

Go-to-Market at reduced risk!

Investment in Cell and Gene therapy, one of the big ideas in biotech

Ref. No. 220929FN-STR025

Date: September 29, 2022 Page 1 of 2

Dear investors,

In **Rius Medical** is an entrepreneur **with a big vision who** wants to create something less ordinary - something that matters, for all of us - a founder's unshakeable intention to address a significant, pressing challenge on our planet and in our society! Products engineered with biotechnology present **a collaborative space for** Bioentrepreneurs and investors to address society big challenges of cancer, type 1 diabetes and other diseases. For Rius Medical, that is under **ONE-Platform technology**!

Yes, I agree that Rius Medical as a life science company is outside the investment scope of many investors. In general, Life Science investment is often perceived as high risk - the sector comprises companies that have an 85-95% failure rate on everything they attempt to invent. Even to achieve success takes about 10 to 12 years, and most biotech businesses do not have any measurable revenue for a long period of time. This view alone, yes! But that is not what Rius Medical does!

De-risking Rius Medical: 14 months to revenue by upgrading existing FDA/EMA approved biologics!

[1] Manufacture of Biologics - accelerate timelines for the development / manufacturing of molecules and disruptive technologies! The Lonza support to Bioqube Ventures www and ALSA Ventures www goes beyond due diligence of candidate biotechs by bringing tailored offering of advice and services to portfolio companies supporting de-risking early development and manufacturing of next-generation modalities. Developing and manufacturing these increasingly complex modalities require sophisticated facility design and expertise, which is often challenging to establish in-house (e.g. Rius Medical). Pnina Weitz, Global Head of Venture Capital Business Development and Relationship Management at Lonza, wants collaboration talks with Rius Medical this week. The collaboration aims to significantly increase the chances for the future success of these therapies by providing early de-risking and development and manufacturing services tailored to each molecule's unique needs and properties.

[2] How do you see Axilium or Hadean Ventures if not Coparion PDF - a venture capital fund for young, German technology companies provided by ERP Special Fund, KfW Capital and European Investment Bank; making EUR 500,000 co-investment alongside Lead Investor EUR 500,000 investment inclusive of 20% refund from German Ministry for Economic Affairs and Climate Protection (BMWK) www? Yes, sharing the EUR 1 million requested funding between two investors. By the way, according to BMWK, the maximum "eligible investment amount for 20% refund" is EUR 500,000 per investor per year. Thus lowering the risk for investor(s) www. By December 2023, significant progress of Rius Medical is technology transfer deals to FR, Erytech Pharma (Enzyme L-Asparaginase) and USA, Travere Therapeutics parent company of CH, Orphan Technologies (Enzyme Thymidine phosphorylase) both FDA/EMA approved biologics! Example: Travere Therapeutics (previously Retrophin) made an upfront payment of USD 90 million in cash at closing of the transaction. Orphan Technologies shareholders will remain eligible to receive up to USD 427 million in additional cash payments contingent upon the achievement of key milestones in the development and commercialisation of OT-58 www. [Encapsulation in 29 days half-life red blood cells from the patient's own blood, Phase 2 clinical trial until December 2022 at St George's, University of London www]. That's right, Lead Investor co-investing with EUR 500,000 for 10% ownership in Rius Medical with EXIT option of EUR 5.2 million on two cell line products as technology transfer deals to third parties by December 2023! Thereafter CDMO Lonza as a partner to Health Solutions product line with red blood cells drug delivery of enzyme or antigen!

[3] Rius Medical Go-to-Market at reduced risk

For life sciences companies, regulatory compliance never becomes any less complex and stringent. Depending on the exact nature of the work and where business is done, multiple regulatory frameworks apply www. Nonetheless this does not apply to Rius Medical! For example Sanofi EUR 308 million buyout of Kiadis natural killer cell projects www. Is based on iPSC technology Kiadis acquired for nothing from Cytosen a year and a half ago. The move in November 2020 by Sanofi came just four months after the French company licensed one of Kiadis's Cytosenderived natural killer cell projects for EUR 17.5 million up front. Rius Medical out-licensing is EUR 20 million up front each on 2x red blood cells drug delivery of FDA/EMA approved enzymes (L-Asparaginase and Thymidine phosphorylase)! Sanofi and others shall handle the regulatory compliance!

