

Insilico Medicine

Category:

Best Startup

Company Name:

Insilico Medicine

Turnover and/or Funding:

>\$500M Raised to date

Sub-Category:

Biotechnology

Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):

Headquartered in Cambridge, MA, Insilico is a globally leading end-to-end generative AI-driven biotechnology company, focused on accelerating drug discovery and development through our proprietary Pharma.AI platform. Our mission is to bring innovative, high-quality therapeutics to patients more efficiently by integrating AI across biology, chemistry, and clinical development.

At the core of our innovation is Pharma.AI, our platform composed of interconnected engines: PandaOmics for AI-driven target discovery, Chemistry42 for generative small molecule design, and InClinico for predictive analytics and trial design. This integrated platform enables rapid, cost-effective development of therapeutics and has been externally validated through partnerships with 10 of the top 20 global pharmaceutical companies, as well as collaborations with leading academic institutions. As of today, the platform has powered the creation of over 30 therapeutic programs, and Insilico has already completed multiple out-licensing agreements, demonstrating our value as both a discovery engine and a business growth driver.

Insilico's lead asset is rentosertib (ISM001-055), a completely novel TNIK inhibitor developed entirely in-house. Rentosertib is one of the most clinically advanced AI-discovered therapeutics in the world to date. The program began with PandaOmics, which mined multi-omics data, biomedical literature, and clinical datasets to identify TNIK (TRAF2- and NCK-interacting kinase) as a high-confidence, novel target involved in

idiopathic pulmonary fibrosis (IPF) - a progressive and fatal lung disease with limited treatment options.

Following target selection, Chemistry42 generated a series of novel TNIK inhibitors using deep generative models, including GANs and reinforcement learning. These compounds were scored for novelty, potency, selectivity, and drug-like properties, leading to the nomination of rentosertib. In less than 30 months from target discovery, the program progressed through preclinical studies and early trials, eventually culminating in a successful Phase IIa clinical trial.

The Phase IIa trial demonstrated clinically meaningful improvements in lung function and confirmed a favorable safety profile - strong indicators of rentosertib's potential as a first-in-class IPF therapy. Recently, the Center for Drug Evaluation (CDE) in China granted Breakthrough Therapy Designation, fast-tracking its development and reinforcing its potential clinical impact. Rentosertib also received an official USAN name, marking it as a validated AI-derived drug candidate advancing toward pivotal trials.

The development of rentosertib not only validates the predictive and generative power of Pharma.AI but also reflects the platform's ability to deliver truly novel therapeutics on accelerated timelines. Unlike traditional approaches to drug development, our integrated AI workflow continuously learns from new data, enabling faster iterations and increasing predictive accuracy across programs.

Insilico has also established robust business development capabilities, securing over \$3.5 billion in potential deal value through pipeline out-licensing and drug discovery collaborations with partners including Sanofi, Fosun Pharma, Exelixis, Menarini, etc. These partnerships not only generate non-dilutive revenue but also validate our science and platform through milestone achievements and continued expansion.

With rentosertib advancing toward pivotal studies, a broad pipeline of novel assets in oncology, immunology, fibrosis, and aging-related diseases, and a continually learning AI engine at our core, Insilico Medicine is redefining how medicines are discovered, developed, and brought to patients.

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

Insilico's lead program, rentosertib, is a first-in-class, AI-discovered small molecule targeting TNIK, identified by our proprietary Pharma.AI platform. Developed for the treatment of idiopathic pulmonary fibrosis, rentosertib has become the most clinically advanced example of an end-to-end AI-driven drug, progressing from target discovery

to Phase IIa data in under 30 months.

The TNIK target was identified using PandaOmics, which integrates transcriptomic, proteomic, clinical, and literature data to uncover novel disease mechanisms. TNIK, previously underexplored in fibrosis, emerged as a top-ranked target due to its role in fibrotic and immune signaling pathways. Once selected, Chemistry42, rapidly designed and optimized small molecules against TNIK, nominating rentosertib after evaluating millions of structures based on potency, selectivity, and safety profiles. This AI-driven discovery and development process from target identification to clinical validation was recently detailed in a peer-reviewed publication in Nature Biotechnology, marking a milestone for the field and reinforcing the validation of this end-to-end approach.

Preclinical studies confirmed rentosertib's ability to modulate fibrotic pathways, reduce collagen deposition, and reverse lung fibrosis in animal models. Within 18 months, the program moved from target nomination to IND-enabling studies, which is a timeline less than half the industry average. It was then advanced into further clinical programs.

In a recently completed Phase IIa trial, patients with IPF were treated with three dose levels of rentosertib or placebo for 12 weeks. The study demonstrated promising safety and tolerability across all doses. Most importantly, rentosertib produced a dose-dependent improvement in lung function, as measured by forced vital capacity (FVC) - the gold-standard endpoint in IPF.

