biobridge·2019
new drugs R&D acceleration program

The first Austrian–Russian

international acceleration program for innovative drug development projects

Contents

About biobridge-2019

Biobridge-2019 is the first Russian-Austrian international acceleration program for drug development projects where all stakeholders of the pharmaceutical industry meet and work together to drive innovation in pharmaceutics. Biobridge-2019 was successfully launched in March 2019 with support of the government and academia organizations from Russian Federation and Austria. Among prominent partners of Biobridge-2019 program are the Ministry of Industry and Trade of the Russian Federation, the Ministry of Science and Higher Education of the Russian Federation, Skolkovo Foundation, Russian Venture Company, LISAvienna, the Vienna Business Agency and some academic partners.

The mission of Biobridge-2019 is to support innovative pharmaceutical projects with everything they need to validate their ideas of improving quality of life at any development stage.

biobridge-2019 program focuses on four areas:

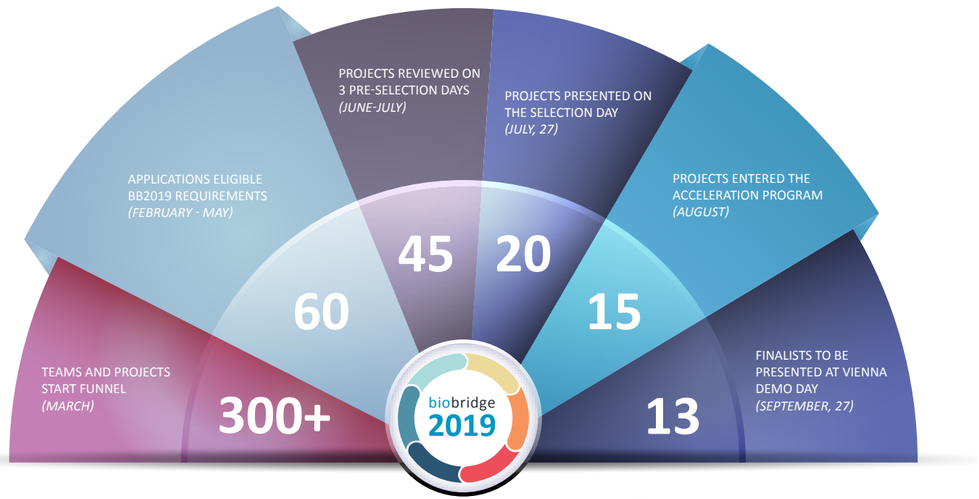
Discovery: In vitro development, novel mechanisms of action and biotargets
Development: Development of innovative pharmaceuticals towards in vivo proof-of-concept
Go2Market: Innovative projects in clinical development stage including already approved, clinical proof-of-concept, Russian and EU market launch
Digital Drugs: Innovative treatment approaches and digital drugs using AI and Big data

The biobridge-2019 Demo Day takes place at Austria's largest art fair viennacontemporary in Vienna. Russian and European private investors, business angels, representatives of venture funds and industrial partners are invited to the event. The international expert council of the accelerator is chaired by Professor Sir Konstantin Novoselov FRS, Nobel Prize Winner in Physics. Some of his artworks will be presented within the framework of a special biobridge-2019 exhibition together with the artworks created by young artists inspired by innovative pharmaceutical projects.

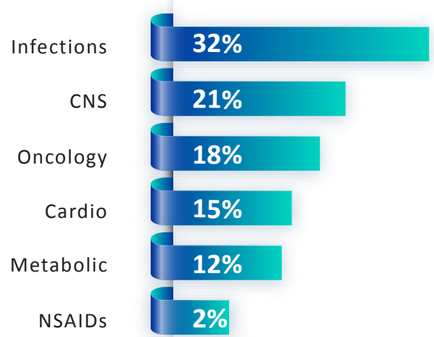
Supported by:

MINPROMTORG RUSSIA · Skolkovo · RVC Russian Venture Capital · Ministry of Science and Higher Education of the Russian Federation · MIPT · STARTUP RALLY · vienna business agency · LISAvie life science a