The pharmaceuticals **and life sciences industry** is uniquely positioned to create value for society as its innovations lay the foundation for universal health and thus prosperity. **COVID-19** emphasizes the central **importance of the industry for** society and the economy. I hereby wish to highlight **key elements that Rius Medical** is doing that might not be clearly depicted in the submitted Pitch Deck. What fits best for your investment strategy, yes that is what I would like to talk on a Zoom call.

Many thanks and warmest regards,

Denis Demarais | Founder and CEO

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Rius Medical

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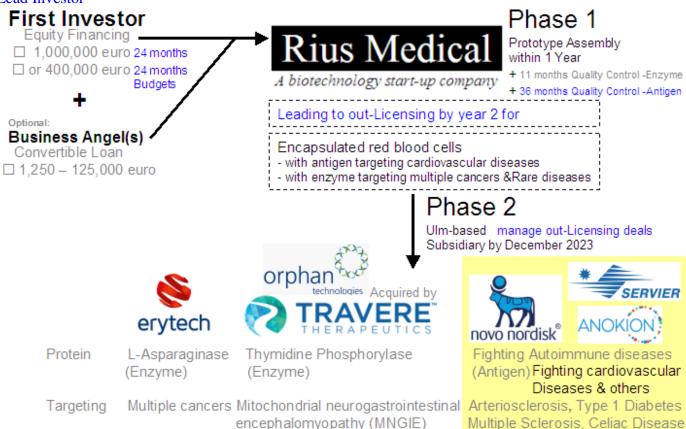
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Lead Investor



Project revenue: 130 million euro on FIVE products by year 2 (i.e. December 2023)

a rare disease

Lead Investor makes a total investment of **at least** 1,000,000 € against 20% ownership if not a co-investment of 500,000 € against 10% ownership in Rius Medical. **Rius Medical** has the following CapTable for negotiating partnership deal /shareholder value.

CapTableRius Medical UGFinanced RoundSeries AInvestment Pre-Money3.350.000,00 €Price per Share1,00 €

	Establishment of the Company		Financing Round A		Fully Diluted	
Shareholder	Shares	in %	Investment	Shares	Shares	in %
Founder 1	3,350,000	100.00%			3,350,000	67.00%
Convertible Loan			125,000.00€	250,000	250,000	5.00%
Investor 1			1,000,000.00€	1,000,000	1,000,000	20.00%
Investor 2			400,000.00€	400,000	400,000	8.00%
Total	3,350,000	100.00%	1,525,000.00 €	1,650,000	5,000,000	100.00%

Founder 1: Denis Demarais, Founder and CEO at Rius Medical UG

Optional Convertible Loan: Bridge financing from third-party as investors, prior to First equity investor

Investor 1: A First equity investor at 1,00 euro per share (LEAD Investor) and/or Investor 2: A second equity investor also at 1,00 euro per share similar to investor 1

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5 Things I Need To See Before Making A VC Investment

Investment in Cell and Gene therapy, one of the big ideas in biotech

Ref. No. 220912FN-STR024 A biotechnology start-up company

Date: September 12, 2022

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What are your "5 things I need to see before making a VC investment" and why. Interviewing Ameena El-Bibany (ARTIS Ventures) www

1. Who is the team, and why are they the right individuals to solve this problem? This is as simple as ensuring we have the conviction that of anyone in the world, this particular team has the knowledge and expertise to solve the problem at hand. Moreover, beyond current members, does this leadership have the ability to excite and recruit the top minds in the space to join their mission?

In this capacity, I Denis Demarais am leading highly talented individuals with unique expertises and skill sets on "Making real innovations, Tomorrow's technology: Next Generation stem cells therapies".

