

Company profile

Rubedo Life Sciences

Rubedo Life Sciences is a biopharmaceutical company that prides itself on developing customised therapeutics to treat age-related diseases and extend health-span. Its investigational compounds are small molecule therapeutics that are selectively activated inside specific cell types, such as senescent cells. The company's multi-disciplinary team includes leading scientists and experts in aging, regenerative medicine, drug discovery and chemistry combined with bio-informatics engineers from academia, life sciences and computer science.

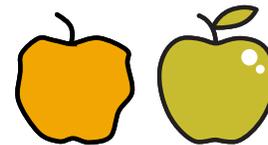
The company's mission is to deliver safe, highly effective targeted therapeutics to treat age-related diseases in patients suffering from chronic degenerative diseases with multiple co-morbidities. Rubedo believes each of its team members adds unique expertise and incredible passion towards its exciting mission. By connecting leaders in multiple fields, Rubedo hopes to solve unmet issues of drug toxicity and selectivity for untreatable age-related diseases.

The research conducted by Rubedo is powered by ALEMBIC™, a proprietary Bio&Chemo informatics platform that enables the proprietary synthetic and medicinal chemistry pipeline discovery. ALEMBIC™ can identify novel targets and unique cellular metabolic signatures to enable Rubedo's proprietary chemistry. The novel composition of matter is based on engineered small molecules that are selectively activated in target cells. Rubedo's unique synergy of proprietary technologies and expertise can quickly advance compounds from discovery to preclinical efficacy *in vitro* and *in vivo*, enabling strategic partnerships and an internal clinical pipeline. The team at Rubedo already has several senolytic

lead compounds in preclinical optimisation for indications in fibrosis and oncology.

These novel lead senolytic compounds were generated in less than two years, demonstrating efficacy both *in vitro* and *in vivo*. Going forward, Rubedo aims to complete lead optimisation to select a clinical candidate for IND-enabling studies ahead of clinical stage evaluation of its first program in lung fibrosis, targeting Idiopathic Pulmonary Fibrosis (IPF). Following this program, Rubedo aspires to file a second IND for indications in the oncology space. The company is considering out-licensing options once compounds reach the clinical development stage. It is also considering strategic partnerships for new indications, involving novel composition of matter, beyond senolytics.

Rubedo has developed a novel class of senolytic targeted small molecules, including prodrugs, designed to be selectively activated in specific senescent cells to induce their clearance from tissues while protecting other cell types. These molecules involve multi-step activation, taking advantage of novel druggable targets and of characteristic senescent cell functions discovered through ALEMBIC™, enabling its proprietary medicinal chemistry. Those prodrugs solve three problems: 1) selectivity - activating only in the rare pathological cells but sparing the other healthy cells; 2) tolerability, protecting elderly patients from side-effects caused by off-targets; 3) efficacy, generating potent active compounds acting on the selected targets. Rubedo prodrugs can be developed from novel molecules and also existing approved drugs resulting in novel composition of matter with superior or novel selectivity and safety, with intellectual property fully owned by Rubedo.



Rubedo's intellectual property has entered the national phase in Canada, China, Europe, Israel, India, Japan, Korea, Mexico and Singapore via International Publication as of 2/11/21. Molecules are currently in lead optimisation ahead of IND-enabling studies. Rubedo's first US patent was granted on the 8th of June, 2021.

Longevity Potential: Small molecular therapy for Idiopathic Pulmonary Fibrosis and more

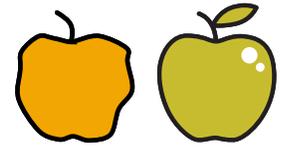
Rubedo is developing a selective targeted therapy aimed to clear the burden of senescent and profibrotic cells in the lung tissue of patients with idiopathic pulmonary fibrosis (IPF), a life threatening degenerative disease. The standard of care for IPF includes two approved medicines, nintedanib and pirfenidone, each with limited efficacy in slowing disease progression in a subset of patients and with side effects that can diminish quality of life and patient compliance. A growing body of preclinical and clinical evidence in the field suggests that senescent cells play a driving role toward fibrosis in IPF. By selectively targeting senescent cell populations, Rubedo hopes that its therapies have the potential to revert the degenerative process with well tolerated therapeutics. To advance its IPF program toward the clinic, Rubedo established a collaboration with the Cedars-Sinai Medical Center in Los Angeles, joining forces with world-class preclinical and clinical experts in interstitial lung diseases (including IPF).

