



Konstantin V. Balakin, PhD, DSci
Director of NP "Orchemed"

*May 2011
Chernogolovka*

**Nonprofit partnership of chemical
institutes of RAS**

«Orchemed»

(Organic Chemistry for Medicine)

**a novel way to transfer innovative
technologies to market needs**

ISTC project #3283

Identification, Characterization, and Application of the Useful Properties of Novel Compounds as Candidate Drugs Based on Preclinical Trials and Technology Transfer

Partner in USA: BioIndustrial Initiatives (BII)

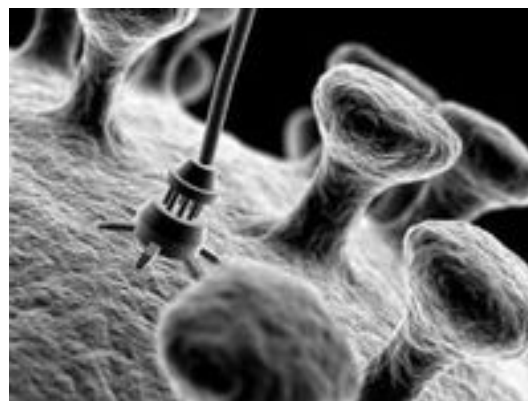
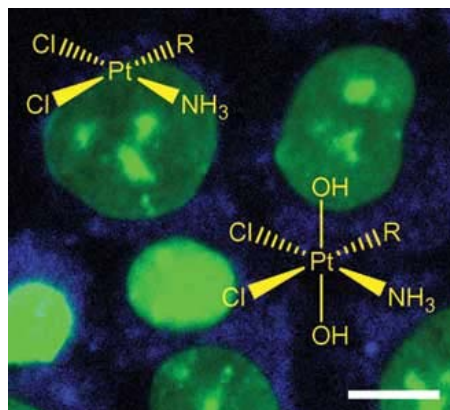
Leading Organization: Not-profit Partnership “Center for the Development of New Potential Medicines” “ORCHEMED”

Phase I: January 2006 – March 2008

Phase II: April 2008 – March 2009

Phase III: from April 2009

Orchemed: structure, mission, activity





General information

Established in 2005

The legal status: nonprofit partnership

Founders: Institutes of RAS

Management:

Scientific Board (chairman – Acad. N.S. Zefirov), Board of experts (chairman – corr. Member of RAS S.O. Bachurin), director (K.V. Balakin, PhD, DSc)

Institutes-members: 13 institutes of RAS, incl. IPAC, IPPC (Chernogolovka), IOC, IEOC, IBCh, IGen (Moscow), ISC (Ivanovo), IOPC (Kazan), IC (Syktyvkar), IOC (Ufa), IOS (Ekaterinburg), IOC (Novosibirsk), IOC (Irkutsk)

Orchemed – Russia’s biggest

cooperative academic initiative in the field of drug discovery and development

Complete cycle of preclinical innovative drug discovery

From virtual screening to preclinical animal studies

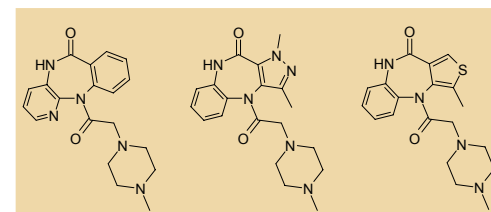
Portfolio of innovative projects

More than 50 projects in actual therapeutic areas

Focus on innovative developments

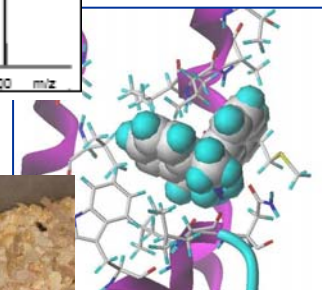
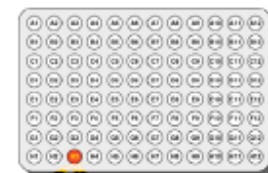
Distinctive feature of academic projects

Orchemed’s Mission: To identify and promote prospective technologies developed in Russian academic institutes, and pave the way to effective technology transfer to national and global pharmaceutical industry



Pirenzepine
(Boehringer Ingelheim)

Pirenzepine
(Ludien)



- Invited experts for State Duma, government, mass media, etc.
- Official codevelopers of Strategy of Development of Pharmaceutical Industry of Russian Federation in 2008-2020 (Pharma-2020)
- Expert evaluation of work projects for business groups
- Initiator of strategic national projects, such as National bioscreening network
- Strategic partnership with Russian innovative (bio)pharmaceutical companies, biopharmclusters, etc.



Presentation of Orchemed's projects in the State Duma



Presentation of NP Orchemed to Minister of economy of RF



Expert's round table in "Rossiyskaya Gazeta"

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Scientific Conferences

September 2008, Chernogolovka
Scientific Conference «Orchemed-2008»

July 2009, Ufa
VII Scientific conference “Chemistry and Medicine, Orchemed-2009”.

