benefit and fail to address the root molecular drivers of fibrosis.

GHB1589 is uniquely designed to reverse fibrotic gene expression programs by silencing disease-associated isomiRs identified through the Code-Breaker™ Platform. Preclinical data from human lung slice models show that GHB1589 potently reduces collagen deposition,  $\alpha$ -SMA expression, and TGF- $\beta$ 1 signaling, key hallmarks of fibrosis. Unlike broad-acting antifibrotics, GHB1589 offers a targeted, precision approach that holds promise to not only slow disease progression but potentially restore lung health - a transformational advance for patients with no curative options.

The innovation embodied by Gatehouse Bio has broad implications for the future of RNA-targeted therapeutics. Beyond IPF, the Code-Breaker™ Platform is being applied to neurodegenerative, cardiovascular, metabolic, and rare diseases, where pathogenic microRNA networks play critical but poorly understood roles. By charting the "dark matter" of the transcriptome - the vast landscape of isomiRs - Gatehouse Bio opens a new frontier for understanding complex diseases, designing tailored interventions, and moving toward a future where medicines are matched to the molecular profile of each patient.

Together, the Code-Breaker™ Platform and GHB1589 exemplify the next generation of precision medicines: scientifically rigorous, computationally driven, and patient-centered - with the potential to profoundly improve the human condition.

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**Please provide appropriate references (PubMed, Abstract, Website) \***

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**Publications:**

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\*Kindly clearly label your files with company name and asset name.