Knowledge and expertise to solve the problem at hand:

- (1) Subcontractor GenScript, USA solves the DNA synthesis in plasmids of required genes. My scientific assignment (2010 – 2013) in leukaemia research at Ulm under Prof. Christian Buske, expanding upon the "HoxB4 work" of Canadian scientist Dr. Keith Humphries www, enabled me at Rius Medical to design the genes solving the scientific and technical hurdles blocking access to life changing protein therapeutics (enzyme or antigen biologics) by "reprogramming stem cells" into cell therapies. [5 months]
- (2) Subcontractor Trans Chromosomics, Japan brings Chromosomes Engineering Technology PDF to Rius Medical as a consumable. Genes that I designed and synthesised as plasmids at GenScript are loaded onto the artificial chromosome vector by Prof. Mitsuo Oshimura Japan prior to being added to stem cells sourced in EU, USA and China for commercialisation in the respective markets. [6 months]

Outsourcing 5 months thereafter 6 months work to subcontractors simply save time and money for Rius Medical doing automation – meaning, "stem cells reprogramming" into a cell line! Rius Medical, developing Advanced Manufacturing, disrupts the biopharmaceutical industry by overthrowing traditional production models in favour of a new model with synthetic biology, genetic engineering and stem cells combine for automation! Automation is the outcome of Rius Medical. The prototype/cell line assembled within 11 months, is a "master copy" that simply self renew long term - starting with "1x donor sample" few bone marrow derived stem cells expand into multiple 2,000 L bioreactors over at least 30 years.

Beyond the current members, the leadership I bring have the ability to excite and recruit top minds in the space to join Rius Medical mission:

[1] Antigen cargo red blood cells targeting autoimmune diseases like type 1 diabetes, multiple sclerosis or celiac disease - Rius Medical addresses the bottleneck of Bristol Myers Squibb's Anokion www. As a completely new product, Rius Medical alongside Agnès Lehuen of Paris France INSERM need further validation data before bringing this protein (antigen) therapeutic product via cell therapy to market. Rius Medical vaccine approach for regulatory T cells has acquisition option by Bayer www or **Bristol Myers Squibb.**

Agnès Lehuen is director of the department "Endocrinology, Metabolism and Diabetes" and head of the laboratory "Immunology of diabetes" at Cochin Institute and University Paris Descartes. She is cofounder of the Laboratory of Excellence INFLAMEX. She did her PhD in Paris, a post-doctoral training in the USA and got a CNRS position at Necker hospital in Paris. Since 2002 she is team leader and in 2014 her laboratory joined Cochin Institute www.

[2] CAR-NK cells to target cancer – Rius Medical addresses the bottleneck associated with CAR-T cells being "only 30-40% of adult patients" will achieve long-term remission www. As a completely new product, Rius Medical alongside Pedro Berraondo of University of Navarra, Spain need further validation data before bringing this protein (CAR) therapeutic product via cell therapy to market. Rius Medical CAR therapies have acquisition option by Sanofi www.

Pedro Berraondo, team leader at CIMA, University of Navarra, hosted a project: To develop strategies that improve anti-tumour responses and reduce NK cell exhaustion - scientists with the CINK project investigated the mechanisms by which NK cell activation is regulated www.

[Grant agreement ID: 746985 / Start date 15 February 2018 - End date 14 February 2020]

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2. What is the problem, and how big is the market? Beyond looking at market numbers, it's important for a startup to deeply understand the problem they are solving. Some teams we see building interesting technology and then searching for a problem to solve, while others we see spending the time to deeply characterize a problem before building the right tech solution. I encourage entrepreneurs not to try to fit a square peg in a round hole. In other words, identify the problem first. Determine the key issues and current bottlenecks in the space, then set out to build the differentiated solution that outcompetes others.

Problem identified first – Cargo red blood cells have **existing bottleneck** by (1) Erytech Pharma (targeting cancer) www - discontinued it's Leukaemia program in June 2018 and instead shifted focus to solid tumor; and by (2) Rubius Therapeutics (rare diseases of metabolism) www - March 2020 scraped lead drug after seeing 'uninterpretable' data. The data capped off a series of setbacks, including "continued manufacturing challenges", for the phenylketonuria asset, that led Rubius to stop the trial and shifted its focus.