October 2009, Antalya (Turkey)
1st Turkish-Russian symposium on organic and medicinal chemistry.

April 2010, Moscow
Scientific conference “National bioscreening network”

June 2010, Saint-Petersburgh
Symposium of NP “Orchemed” «Development of drugs and physiologically active compounds from natural sources»

June 2011, Saint-Petersburgh
2nd Symposium of NP “Orchemed” «Development of drugs and physiologically active compounds from natural sources»



Содержание

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- 1.1. Стратегические принципы разработки Стратегии
- 1.2. Цели и приоритеты государственной политики Российской Федерации по развитию национальной фармацевтической промышленности
- 1.3. Ожидаемые результаты реализации Стратегии

2. Анализ состояния фармацевтической промышленности

- 2.1. Основные мировые тенденции на рынке продукции (услуг) фармацевтического сектора, глобальные направления научно-технологического развития
- 2.2. Место и роль фармацевтической промышленности в экономике России, общая характеристика отрасли

3. Системные проблемы фармацевтической промышленности

- 3.1. Проявления возможных системных проблем
- 3.2. Определение системных проблем
- 3.3. Анализ составляющих факторов системных проблем

4. Альтернативные сценарии развития отрасли

- 4.1. Иммерсионный сценарий
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Заключение

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- А) Анализ производства ЛС;
- Б) Анализ потребления ЛС.

Приложение 3. Анализ международного фармацевтического рынка:

- А) страна США;
- Б) страна ЕВ;
- В) страна СНГ

Приложение 4. Формативный план развития фармацевтики до 2020 г.

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Приложение 7. Региональные факторы развития фармацевтической промышленности.

Приложение 8. Финансово-экономические обоснования.

Приложение 9. Кадры для фармацевтической промышленности.

As an independent expert group, which represents Russian academic institutes, NP "Orchemed" officially took part in development of a novel **Strategy of Development of Pharmaceutical Industry of Russian Federation in 2008-2020 (Pharma-2020)**. The Strategy was developed in 2008-2009 by the Ministry of Industry and Trade of Russian Federation by order of the President and Security Council of Russian Federation.

www.pharma2020.ru

According to Strategy, 150-200 innovative drugs should be developed in Russia by 2020

National Bioscreening Network

Project №15 in the state register of promising pharmaceutical projects



Strategic goal:

Launching integrated national bioscreening network in Russia, as a systematic way to generate and develop innovative drugs

Developers: "Orchemed", IPAC RAS, IGG RAS

Applicant and leading organization: "Orchemed"

National Bioscreening Network

Molecules under development:

1. Advanced preclinical candidates

>50 leaders in actual pharmacological areas.

2013-2014: up to 10 candidates in phase I/II clinical trials, including: anti-TB (2 cmpds), antitumor (2 cmpds), cardiovascular (2 cmpds), CNS-active (2cmpds), other (2 cmpds).

2. Clinical candidates

-oncolytic; cardiovascular; oncolytic; antiparkinson

2015: 2-3 candidates in phase III clinical trials.

From 2014: NSBS will generate each year >30 advanced preclinical candidates ready to enter clinical investigations

IP rights will belong to NP “Orchemed” or to other private companies, not to governmental organizations (RAS, institutes, gouvernement etc.)

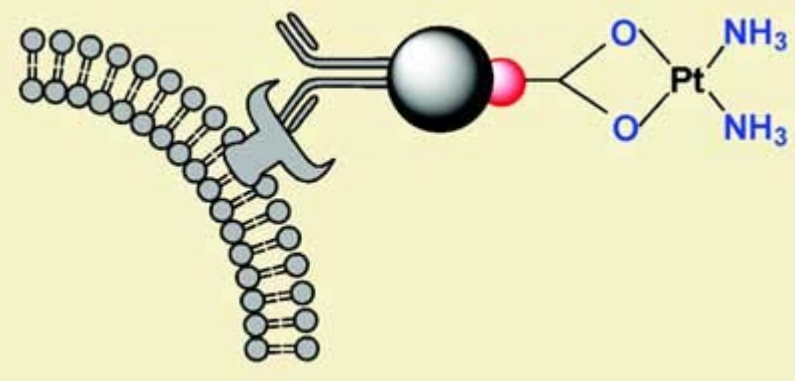
Strategic partnership with Russian innovative (bio)pharmaceutical industry

JSC «Binnopharm», JSC «Medbiopharm»

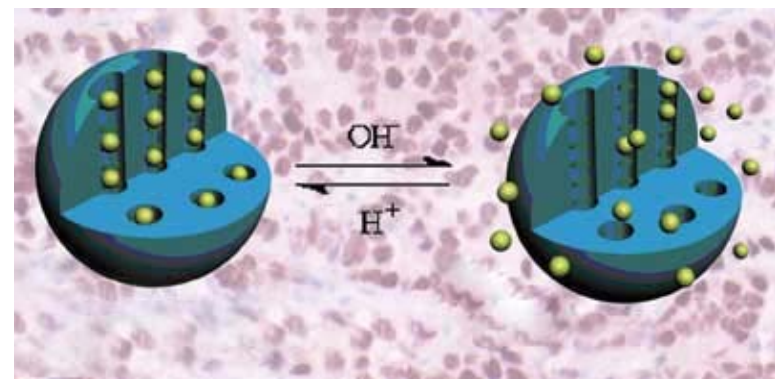
Pharmclusters (Kaluga, Yaroslavl, Sankt-Peterburg)