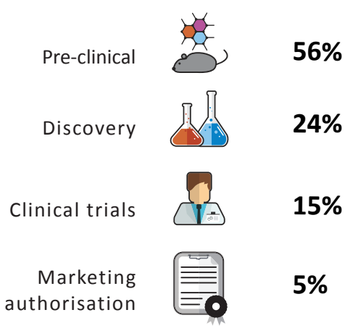
Selection process



Therapeutic Areas



Development stages

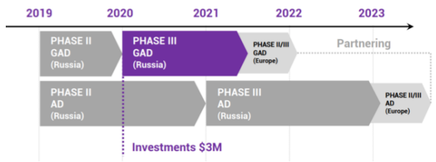


avineuro

Description of the problem

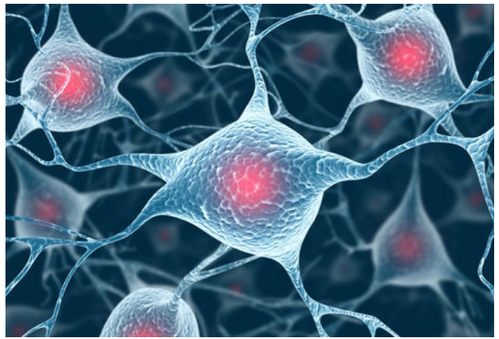
Anxiety disorders are common mental diseases that are characterized by persistent and unrelenting worry about everyday things. According to WHO estimation, it affects 300 million people worldwide. Current anxiety disorder medications have significant limitations in particular due to their ineffectiveness and, in some cases, intolerable side effects.

Pipeline



Project synopsis

AVN-101 is an innovative drug candidate with a multimodal mechanism of action. The unique receptor profile of molecule allows treating several symptoms at once. AVN-101 has strong precognitive activity and significant anxiolytic effect. In addition to being highly active in animal models, AVN-101 has good bioavailability, high brain distribution, and low toxicity. Phase II of clinical trials has been successfully completed in patients with generalized anxiety disorder. Eight weeks of treatment with AVN-101 produced significant improvement in HARS total score, anxiety was reduced by half.



Business model

The market for Anxiety Disorder Treatment in Russia is now about $240 million (while globally this figure exceeds $15 billion). Market growth is 15% per year. AVN-101 is expected to enter the market in 2022 and reach peak sales by 2026. If we take at least 5 % of the market, which is more than feasible for an innovative drug, peak sales will make approximately $36 million, with IRR reaching 131%.

Liudmila Yamukova

Company / team

Avineuro is a high-tech R&D pharmaceutical company comprising a team of prominent scientists. We specialize in creating innovative solutions for diseases of the central nervous system. Our portfolio includes molecules for treatment of Alzheimer's, Schizophrenia, Bipolar affective disorder, and Generalized anxiety disorder.

VALENTECH

Valentech
FAP-2015

Maxim Zapolsky

The problem the project solves / relevance of the problem

Impulsivity and related behavioral disorders that include gambling, alcoholism, and drug addiction are a problem affecting up to 20% of the healthy population and up to 60% of patients with functional mental disorders.

For patients with psychiatric diagnosis (e.g. schizophrenia, bipolar affective disorder, ADHD, etc.), comorbid impulsivity poses a serious problem, often leading to aggressive, self-aggressive behavior, or even suicide. Violent outbursts can endanger life or health of the patients, their families, and doctors.

Impulsivity was introduced as a new diagnostic category in the Diagnostic and Statistical Manual of Mental Disorders, DSM-5 (F63, Impulse Disorders) and recognized as a separate therapeutic category requiring new modern drug therapy. A number of western companies started clinical trials, but their research has been limited to repositioning the existing drugs according to new indications. Still, there is no specific therapy for impulsivity, nor is there a medication in the market having impulsivity in indications for use.

Summary of the project

FAP-2015 is the first original drug to specifically treat impulsivity in various functional mental disorders with strong

IP support. Potentially, the product is the first-in-class with regard to the market entry. Preclinical studies confirmed the effectiveness of FAP-2015 in the therapy of impulsivity. The drug is ready for clinical trials scheduled for 2020.