To reduce the side effects that are associated with targeting senescence, and to increase selectivity, Rubedo's proprietary therapeutics are small molecules designed to initially be inactive (such as prodrugs). By taking advantage of characteristic metabolic and cellular functions of senescent cells, these small molecules are then selectively activated in multiple steps by targeted senescent cell types. For example, senescent cells are characterised by a notable change in biological

properties such as an increase in mitochondria levels, reactive oxygen species, lysosomal content and upregulation of lysosomal enzymes like senescence-associated β -galactosidase (SA- β Gal). Using a drug that is selectively activated in senescent cells, by the hydrolase activity of SA- β Gal and by other cell specific enzymes, creates the potential to remove senescent cells without any noticeable side effects.

By using activated small molecules, the therapies can be delivered systemically. The portfolio of chemistries developed by Rubedo can be applied to different small molecules, targeting different cell types and different molecular targets, in the context of multiple tissues and diseases. (Further details on the small molecules used are still undisclosed.)

Rubedo's portfolio of lead compounds includes developed small molecules that can selectively target both senescent and cancer cells, systemically and within the tumour environment, aimed to treat unmet needs in oncology. Additionally, recent breakthroughs in its chemistry resulted in novel intellectual property that enables new opportunities for drug discovery in senescence, enabling different clinical indications and facilitating new therapeutic opportunities for strategic partnerships beyond senolytics.



Pre-Clinical and Clinical Studies



Rubedo's strategy has the potential to address multiple conditions simultaneously by targeting a master regulator of the degenerative age-related process. Additionally, Rubedo therapeutics are designed to be well tolerated in individuals who are aged, frail and afflicted by several chronic conditions and co-morbidities.

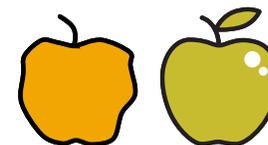
Technological (Platform) Analysis

Rubedo has built a sophisticated bioinformatics and chemoinformatics platform named ALEMBIC™, driven by a combination of AI and other algorithms. ALEMBIC™ can analyse large datasets across different integrated dimensions, such as multi-omics data, age, patient populations, tissues and diseases. This allows identification of novel targets and cell "IDs", or signatures, that enable application of proprietary chemistries to generate novel small molecules such as prodrugs. This approach at Rubedo can uniquely advance the drug discovery process: after target identification, ALEMBIC™ enables generation of proprietary novel composition of matter, starting either from completely novel compounds or from existing clinically approved molecules, engineered for improved selectivity and safety profiles.

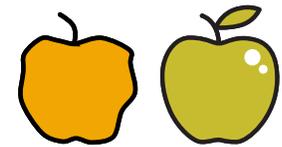
Standard models along with novel age-related preclinical rodent models have been developed at Rubedo, showing promising initial efficacy. Early pharmacokinetic (ADME/DMPK), tolerability and efficacy studies have been conducted in rodent and non-human primate animal models.

For example, reported initial studies using a tool prodrug targeting initially only SA-βgal activity in geriatric mice showed significant improvement in 1) frailty profile; 2) skeletal muscle function; 3) muscle stem cell function; 4) cognitive function; and 5) survival. These studies are ongoing along with different lead compounds in the optimisation stage, ahead of IND-enabling studies.

The initial indication for Rubedo's technology is IPF, followed by additional age-related indications, possibly and similarly driven by the accumulation of senescent cells. A clinical endpoint for IPF will likely involve forced vital capacity.