Strategic problems of Russian pharmaceutical industry cannot be solved without close collaborative efforts of science and business

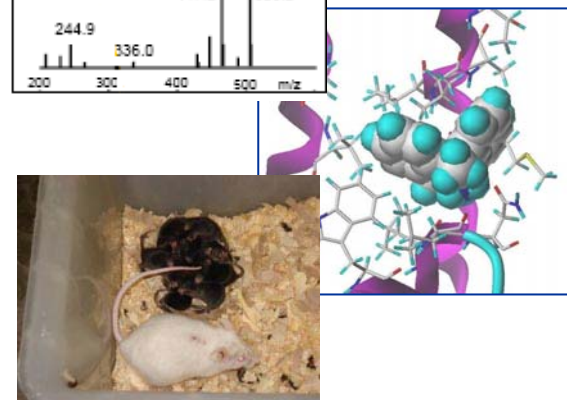
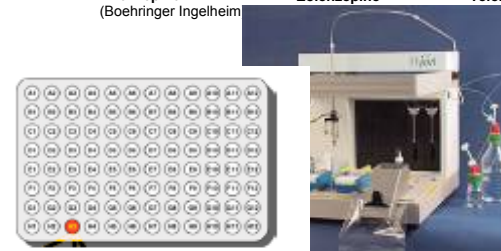
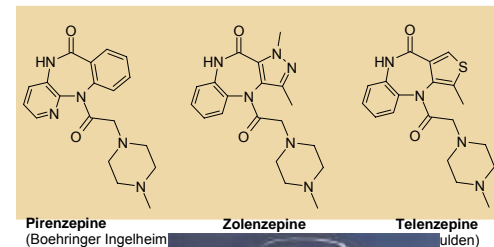