About the company

Valentech is a private startup company set up in 2011. It specializes in R&D of drugs in mental and neurological disorders. The team is a group of scientists with over 25 years of experience in basic and applied research as well as clinical trials. We have accomplished more than 20 projects, including Phases I, II, and III in international multicenter trials of most modern drugs.

AnnSIGHT

Project goal / description of the problem
AnnSIGHT is a project aimed at developing a system with a potential to completely cure type 1, i.e. insulin-dependent diabetes.
Currently, there are more than 400 million people with diabetes worldwide and their number is growing by more than 10 million per year.

Short description of the project
The project is developing a therapy based on the use of a specially designed cellular product. We use direct reprogramming of the patient's own cells to create insulin-producing glucose-dependent cells. Then the cell product is packed into special capsules. Their walls, which are permeable to insulin and glucose, protect the product from the immune response. The capsules are inserted into the muscle, ensuring complete command over the injected material and minimizing the risk of complications.

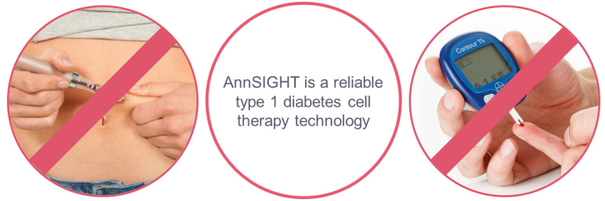
Advantages of the system
- Reproducibility and scalability
- Use of patient's own cell material
- Absence of the immune response
- Full control of the administered material
- Low-invasive procedure

Stage of the project
The project is currently at the research-and-development stage.

Team / motivation
Our team consists of 13 people, including 11 cell technology experts. The founder of the project is Vladimir Kozlov. Ann in the name of his younger sister who has lived with type 1 diabetes for 17 years. An opportunity to help her has been the driving force of this project, but we hope to help everyone who suffers from the same disease.

Prospects
High demand, effectiveness, simplicity, and safety of AnnSIGHT technology ensure its viability for clinical use.

Vladimir Kozlov



AVIVIR
Chemrar group company

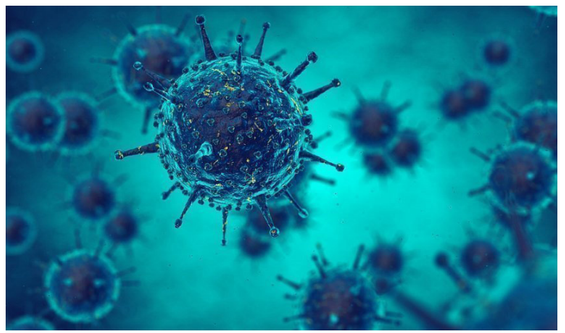
Information about the company
Avivir is an internal startup of ChemRar Group of Companies conducting research, development, and implementation of innovative antiviral drugs.

Relevance of the problem the project solves
According to the WHO every year 10 to 30% of the population suffers from various forms of SARS. The global incidence of influenza is approximately 1 billion cases, including 3 to 5 million severe cases resulting in up to 500,000 deaths. Despite the relatively short duration of the disease, influenza is one of the main challenges and risks to health and safety of mankind. It can cause complications, such as pneumonia, bronchitis, otitis, etc.

Summary of the project
ChemRar is developing AB5080 molecule, an innovative drug candidate for the treatment of diseases caused by the influenza virus. It belongs to the class of influenza neuraminidase inhibitors, which is currently the only class of medication proven effective in treating influenza over the past 10–15 years.

Stage of development
The first phase of clinical trials of AB5080 was conducted in 2017. The candidate was recommended for further clinical studies. This year we have successfully completed the second phase of clinical trials in patients with influenza.

Advantages of the drug candidate
The potency of AB5080, as well as its efficacy in vivo, is on a par with the leading neuraminidase inhibitors, such as Oseltamivir, Zanamivir, Laninamivir, and Peramivir. However, what distinguishes AB5080 is that it acts on the strains, which have developed resistance to them. The data obtained in the course of clinical studies have unambiguously proved efficacy, effectiveness, safety, and good tolerance of AB5080.