Patients receiving the highest dose (60 mg QD) experienced a mean FVC increase of +98.4 mL, while those on placebo declined by -20.3 mL. Among patients not on background antifibrotics, the improvement was even greater - +187.8 mL, exceeding the minimal clinically important difference. Proteomic analyses further validated target engagement and mechanism of action. Patients treated with rentosertib showed marked downregulation of fibrosis-associated proteins as well as suppression of extracellular matrix and immune-related pathways. These biological signals support the hypothesis that TNIK is a critical node in IPF pathology and that rentosertib is effectively modulating it.

These results were recently published by Nature Medicine this June, highlighting how rentosertib not only halts decline but may actively restore lung function, an outcome rarely observed in IPF trials. This marks a pioneering step for both AI-driven drug discovery and the advancement of innovative therapies. The historical milestone marks the first-ever published proof-of-concept, with promising safety and efficacy results, of a drug discovered and designed using generative AI. Our platform continues to generate novel assets across fibrosis, oncology, and aging-related diseases, with 10 receiving IND clearance, rentosertib stands as our most advanced program and a proof point that AI can transform how new medicines are created and brought to patients.

Insilico is currently engaging with regulators in China and the USA to design and initiate

pivotal trials for rentosertib, with the goal of advancing the first fully AI-discovered therapy toward regulatory approval and clinical use globally.

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

Rentosertib represents a novel breakthrough not only for patients suffering from idiopathic pulmonary fibrosis (IPF), but for the way we think about discovering and advancing new medicines. Its innovation is highlighted both by what the drug is, a first-in-class therapeutic targeting a highly novel biological mechanism, and how it was created through a fully AI-driven process. This dual significance gives rentosertib far-reaching implications for science and the biotech/pharmaceutical industry.

Most drugs in fibrosis target well-known pathways and rely on years of incremental research. Rentosertib challenges that model by introducing a mechanism not previously associated with fibrosis in clinical development. Insilico's technology and rentosertib also challenge the structure of traditional drug discovery itself. Developed entirely through a generative AI system, rentosertib emerged from an R&D process that used advanced neural networks to sift through massive datasets, generate novel hypotheses, design drug-like molecules, and guide decision-making through preclinical and early clinical stages.

Rentosertib has already demonstrated that its new approach can yield meaningful outcomes in the clinic. What makes this important is not just that the drug has worked but that the process behind it has begun to be validated. By showing that AI can go from discovery to clinical data in a fraction of the time and cost of traditional methods. The story of rentosertib opens the door to solving other diseases previously deemed too complex, expensive, or difficult to discover and develop.

In general, broader implications for research are great. If a fraction of the efficiency achieved with rentosertib and Insilico's other programs can be replicated across other programs, it would represent a structural shift in the economics of drug development. Therapeutic areas that are data-rich but mechanism-poor like those of neurodegeneration, rare diseases, and aging-related conditions, stand to benefit most. Additionally, barriers to entry for discovering first-in-class drugs could be significantly lowered, making it feasible for more organizations and even countries to address important drug discovery needs.

IPF is a progressive, fatal disease that currently has no curative therapies. For many, it means watching their lung function decline year over year, with little hope of reversal. A therapy that can meaningfully improve lung capacity, even modestly, could translate into more mobility, less oxygen dependency, and a higher quality of life. Rentosertib is being developed with that human outcome in mind and has the real opportunity to improve the standard of care across IPF.

As the first AI-discovered fibrosis therapy to reach mid-stage trials with promising efficacy and safety signals, rentosertib serves as a template for what is possible with AI-drive drug discovery.

Please provide appropriate references (PubMed, Abstract, Website):

Website: <https://insilico.com/>

All Publications: <https://insilico.com/publications>

Key Publications:

- Nature Medicine 2025: A generative AI-discovered TNIK inhibitor for idiopathic pulmonary fibrosis: a randomized phase 2a trial (<https://www.nature.com/articles/s41591-025-03743-2>)
- Nature Biotech 2024: A small-molecule TNIK inhibitor targets fibrosis in preclinical and clinical models (<https://www.nature.com/articles/s41587-024-02143-0>)
- ACS Publications 2024: PandaOmics: An AI-Driven Platform for Therapeutic Target and Biomarker Discovery (<https://pubs.acs.org/doi/10.1021/acs.jcim.3c01619>)
- ACS Publications 2023: Chemistry42: An AI-Driven Platform for Molecular Design and Optimization (<https://pubs.acs.org/doi/10.1021/acs.jcim.2c01191>)
- Nature Biotech 2019: Deep learning enables rapid identification of potent DDR1 kinase inhibitors (https://www.nature.com/articles/s41587-019-0224-xfbcid=IwAR2rwRqmRxj7eyz6WX13_oHXFWRTahQsZoobZGdGde7HRDVCUm4kj7ewad4)

References File Document upload:

Nature Biotech_A smallmolecule TNIK inhibitor targets fibrosis in preclinical and clinical models.pdf
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InsilicoMedicine_Rentosertib_Hallmarks of agingbased dualpurpose disease and ageassociated targets predicted using

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