Technologies

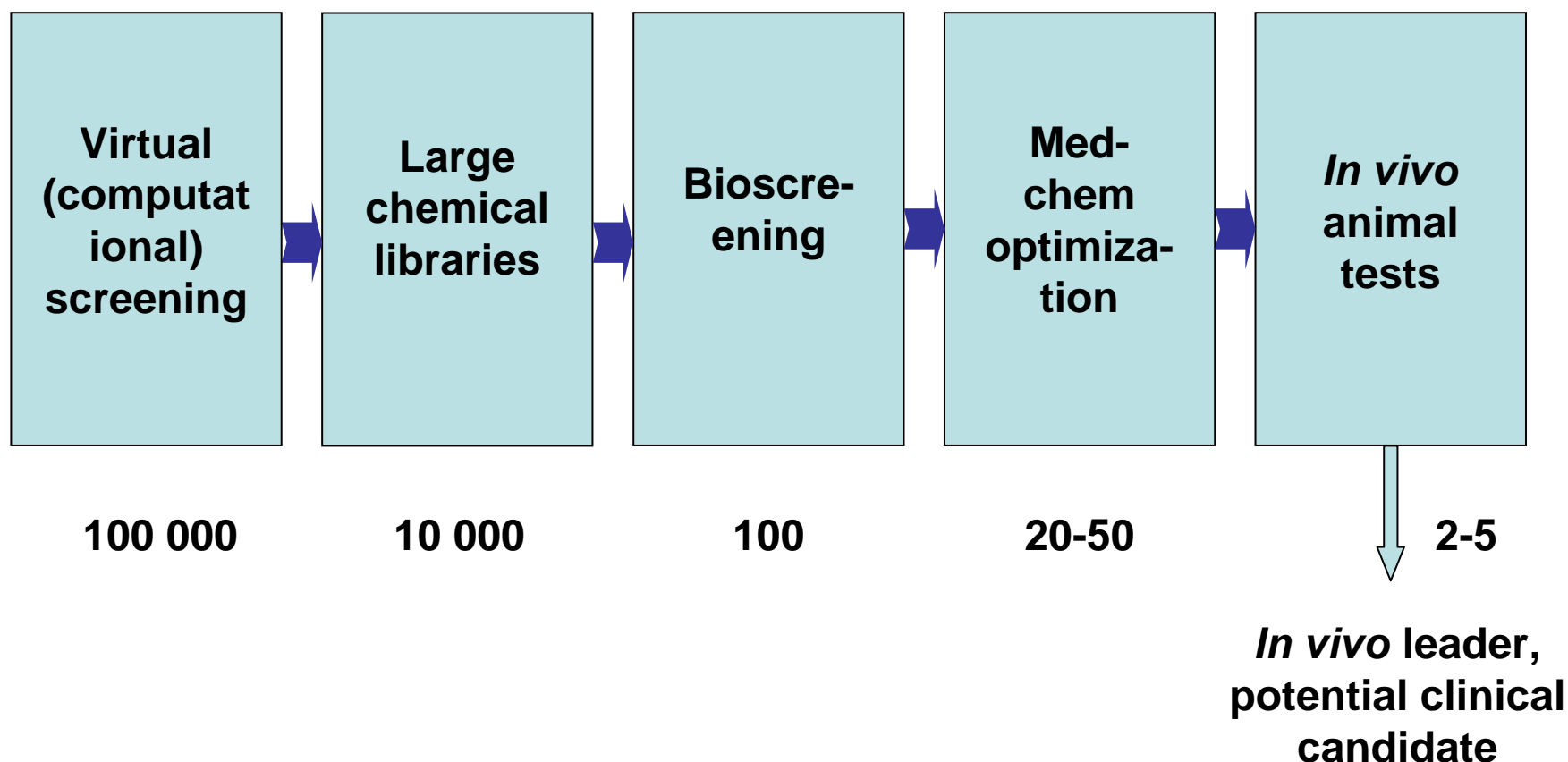


Full cycle of preclinical drug discovery

- ❑ Computational virtual screening
- ❑ Libraries of synthetic and natural compounds
- ❑ Biological screening
- ❑ Med-chem optimization
- ❑ Studies of molecular mechanisms of drug action
- ❑ Studies of phys-chem, pharmacological, metabolic profile of potential drugs
- ❑ Development of advanced drug delivery systems
- ❑ Preclinical animal studies



Technological aspects: the way to compound-leaders



«Orchemed»: functional structure

Compound sources: Institutes of RAS

Project evaluation: The internal board of experts, independent experts

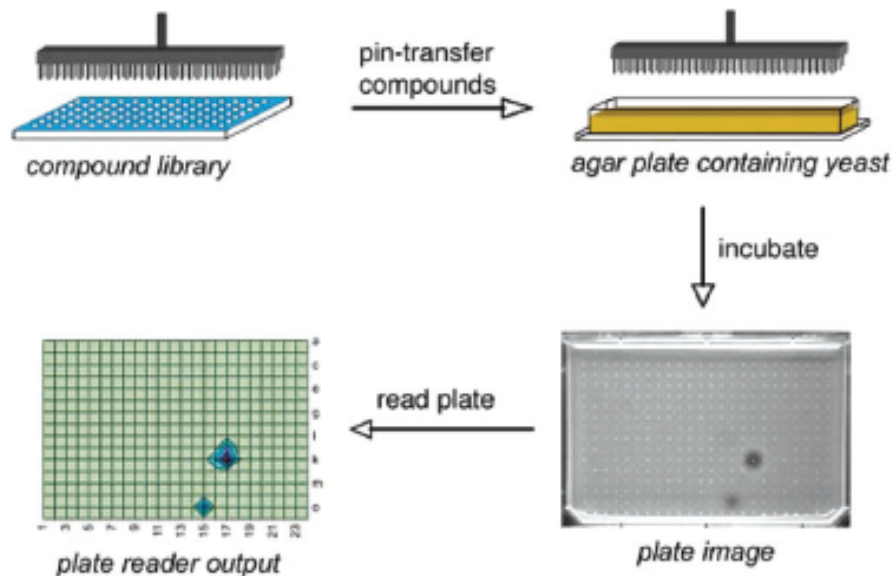
Technological laboratories of joint use:

- biological screening,
- virtual (computational) screening,
- preclinical animal studies («JSC TRUST»),
- studies of phys-chem properties, ADME/Tox profile, etc.
- development of advanced drug delivery systems

Marketing and legal support

- Project portfolio management, patent applications, market analysis, evaluation of IP landscape, etc.