Prospects / estimate
By 2022 Avivir plans to complete Phase III of clinical trials and bring the drug to the market.

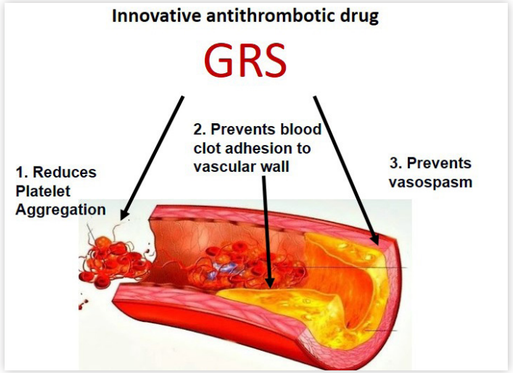
Aslan Pshikhachev

Veniamin Khazanov

Problem:
18 M people die from thrombosis every year on regular treatment.
200M people are in the risk groups.
GRS solves the problem of cardiac and cerebral arterial thrombosis in patients with cardiovascular diseases.

Existing drugs have a narrow therapeutic range (5–30) and serious shortcomings:
- None of them inhibit the development of pathology.
- Effective only at the final stages of thrombosis and target strictly one process.
- For efficacy used in combination, aggravates adverse effects and dangerous drug-drug interaction (DDI).
- Changes in metabolism can lead to lack of effect and risk of life-threatening complications (e.g. internal bleeding).

Advantages:
GRS is the first-in-class drug with a new target, soluble guanylate cyclase enzyme.
- Thanks to a new mechanism of action, acts on 3 main causes of thrombosis:
- Atherosclerotic damage of vascular wall
  – Vascular spasm
  – Platelet aggregation
- Therapeutic range is 10 times wider than any competing drug.
- Inhibits the progression of pathology and affects target reversibly, reducing the risk of life-threatening complications.
- Effect does not depend on liver metabolism, eliminating DDI risk and efficacy fluctuations.



The unique combination of safety and efficacy makes GRS number one drug for life-long use by patients following cardiovascular events or invasive surgeries (e.g. stenting, implantation, endoprosthesis).

Project track:
$2M+ invested in 2013–2019
API and dosage forms developed
Preclinical trials completed by IPHAR R&D center
Phase I clinical trials: in progress (2019)
IP: Patented in Russia, US, and EU
Prospective partner on the Russian market, "Organica" (Novokuznetsk), invested in clinical trials and tech transfer
Start of sales in Russia is planned for 2024

We plan to attract $10M in EU and US for Phase II clinical trials (thrombosis-induced heart attack and stroke) with subsequent sale to a strategic investor.

GRS is a spin-off project of IPHAR R&D center, which comprises a team of professionals with 10–40 years of experience in drug development and 200+ preclinical and clinical projects completed.

L-BIO

Igor Levshin

Company

L-BIO is a pharmaceutical company developing innovative drugs for infections caused by pathogenic fungi. The team of professionals with experience in creating highly effective drugs, clinical trials and bringing the drugs to the commercial market.

Description of the problem

The world death toll associated with invasive mycoses has reached 1.35 million cases per year.

It is comparable to the mortality rate from malaria and tuberculosis, but in contrast to them, it increases.

Very common infections are in immunocompromised patients, HIV, or after organ transplant operations. The problem is the ever-increasing resistance to the currently used drugs (antimycotics). We found the effective medication that will overcome the barrier of resistance.

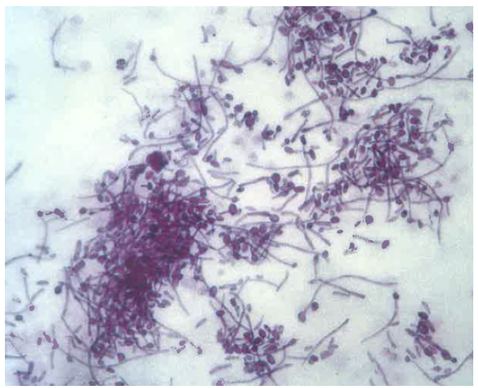
Synopsis

We developed a number of auspicious molecules based on thiazolidine and triazole to treat the life-threatening systemic mycoses. The unique double mechanism of action of hybrid molecules solves the resistance of microorganisms and thereby helps to avoid serious complications or fatalities.