Competitions to Rius Medical have emphasis on traditional production models with all the cells made by hand in batches, by highly trained scientists sitting in a clean room. That's not scalable. Rius Medical developing Advanced Manufacturing disrupts the biopharmaceutical industry by overthrowing traditional production models in favour of a new model with synthetic biology, genetic engineering and stem cells combine for automation.

3. What is the unique edge you bring? Is it your tech, your business model, your team, or something else? The unique edge is as simple as what your company is doing to outcompete others and what strategy helps you maintain that moat. In some cases, the tech provides differentiation; in other cases it may be a unique strategy or business model that brings an edge to execution.

The unique edge I bring via Rius Medical is on three levels to outcompete others:

[1] Tech provides differentiation

Synthetic biology with a strong platform approach is what you will find in Rius Medical - a scientist founder driven biotech company. By doing so, Rius Medical propels science and humanity forward in solving massive, global problems with **the power of technology**. The world's best scientists with "1995 HoxB4 self renewal" by Keith Humphries - genetic engineering **revisited with** Japan synthetic biology with artificial chromosome vector on stem cells is what Rius Medical does.

The differentiation is obvious relative to (1) Erytech Pharma doing enzyme or antigen biologics added to 29 days half-life blood donation derived red blood cells and (2) to Rubius Therapeutics doing 120 days lifespan stem cells derived red blood cells in a "single batch approach" from 1x donor, traditional method and "continued manufacturing challenges". Rius Medical outperforms Rubius Therapeutics to enable "multiple batches approach" from 1x donor long term. The mission of Rius Medical is to fully automate cell and gene therapy (CGT) manufacturing to increase throughput, improve quality and decrease costs in order to enable patient access to this new generation of life-saving treatments.

[2] Unique strategy

Rius Medical **overthrows traditional production models** in favour of a new model with synthetic biology, genetic engineering and stem cells combine <u>for automation!</u> Traditional production models have all the cells made by hand in batches, by highly trained scientists sitting in a clean room. **That's not scalable**.

Rius Medical is firmly positioned on network effects - **those where** a product, service or platform gains exponential value as usage increases! **Manufacturing biologics** as cell therapy has only one objective, prevent severe immune-mediated adverse reactions and anaphylaxis of existing medication!

Despite commercial Asparaginase medicine/ASNase relevance in acute lymphoblastic leukemia (ALL) treatment, since the first approved *E. coli* formulation of ASNase (Elspar®) by the Food and Drugs Administration (FDA) in 1978, only two biobetters have been commercially available, the PEGylated ASNase (Oncaspar®) which was approved in 1994 where the 20 hours half-life <u>is extended to</u> **7 days by PEG** – the addition of molecule Polyethylene glycol (PEG) to increase enzyme activity, and an ASNase from *Erwinia chrysanthemi* (Erwinase®), approved in 2011 because development of hypersensitivity in

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"10-30% of patients" to *E. coli* formulation of ASNase (Elspar®). All three commercial Asparaginase medicines have **toxicity from** immune reaction and to a secondary L-glutaminase activity.

Biologic enzyme L-Asparaginase for starving cancer cells in AML, ALL, pancreatic cancer and breast cancer... works only if the drug delivery hurdles are addressed - hence **the solution by** Rius Medical. The same therapeutic platform requires only switching the enzyme to target **rare diseases of metabolism** (MNGIE and PKU) - network effects!

[3] Business model that brings an edge to execution

Rius Medical does drug development and is interested in partnering for drug manufacturing with a CDMO like Lonza to address EU, USA and China markets - Modelled after CDMO Catalent partnership for Erytech Pharma's commercial cell therapy www! Rius Medical is an early-stage company committed to creative problem-solving and recognizes the need to rethink how the world's needs are addressed—by applying revolutionary technologies to improve life and generate substantial economic return. That also applies to Immune Tolerance for Autoimmune diseases type 1 diabetes, multiple sclerosis (MS) and Celiac Disease in relation to Anokion partnership with Astellas Pharma www and partnership with Bristol Myers Squibb www.