Biological screening



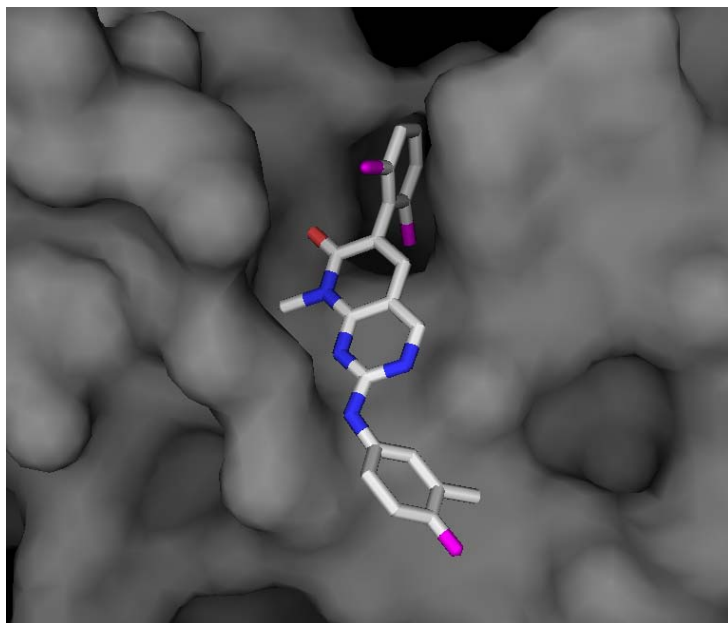
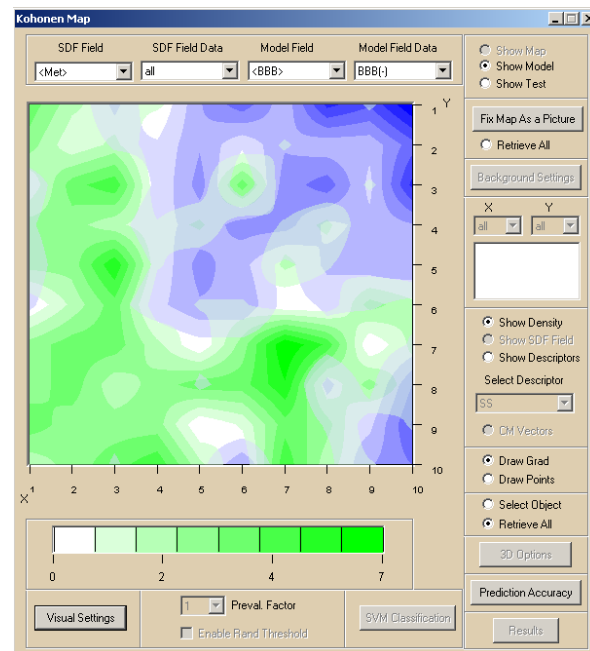
The key technological stage:

The bridge from large chemical libraries available in the institutes (10^6 cmpds) to preclinical and clinical candidates (10-100 cmpds)

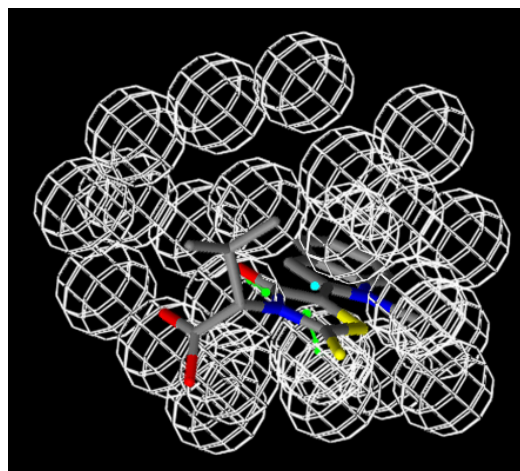
In vitro tests on individual biotargets, cell-based assays, ADMETox, phys-chem properties, etc.

Computational screening

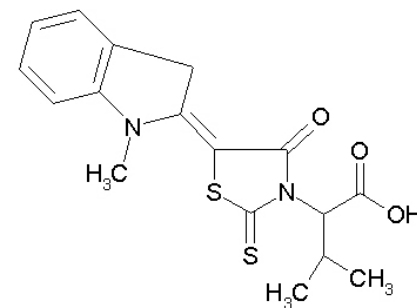
Data mining techniques



Molecular docking



3D pharmacophore design



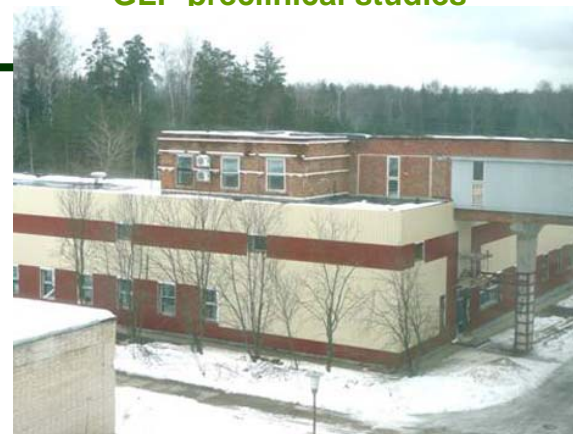
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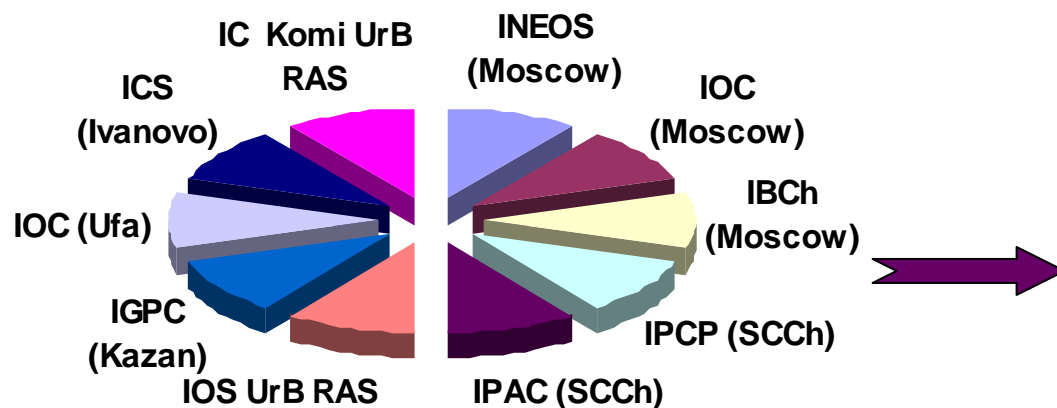
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Preclinical animal studies