The drug tested in comparative experiments with generalized Candida infections in animal models and showed obvious advantages over the existing drugs:

- Efficacy on a broader spectrum of strains
- Strong antimicrobial effect on resistant strains
- Excellent tolerance, classification as a non-toxic drug

The project is at the preclinical stage and selection of a lead, i.e. molecule that meets all requirements for a highly effective drug.



Patent

IP is protected by patents in Russia and PCT 2019.

Market feasibility

The main competitor Fluconazole and its hybrid analogs have drastically weakened their position due to the cross-resistance of various pathogenic fungi of the genus Candida. Thus created the favorable conditions for a successful launch of the innovative drug. The advantage of the project is its early stage, while the conducted studies confirm the high probability of drug to have a commercial success on the market.

Cardio System Pharma

Normacor

What's the problem?

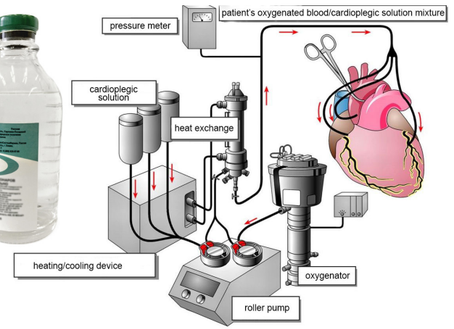
Over 1 million open heart surgeries are performed worldwide every year.

Cardiac surgeons still have no convenient universal technique to optimally protect and preserve the heart at the final stage of the surgery and prevent additional damage to it.

There are two types of contemporary cardioplegic techniques:

- **#1 cold (hypothermic) techniques**
  They cause ischemia, which often leads to intraoperative myocardial infarction;
  They cause additional reperfusion damage at the final stage of the surgery.
- **#1 warm (normothermic) I techniques**
  They are not very convenient for surgeons, as they require re-infusion and limit cardiac procedure duration.

Solutions for them are mixed "in-house" just before the surgery, and consequently, come out devoid of proper shop-floor quality control and assurance.



Solution - Normacor

Normacor is a normothermic cardioplegic solution, which combines all the advantages of contemporary myocardium protection techniques in open heart surgeries, yet allows to eliminate their shortcomings. This is possible because of the two key properties of Normacor:

1. Absence of ischemia during the cross-clamp period;
2. Absence of reperfusion damage at the final stage of a cardiac procedure.

These properties ensure a predictable outcome for long-lasting and complex interventions even with a single infusion of Normacor.

Stage of development/Application prospects

The medicine is registered, manufactured and successfully used in the Russian Federation.

This innovative solution can benefit the entire field of cardiac surgery, and increase the profitability of European pharma companies specializing in the sector.

Maxim Podkolzin

Company description:

CardioSystemPharma JCS is the developer of Normacor medical product and holder of the marketing authorization for the Russian Federation.

NewVac
Chemrar group company

Quisinostat

Yulia Baybikova

The problem the project solves / Relevance of the problem

The project aims to develop a combinational drug to treat synovial sarcoma, an aggressive tumor that particularly affects teenagers and adolescents. To date, there are no available treatment options apart from standard chemotherapy associated with severe adverse reactions and poor efficacy.

Summary of the project

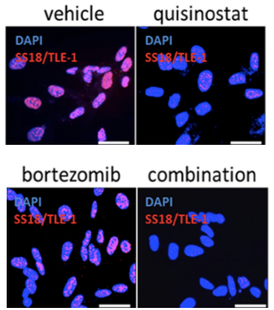
Quisinostat is the best-in-class oral HDAC inhibitor with unique PK properties allowing it to be used to treat solid tumors. The drug was originated by Johnson & Johnson and co-developed with NewVac in 6 phase I-II clinical trials in oncological indications. Afterward, NewVac obtained exclusive global rights to develop and commercialize the drug.