Partnership is what drives Rius Medical for it is a relay race and not a marathon! Anokion core strength is in patient recruitment for promising Clinical Trials. Instead of blood-donation, Rius Medical core strength is in upgrading stem cells for cargo-carrying red blood cells. That is upgrading donated stem cells with foreign DNA/genes using an artificial chromosome vector. Technology transfer deal to BIG PHARMA is the norm in cell therapy as depicted with Sanofi (i.e. Sanofi EUR 308 million buyout of Kiadis natural killer cell projects www) if not Bristol Myers Squibb - Anokion acquisition with Antigen cargo red blood cells for Autoimmune Diseases www.

Biotechnology, often abbreviated to biotech, is the area of biology that uses living processes, organisms or systems to manufacture bio-related products or technology intended to improve the quality of human life. The primary focus is on generating enough data that are compelling to Big Pharma **acquisition**. The business model is to get acquired!

4. Who is excited to adopt this? Who is your customer, and how well do you understand them? While this might seem like it falls into market assessment, it is about having a nuanced understanding of who all the stakeholders in the purchase process are. Who is the end user and how excited are they to adopt the solution? Additionally, who is the payer and what is their feedback on the product, pricing, and business model? If the company is still pre-commercial, there may not be signed contracts; in this case, showcasing evidence that supports product-market-fit can help.

Rius Medical doing drug development capitalizes on unmet medical needs. Manufacture of Biologics - accelerate timelines for the development / manufacturing of molecules and disruptive technologies is at the core of Rius Medical. Rius Medical solves the scientific and technical hurdles blocking access to life changing protein therapeutics (enzyme or antigen biologics) by "reprogramming stem cells" into cell therapies with synthetic biology, genetic engineering and stem cells combine for automation. Rius Medical is validated by the German Federal Ministry For Economic Affairs And Climate Action www.

My understanding of all the stakeholders in the purchase process start with the three commercial Asparaginase medicines having **toxicity**, i.e. severe immune-mediated adverse reactions and short enzymatic activities of 20 hours if not 7 days. The end users are patients with unmet medical needs.

Rius Medical enzyme cargo red blood cells target AML cells with NO adverse reactions. In addition, enzyme-loaded red blood cells 4 months / 120 days lifespan (Rius Medical) is **4x that of existing traditional method**, i.e. 1 month / 29 days (Erytech Pharma) enzyme activity. **In cancer care**, a business partnership with Rius Medical delivers on cancer patients having less frequent administration of "L-Asparaginase medicine", requiring very fewer visits to daycare, and is therefore **more patient-friendly**.

Biologic enzyme L-Asparaginase for starving cancer cells in AML, ALL, pancreatic cancer and breast cancer... works only if the drug delivery hurdles are addressed - hence **the solution by** Rius Medical. The same therapeutic platform requires only switching the enzyme to target **rare diseases of metabolism**

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(MNGIE and PKU)! This is my understanding of **the stakeholders in** the purchase process. I acknowledge the strength of Erytech Pharma and Rubius Therapeutics in being clinical stage biotech companies. Furthermore having the conviction that partnership is the best way forward, Rius Medical as a pre-commercial entity demonstrates **evidence that supports** product-market-fit.

A contract development and manufacturing company (**CDMO**) is a company within the pharmaceutical industry that provides drug development and manufacturing services. Pharmaceutical companies partner with CDMOs as a way to outsource drug development and drug manufacturing. Yes the enzyme cargo red blood cells targeting cancer or rare diseases of metabolism - has emphasis on manufacturing as an **upgrade to existing bottleneck** by Erytech Pharma www and Rubius Therapeutics www.