JSC «TRUST»
GLP preclinical studies



Nonprofit partnership «Orchemed»

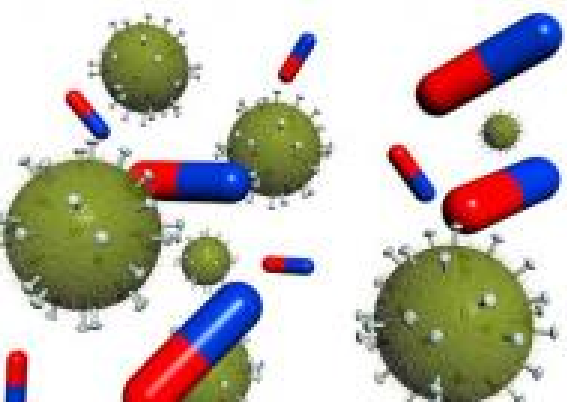


Expert evaluation of innovative projects

Orchemed: recognized expert group providing first-rate, multilevel evaluation of innovative drug discovery projects by order of academic, governmental and business organizations in Russia.

- ❑ Board of experts
- ❑ Independent experts (subcontracts)
- ❑ Multilevel project evaluation, including scientific, IP, market and technological stages
- ❑ Theoretical and experimental evaluation of active molecules





Project portfolio

>50 projects in actual pharmacological areas



INEOS RAS (Moscow): antiviral BG-122

Action of BG-122 on chickens, infected with H5N1 (dose 50 LD50).

№ group	Drug	Time of administration	survived/total	% of survived
1	BG-122	24 hours before infection	10/10	100
2		Simultaneously with infection	10/10	100
3		24 hours after infection	9/10	90
4		48 hours after infection	8/10	80
5	Control	-	0/10	0

After repeated infection of survived chickens (H5N1, dose 100 LD50) we observed 100% survival (0% in untreated control).

IOS UrB RAS (Ekaterinburg): anticoagulant LS-27

Strong antitrombotic action in a wide concentration range (0,01-1 mM).
The effectivity is validated in ex vivo experiments with human blood and in vivo experiments in rats.

Dose (mg/kg)	Time after administration (min)	Duration of blood flow (sec)	
		Control	LS-27
20	100	48±7	73
	220		59
80	100		81
	220		66

Effect of LS-27 on duration of parenchimal blood flow in rats liver after peroral administration

IPAC RAS (Chernogolovka): antineurodegenerative drug RU32-1

Dimebon (IPAC RAS, Medivation, Pfizer) – phase III clinical trials for neurodegenerative diseases.

Novel functional analogs of dimebon.

RU-32-1 is highly effective cognition enhancer in in vivo behavioral tests. Multitarget agent of novel generation which influences complex pathogenic mechanisms



WOUND HEALING DRUG (Chernogolovka - Moscow)

Compound type	Hybride molecule: natural prostaglandine + NO donator part
Developer	Institute of physiologically active compounds RAS, Institute of bioorganic chemistry RAS
Indications	Treatment of burns, wounds, dermatitis, psoriasis and other dermal diseases
Toxicity	Very low at therapeutic concentrations (SI > 1000)
Features	Preferable use in form of liniments or gels, also in cosmetic compositions
Development status	Advanced preclinical stages

Antiinflammatory drugs

Yaroslavl-Moscow-Chernogolovka

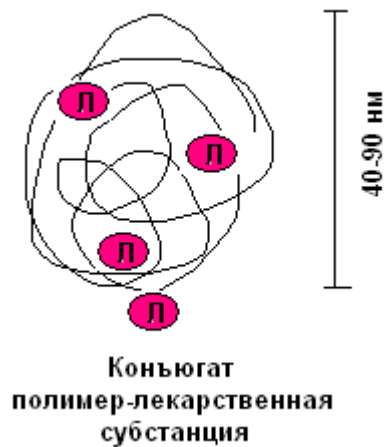
A series of hybrid molecules adamantane-amino acid derivative + NO donor

Strong antiinflammatory activity as compared to market available NSAID, low ulcerogenic, low toxic