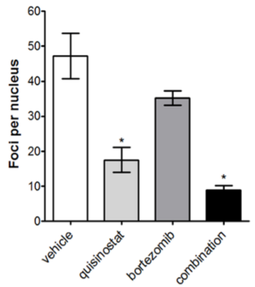
Stage of development

Quisinostat showed good tolerability in a combination including bortezomib. Besides, combined with background chemotherapy, the drug demonstrated high efficacy and safety in patients with platinum-resistant ovarian cancer showing an objective response rate of 58.1% and median PFS of 8 months, dramatically exceeding current treatment standards.
Quisinostat IP is protected worldwide until 2032. There is an open IND in the USA.

Advantages

IQuisinostat showed the highest score in vitro among 900 selected compounds, confirmed by in vivo experiments. Moreover, the synergy with the next effective class drug, bortezomib, was observed (Figs. 1 and 2). Since there are no effective treatment approaches for these groups, high unmet need from patients and medical society will provide a smooth launch of a new treatment standard worldwide with minimal marketing costs.
Quisinostat is orphan/breakthrough therapy designation-feasible, thus significantly reducing regulatory costs and enabling sales in parallel with clinical development





5. Team

The project team comprises participants with extensive experience in development, commercialization, and successful launch of new drugs worldwide in collaboration with major international pharmaceutical companies.

NP PharmaTech

KFU-01

Challenge

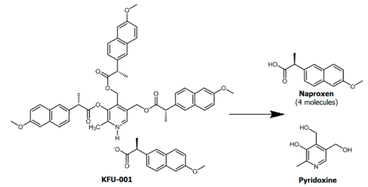
Up to 30% of the global adult population suffers from rheumatoid arthritis and osteoarthritis. Among those, at the age above 60, this pathology is even more common. Almost 50% of the population is diagnosed with joint diseases. Almost every person encounters such acute conditions as ischialgia and lumbago. NSAIDs have limited efficacy and toxicity (cardiovascular, gastric, nephrotoxicity, etc.).

Project resume

KFU-01 belongs to a new generation of non-steroidal anti-inflammatory drugs (NSAIDs). It is a prodrug molecule that releases two active components that have a unique synergistic effect. As a result, KFU-01 significantly outperforms all market-available NSAIDs in terms of anti-inflammatory efficacy and safety (the absence of gastric toxicity and other undesirable effects even after prolonged use). Even in older patients, KFU-01 can effectively treat arthritis, arthrosis and other diseases without the threat of adverse gastric, cardiovascular, or other complications. Given the unique competitive advantages, KFU-01 can occupy a significant share of the global NSAID market (sales > US$12 bln) oversaturated with generics.

Development status

Preclinical phase successfully completed, clinical phase I initiated.



Advantages

KFU-01 has significant advantages over all market-available NSAIDs:

- High efficacy in the treatment of acute inflammations.
- Significantly increased anti-inflammatory activity in the treatment of chronic inflammations.
- Increased analgesic activity, comparable to “soft” opioid analgesics.
- Significantly decreased acute toxicity.
- Dramatically decreased gastric ulcerogenicity.
- Decreased toxicity after chronic 6-months’ administration.
- Improved pharmacokinetics profile, prolonged effect, once-a-day administration.
- Alternative therapeutic indications.

Yuri Shtyrlin

Project company

NP-Pharmatech LLC, a resident of the Skolkovo Innovation Center, established in 2019. The IP rights are protected in the world’s top markets (Russia, EAEC, EU, USA, China, India, Japan). The IP rights belong to Tatkhimpharmpreparaty JSC (Kazan, Russia).