From an investor perspective, it is also the fastest drug development to market of <u>11 months</u> thus ensuring **return on investment** on 10% ownership as EUR 1,8 million dividends if not EUR 5,2 million EXIT option by December 2023.

5. How will we as investors bring value to this? ARTIS approaches investments as a true partnership, not just a check, so with each investment, we carefully consider what value we can add to the company. Once we reach conviction around an investment, then we look at ourselves and ask what edge we can bring, whether that's through strategy, customers, partners, or talent. We do this in two ways. The first is by rolling up our sleeves and directly working with founders on anything from helping to identify gaps in data to early strategy to aiding with recruitment, etc. The second way we add value is through that network of Healthcare Pioneers, which includes executives from the top biotech, pharma, and life sciences institutions that both mentor and advise our portfolio companies.

After reviewing the deck with the investment team, I look forward to **investor(s) feedback** and further talks on Rius Medical **first-in-class biologic assets** (enzyme or antigen biologic via cell therapies).

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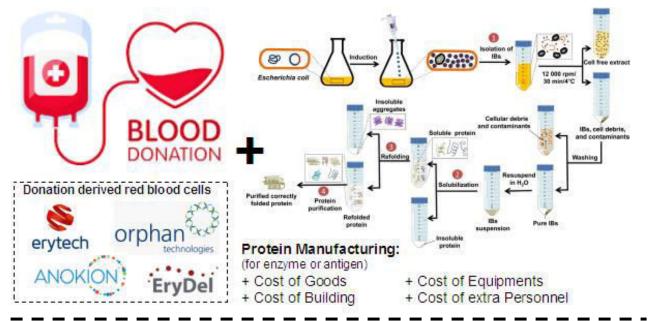
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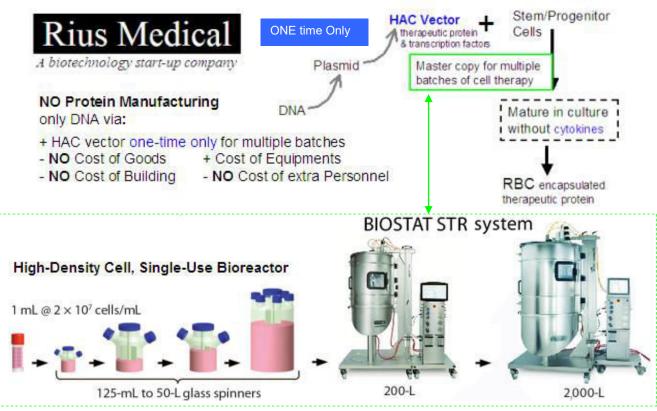
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[1]





As depicted the Rius Medical "Master copy" expands substantially long term over multiples of 30 years as Mammalian expression system for recombinant Plasma Proteins with excess cells maturing on-demand into desired Drug-loaded erythrocytes / cargo-carrying red blood cells!

The simplicity of Rius Medical proprietary cell lines for drug delivery is depicted above. Competitors' emphasis on Protein Manufacturing implies gene added to bacteria for protein therapeutic thereafter added to blood donation derived 29 days half-life red blood cells. Rius Medical has the engineered stem cells making the therapeutic protein within maturation of 120 days lifespan red blood cells.