Technology Platform Analysis	Description	Rubedo Biotechnologies
Class of Senotherapeutic	Senolytic, Senomodulator, SA-immunomodulator, Senoblocker.	Senolytic: Targeting cellular pathways that make senescent cells vulnerable to death.
Target specificity	Features of therapeutic that facilitate targeting of senescent cells without off-target effects; dependent on senescent biomarkers.	The use of selective small molecules, designed to activate only under certain senescence conditions, creates the potential to remove senescent cells with increased selectivity and without any noticeable side effects.
Delivery	Approaches (local or systemic), technologies (delivery vehicle), and formulations needed to safely and reliably deliver therapeutic to its target.	Rubedo uses novel small molecules designed specifically for its target. Due to the small molecules only being activated by cellular functions of senescence, the therapeutic can be delivered systematically.
Adaptability	Foundational technology that can be utilised to systematically improve, or build upon, robustness of therapeutic.	ALEMBIC™ can analyse large datasets to identify novel cell “IDs” that enable applications of proprietary chemistries to generate novel small molecules. This platform has created a portfolio of chemistries that can be applied to different small molecules, targeting different cell types and different molecular targets, in the context of multiple tissues and diseases.
Regulation	Context specific control over therapeutic action once it has reached its target (spatial, temporal, sensitivity, degradation).	Rubedo’s proprietary therapeutics are small molecules designed to initially be inactive (such as prodrugs). By taking advantage of characteristic metabolic and cellular functions of senescent cells, these small molecules are then selectively activated in multiple steps by targeted senescent cell types.
Toxicity	Level of damage that therapeutic can cause to organism; Can include, but not limited to: off-target effects, on-target side effects, immunogenicity, etc.	The novel small molecules designed by Rubedo have not been disclosed.



Safety and Risks

Many of the senolytic drugs used to deplete senescent cells cause profound toxic side effects due to lack of specificity toward senescent cells. This can lead to hematological toxicities including neutropenia and thrombocytopenia. The specificity issues of current senolytic drugs limits their application to local delivery and/or to acute treatments as opposed to chronic systemic administration. Creating a therapeutic that selectively kills senescent cells whilst sparing other cell populations remains a challenge.

Rubedo's proprietary therapeutics are designed to be well tolerated, selective and to be delivered via multiple routes of administration. The chemistry strategies invented at Rubedo enable the design and generation of different targeted therapeutics, such as complex prodrugs among other types of small molecules. Rubedo is developing targeted technologies to prevent or overcome limitations due to side effects, off-target effects and poor selectivity that typically limit the therapeutic development of small molecules. Moreover, considering the heterogeneity and tissue specificity of senescent cells, Rubedo aims to develop customised senolytic therapies along with different targeted therapeutics for other cell types, including cancer cells or dysfunctional stem cells.

Target Market

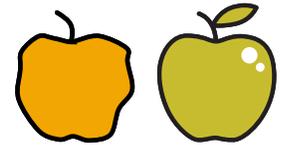
Rubedo's first developed target therapy for IPF has a market size valued at US\$2 billion in 2018 and is estimated to expand at a CAGR of 12.7% over the forecast period, amounting to US\$5.2 billion by 2027. These projections do not include the global impact of the pandemic. As COVID-19 survivors appear to suffer from accelerated biological aging in the lung tissue, due to SARS-Cov2 driving cellular senescence in the lungs, this population is at an increased risk of developing IPF in the future. This is a factor potentially driving an increase in the IPF population over the next

decade, with expected market growth surpassing initial predictions. Beyond IPF, Rubedo states that its senolytic compounds have been designed to tackle other pulmonary diseases, such as chronic obstructive pulmonary disease and to other indications related to fibrosis and to unmet oncology needs. Rubedo's targeted therapies are designed to be "healthy" potent senolytic chemotherapies with the goal to enable efficacy with greater tolerability in selected therapies for aged populations with co-morbidities.

Success Factors

Team and Reputation

- Rubedo Life Sciences has a strong team. Its C-suite covers multiple aspects of a successful senotherapeutic start-up including entrepreneurship, senescence biology expertise, software engineer proficiency and big pharma insights;
- Marco Quarta, the co-founder and CEO of Rubedo LifeSciences is a leading expert in aging and regenerative medicine from Stanford University. Marco is backed by over 15 years of research with an extensive track record of scientific publications in top tier journals. He also co-founded biotech companies in Europe and the US, including regenerative medicine biotech WetWare Concepts and longevity start-up Turn Biotechnologies;
- The scientific team is headed by Mark Gallop, co-founder and a leading scientist in multiple chemistry fields, with world-class expertise in prodrug chemistry and development, and more than 30 years of drug discovery experience in the bio-pharmaceutical industry, including senior director role at Affymax. Mark has co-founded and led drug discovery companies such as Nurix and Xenoport and has multiple track records of IPOs, acquisitions and FDA approved drugs brought to market;