Drug	ED_{50} (mg/kg) acute inflammation	UD_{50} (mg/kg)	LD_{50} (mg/kg)	UD_{50}/ED_{50} (safety index)	LD_{50}/ED_{50} (therapeutic index)
KFU-01	**15**	**> 2000**	**> 5000**	**> 130**	**> 330**
Ibuprofen	48	310	750	6.45	16
Diclofenac	8	48	370	6	46
Naproxen	15	49	620	3.2	42
Piroxicam	20	36	290	1.8	15
Phenylbutazone	56	120	430	2.1	7.7
Acetylsalicylic acid	98	240	1600	2.45	16
Indomethacin	10	10	47	1	4.7

PS PharmaTech

KFU-05

Challenge

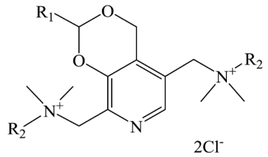
Existing antimicrobial agents are rapidly losing their effect; still, there is insufficient investment in new disinfectants, diagnostics of resistant microorganisms, and new biological and chemical agents for controlling infections. According to WHO data, the arsenal of tools to combat resistant microorganism will soon be depleted. Without new effective antibiotics and antiseptics, the success of surgery and chemotherapy would be compromised.

Project resume

KFU-05 is an antiseptic drug for external use with a broad-spectrum microbicidal activity against the most common and dangerous bacterial, fungal, and viral pathogens, including drug-resistant strains. KFU-05 is also active against the biofilm-embedded pathogens. A unique feature of KFU-05 is suppression of pathogens' ability to develop resistance. As a result, this agent doesn't lose its microbicidal efficacy even after prolonged use. KFU-05 can occupy a significant market share: expected sales >US$17 bln.

Advantageous pharmacological profile

- Increased antibacterial, antifungal, antiprotozoal, and antiviral activity versus available antiseptics. KFU-05 has been tested on a panel of widespread pathogens of wound infections (87 clinical isolates). All 87 bacterial strains were sensitive to KFU-05 (MIC ≤64 μg/ml).
- KFU-05 suppresses the ability of pathogens to develop resistance.
- Decreased acute toxicity in rodents (oral LD50 = 1,706 mg/kg), as compared to the widely used antiseptics Miramistin (LD50 1,000 mg/kg), benzalkonium chloride (LD50 150 mg/kg), and chlorhexidine (LD50 1,260 mg/kg).
- Preclinical phase successfully completed in 2019.
- Favorable profile of physical and chemical properties, high chemical stability after prolonged storage.



Strain	KFU-05	Octenisept	Miramistin	Chlorhexidine	Benzalkonium chloride
S. aureus ATCC 29213	4	64	16	2	2
B. subtilis 168	2	64	2	2	0.5
S. intermedius 1061 MRSI	1	32	8	4	4
S. aureus 1168 MRSA	1	16	8	2	2
S. aureus 22	1	8	8	2	0.5
E. faecium 31	0.03	8	4	4	0.25
K. pneumoniae 1813	2	32	>64	2	>64
P. aeruginosa ATTC 27853	4	32	>64	4	>64
Moraxella spp.765	4	64	64	32	32
Acinetobacter spp. 1	16	64	64	64	>64
Pseudomonas spp. 5	8	64	>64	64	32
E. coli 13	8	64	32	64	2

Nikita Shtyrlin

- The proposed mechanism of action is disruption of the cytoplasmic membrane of microorganisms. At the same time, intracellular targets cannot be excluded.

Project company

PS-Pharmatech LLC. The IP rights are protected in the world's top markets (Russia, EAEC, EU, USA, China, India, Japan). The IP rights belong to Tatkhimpharmpreparaty JSC (Kazan, Russia).

CRYNO BIOTECH

The Problem the Project Solves

Type 2 Diabetes (T2D) is one of the major healthcare challenges of the 21-st century and it is on the rise. According to the forecasts, the number of patients with T2D will increase by 48–50% by 2045.

Diabetic neuropathy (DN) is one of the most common complications of T2D, which affects up to 50% of patients. DN significantly decreases the quality of life and often results in disability. However, no therapy slowing down nerve tissue degradation is currently available in the market.

Project Summary /Advantages/ Stage of Development

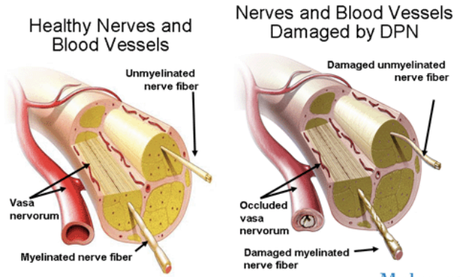
Cryno Biotech is developing a novel GLP-1 receptor agonist (CRY-001) with promising preliminary preclinical results in treatment of type 2 diabetes and prevention and treatment of diabetic neuropathy.