Analgesic and antipiretic activity, without sedative effects

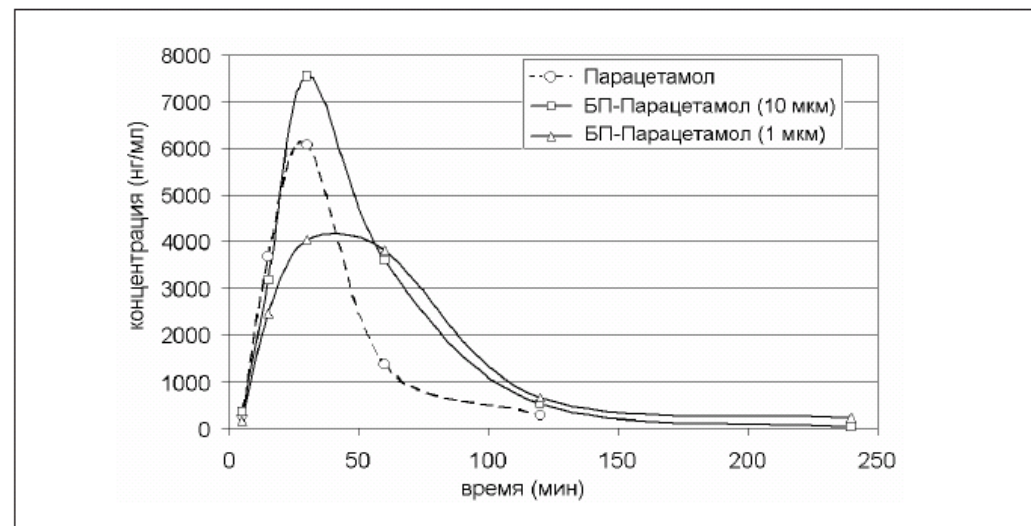
Development status: advanced preclinical studies

Advanced drug delivery systems based on nanosized noncovalent conjugates polymer-drug (Chernogolovka)



- enhanced bioavailability;
- prolonged action;
- complex modification of pharmacological parameters

Влияние размера частиц на содержание парацетамола в крови кроликов после однократного перорального введения в дозе 30 мг/кг



A.V. Sosnov, R.V. Ivanov, K.V. Balakin et al.
Good Clin. Pract. (Russ.). 2008, 2, 4-12

Active concentration of Dimebon in the noncovalent nanosized conjugate is 10 times smaller than for the nonmodified substance!

Ophthalmologic drugs (Moscow)

	indications	Clinical development phase	Drug form
Oro-001	catharacta	Phase III	Eye drops
Oro-002	miopia, eye trauma	Phase II	Eye drops
Oro-003	pathologies of rethina	Phase II	Eye drops
Oro-004	pathologies of rethina	Phase II	Eye drops

Peptide-protein complexes, isolated from animal tissues.

Based on specific bioregulators which activate cell regeneration in eye tissues (e.g. pluripotent stem cells), control basic biological processes (adhesion, migration, differentiation, proliferation of cells. Activity of these bioregulators is tissue specific but not species specific.

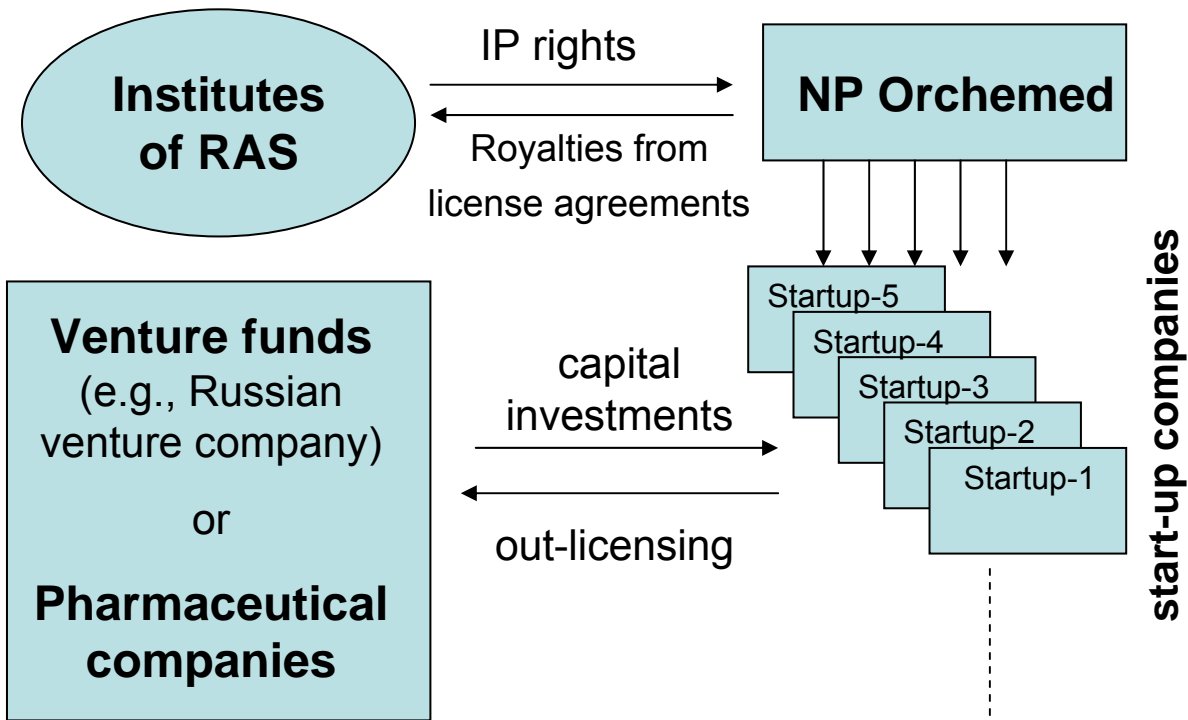
Oncologic and radioprotective drug (Moscow)