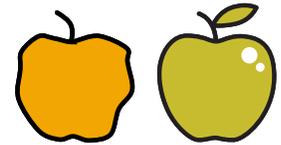


- Julian Klein, co-founder, is an expert in senescence biology who trained under academic leaders and pioneers in the field, contributing to top tier scientific publications;
- The VP of drug discovery, Jeff Jasper, has over 25 years' experience in the bio-pharmaceutical industry including positions at Merck, Roche, Theravance and Cytokinetics. He is co-founder of Altos Therapeutics (acquired by Takeda Pharmaceuticals). He has an extensive track record of approved medicines brought to market;
- The drug discovery platform, ALEMBIC™, was built by the chief technology officer, Alex Laslavic, and his team. Alex is an experienced software engineer having been a former lead at Facebook and other IT companies. His unique skills in building infrastructure software, distributed systems, and pipelines for large-scale data analysis was fundamental to the design of ALEMBIC™. The team at Rubedo Life Sciences continues to grow rapidly. Currently a small, 18-person organisation, Rubedo aims to bring-on additional key members in the future including clinical and business development;
- Rubedo Life Sciences also benefits from a compelling scientific and clinical advisory board, including Prof Cory Hogaboam from Cedars-Sinai (IPF and Senescence), Prof Mark Pegram and Prof Lidia Shapira from Stanford University Oncology) and Distinguished Prof. Paul Insel from UCSD (Pharmacology). Academic collaborators include Prof Thomas Rando and Prof Tony Wyss-Coray from Stanford University, leaders in the field of aging and the rejuvenation field;
- Rubedo is very collaborative and is currently discussing strategic partnerships to expand its portfolio to other indications and is open to initiate new conversations. The company recently released a preprint publication (under review) of early proof of principle with leaders in the field from Stanford University. The work is based on a targeted senolytic prodrug in geriatric mouse models. The company aims to continue contributing to the scientific field with its own research and advancements;

- The current team has a strong breadth of knowledge that has aided product development and a strong senotherapeutic platform. Progression to Series A funding would benefit from a business development and clinical manager to ensure generation of long-term profit and sufficient clinical data.

Intellectual Property

- Rubedo Life Sciences creation of the sophisticated bioinformatics and chemoinformatics platform, ALBEMIC™, that identifies novel targets for small molecule generation, gives the company a plethora of opportunity for patents;
- As ALBEMIC™ will identify cell IDs associated with cellular senescence as targets, the small molecular therapies designed by Rubedo should have a higher selectivity and safety;
- There is early proof of concept, released in a preprint publication, that validates a targeted prodrug senolytic strategy. This positive early work gives Rubedo's scientific team confidence in its initial hypothesis. Rubedo hopes to advance these initial positive results to higher levels of sophistication, including new targets and new chemistry strategies;
- Standard models, along with novel age-related preclinical rodent models, have been developed at Rubedo and have achieved initial efficacy results. Further, the company states it has achieved an improved safety profile in multiple species;
- The first indication, IPF, is expected to be the initial step in a series of different possibilities to expand the label to other forms of interstitial lung diseases;
- The company has also stated that it has had recent breakthroughs in its chemistry efforts that have generated new IP and extended Rubedo's capacity beyond initial expectations. Based on these efforts, Rubedo now has several new patent applications in construction;



- Rubedo has other compounds in the pipeline in development for different indications. It hopes to pursue these new drug discoveries by developing strategic partnerships.

Funding

- Rubedo Life Sciences has raised \$12m in seed financing since incorporation, led by Khosla Ventures, including participation from Longevity Funds, Refactor Capitals, Shanda Group and others;
- Rubedo Life Sciences is moving to Series A funding in the summer or 2021. This funding phase will help prepare the IND-ready package and submission for the first-in-human and move to Phase 1 clinical trial in IPF;
- Funding will also support advancing a second indication to IND, expanding the current team, research facilities and IP portfolios;
- The team also aims to secure strategic partnerships that will enable parallel drug discovery programs, expand the IP portfolio and licensing opportunities;
- The growth and aims of the company is dependent on raising sufficient additional capital in series A funding. Strong preclinical results, including efficacy and safety data, as well as regulatory and strategic planning for the path to the clinic (patient inclusion criteria and stratification, endpoints and biomarkers) and to market (competitive landscape, reimbursement strategies and market evolution), will help assure investors when raising additional capital.