The specific structure of the molecule of CRY-001 with polyarginine vector helps:

- Increase stability and half-life of the molecule
- Improve the blood-brain barrier and cell membrane permeability. In vivo, CRY-001 studies have shown:
- Good neuroprotective effect, including remyelination of the nerve tissue
- Decrease of neuropathic pain
- Promising hypoglycemic effect
- Anti-ischemic and moderate analgesic effect

The molecule has a solid potential to become a market leader in GLP-1 class. CRY-001 will be supplied as a finished pharmaceutical formulation with extended release for subcutaneous administration once a week or once every 2 weeks.

Diabetic Peripheral Neuropathy



Vinik AI. *Diabetic Microvascular Complications Today*. 2006;3:23-26.

Developing Company

Cryno Biotech was founded in 2017 with private funding. In 2018, the company received a grant for pre-clinical studies and was selected to join Johnson & Johnson and SK Biomed accelerator.

The project seeks commercialization by out-licensing of Intellectual Property and/or acquisition of Cryno Biotech by a large pharmaceutical company upon completion of Phase I or Phase II of clinical trials.

Dmitry Shobolov

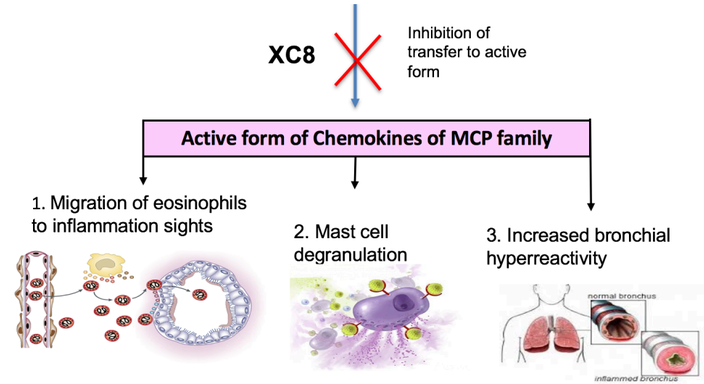
Problem the Project Solves
The eosinophilic phenotype of asthma is characterized by the high frequency of hospital admissions and a large burden on healthcare. The recent approval of targeted biological drugs has partially solved the problem for patients with **severe eosinophilic asthma**, and these products have become blockbusters (>$1B revenue). However, these biological drugs are not applicable to patients with **mild-to-moderate eosinophilic asthma** due to the high price and parenteral route of administration.

Summary of the Project
EURRUS GMBH develops XC8, a novel oral drug candidate for the treatment of mild-to-moderate eosinophilic asthma. XC8 is aimed at targeting the broad market niche, which is currently not filled with highly demanded drugs.

IP protection till 2033

Pipeline
Efficacy and safety of XC8 was demonstrated in several clinical trials. Administration of XC8 in patients with mild-to-moderate eosinophilic asthma for 12 weeks resulted in clinically and statistically significant improvement in FEV1 compared to placebo.

Helmut Schmutz



Business Model
Investment is now sought for completion of the next stage of clinical development of XC8 in 2019-2021,which is likely trigger acquisition of the product by a strategic investor. Approximate volume of such transactions is 100 million euros.

Founders & Partners

The industry alliance Neuronet
A state industry alliance with numerous research and technological centers, educational and business institutions engaged in social and commercial projects in the areas of neuropharmacology, neuromedicine, neuroentertainment and sports projects, neuroeducation, neurocommunication and marketing, neuroassistants. www.rusneuro.net

RDI Group
RDI Group is a holding company operating in the most prospective sectors of the economy. It unites several companies operating in various sectors, which enables it to build up a diverse business stable to risk. The group's main areas of activity are development and investment in real estate. www.rdigroup.ru

ChemRar Group
ChemRar Group unites R&D service and investment companies in the field of innovative pharmaceuticals for the development and commercialization of innovative medicines, diagnostics, preventive care and new treatments of life-threatening diseases in Russia and abroad. www.chemrar.ru

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