Type	Fractioned tissue extract from water animals <i>Margaritifera margaritifera</i> and <i>Holothuroidea</i>
Developer	Institute of elementorganic compounds RAS, Institute of developmental biology RAS
Activity	Profilactics and therapy of oncological diseases, radiotherapy. The drug stimulates processes of reparation in pathologic and damaged tissues, as fine tuner of haemostasis on organ-tissue level. The drug also possesses antiaging activity.
Drug form	Water solution of fractioned extract with concentration of peptide bioregulator 10^{-10} mg/mL
Toxicity	No toxicity observed. Compatibility with all other drugs

The drug is at final stages of preclinical studies

Project portfolio: summary

Pharmacological area	Number of projects
Oncolytic drugs	7
Anticoagulants	3
Antiviral drugs	3
CNS drugs	9
Anti-inflammatory drugs	6
Antibacterial drugs	3
Ophthalmologic drugs	6
Others	10
Novel diagnostic assays	2
Novel drug delivery systems	>10



Typical distribution of shares in start-up:
 Scientists-developers – 75%
 NP Orchemed – 25%

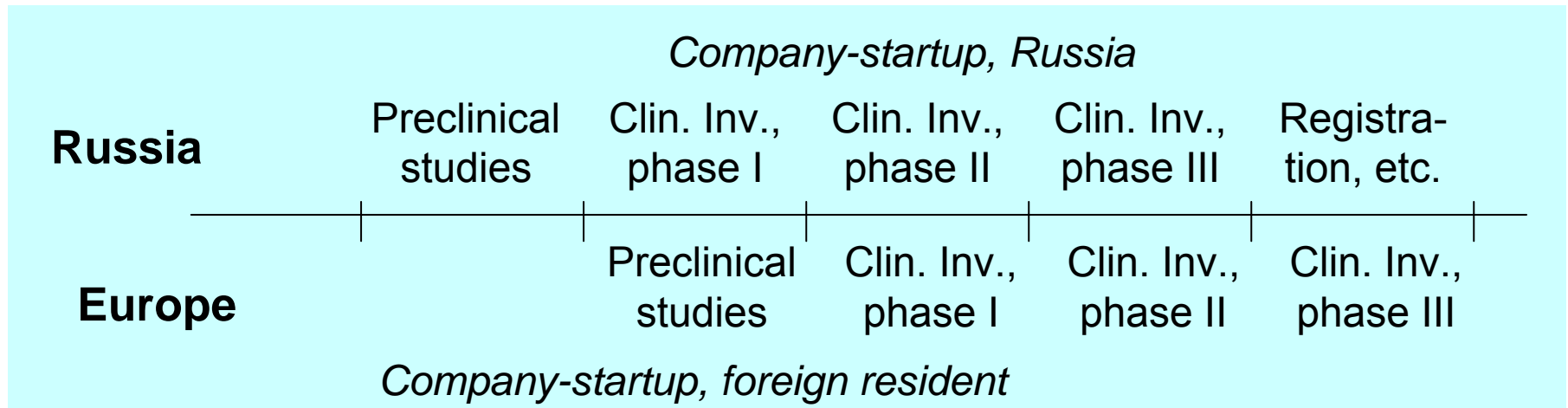
- ### Business partners
- Russian Venture Company
 - Innovation Center Skolkovo
 - Vnesheconombank
 - Binnopharm
 - Pharmacluster BioCity
 - Maxwell Biotech
 - International fund of techn. and Investment
 - Obninsk pharmcluster “Park of active molecules”
 - and many other scientific and business organizations in Russia and former USSR

Proposals for collaboration

- Scientific collaboration, joint grant applications, etc.
- Preclinical drug D&D studies, including GLP studies (outsourcing model)
- Joint development of projects from Orchemed's portfolio or projects from our foreign partners
- Orchemed can represent interests of the foreign partners at Russian scientific and education community, governmental and business structures, etc.
- Orchemed can be a point of entry for scientific projects from foreign partners to big innovative initiatives such as "Skolkovo innovation city", National bioscreening network, etc.

Joint development of Orchemed's projects

Project X: start-up company with IP rights (license) on a molecule from Orchemed's portfolio



Risk share model:

- foreign partner invests money to start-up;
- joint development in Russia and, with a time shift (depending on success in Russia), in other countries;
- joint IP



Thank you for attention!



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