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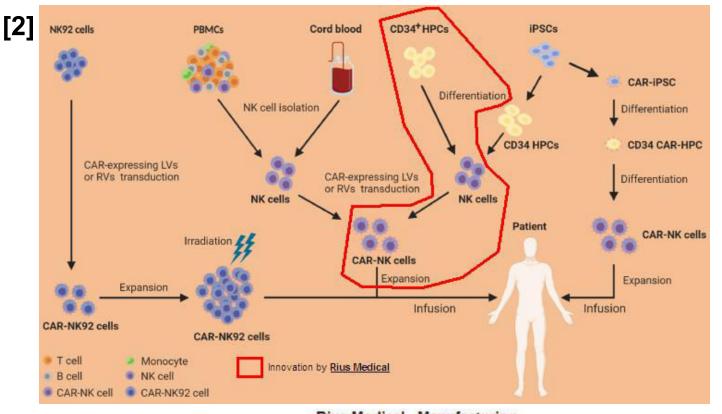
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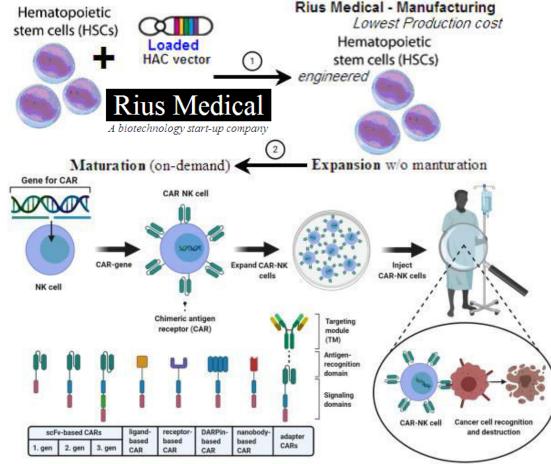
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NK cells against cancer is an interest for Rius Medical:

Rius Medical is developing
Advanced Manufacturing
to help patients with
cancer and other diseases
by solving the problem of
Drug Delivery through
reprogramming stem cells.

Chimeric antigen receptor and other antigens have demonstrated the relevance of NK cells therapy in clinical use.

Isolation challenges:

Natural killer cells represent 5–20% of circulating lymphocytes in humans whereas T cells comprise 51-88% of circulating lymphocytes.

Stem cells derived as an alternative to isolation is hereby being evaluated.

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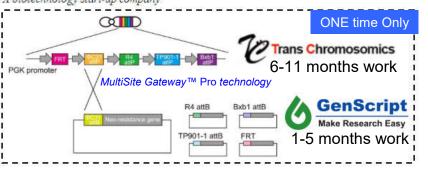
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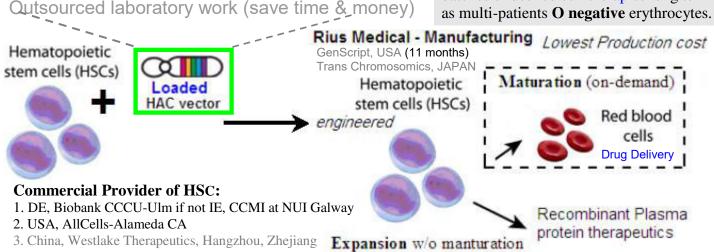
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DE, Rius Medical <u>adds genes</u> to blood stem cells (i.e. CD34+ cells) through the <u>Human Artificial Chromosome</u> vector for **red blood cells** maturation!



Outsourced laboratory work [ONE time Only]
11 months development stage is a
ONE time only event as once the
Human Artificial Chromosome vector is
loaded with foreign genes/DNA designed
by Rius Medical, the engineered stem cells
self-renew long term in large volume
bioreactor culture. This provides multiple
batches of desired cell therapies long term



B2B marketplace: Rius Medical **is best positioned** as a Technology Transfer supplier to other companies. Adopting a supplier's perspective <u>and providing value-added services</u> when compared to the "alterative supplier" blood-donation, Rius Medical goes beyond EU-market, to USA-market and China-market.



Thus effectively enabling 3x dividends financial benefits on Equity Capital

By December 2023, significant progress of **Rius Medical** is technology transfer deals to FR, Erytech Pharma (Enzyme L-Asparaginase) and USA, Travere Therapeutics parent company of CH, Orphan Technologies (Enzyme Thymidine phosphorylase). Example: Travere Therapeutics (previously Retrophin) made an upfront payment of \$90 million in cash at closing of the transaction. Orphan Technologies shareholders will remain eligible to receive **up to \$427 million** in additional cash payments contingent upon the achievement of key milestones in the development and commercialisation of OT-58 www.. [Encapsulation in **29 days half-life** red blood cells from the patient's own blood, Phase 2 clinical trial until December 2022 at St George's, University of London www.]

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