



GEROPHARM



INTERNATIONAL RAPIDLY GROWING BIOTECHNOLOGICAL COMPANY WITH ALL INSULIN BLOCKBUSTERS IN PORTFOLIO



Development and production of medicinal products to treat socially important diseases



Production of active pharmaceutical ingredients



Investment into technological development and creation of modern pharmaceutical infrastructure



Implementation of the import substitution tasks within state federal programs

FROM IDEA TO GLOBAL MARKET

**Petr Rodionov,
GEROPHARM CEO**



ABOUT COMPANY

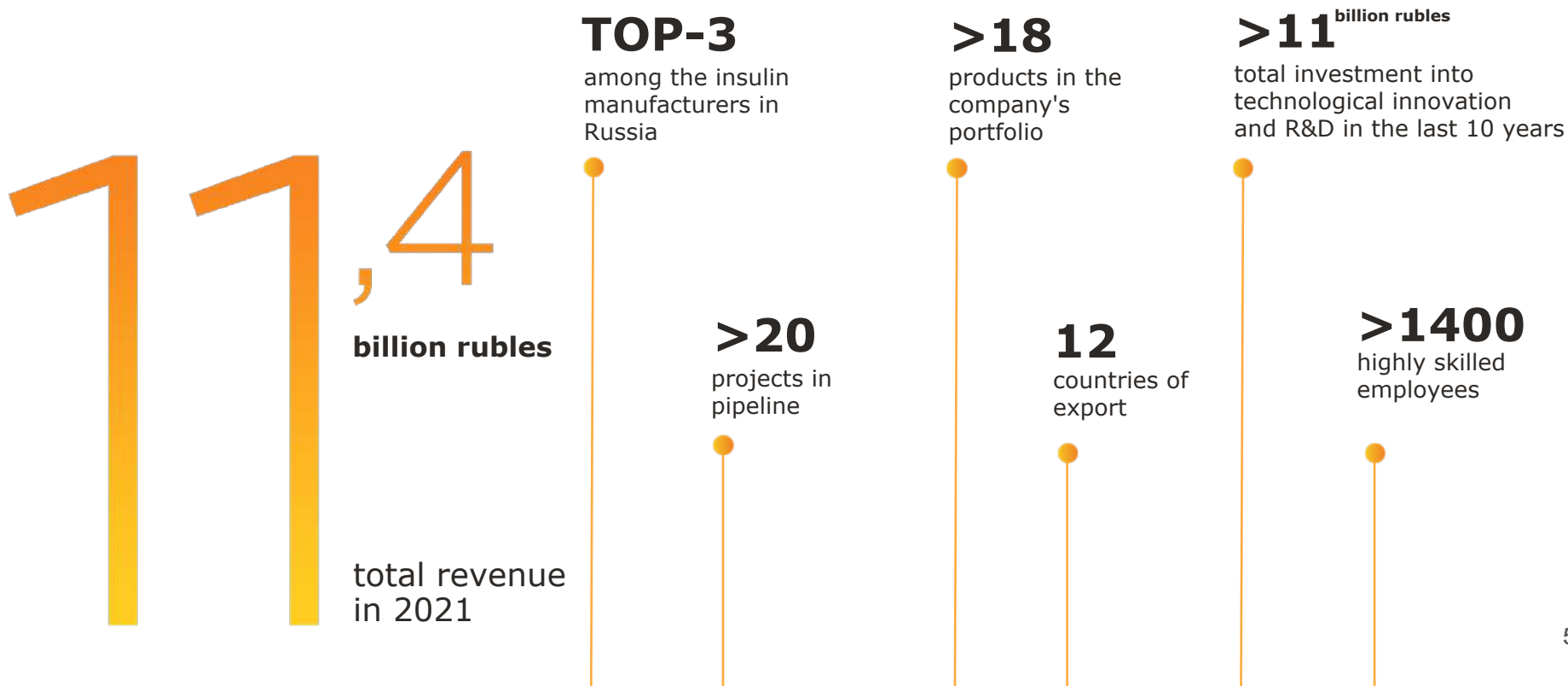


- Over 20 years on the pharmaceutical market
- One of the TOP-3 insulin manufacturers in Russia
- Own R&D Center and 2 Manufacturing Sites
- Full-cycle drug development, clinical research and production of insulins bioanalogues accordance with GMP, GLP, GCP, GVP standards
- More than 1400 highly skilled employees
- 12 countries of export: all CIS members, Turkmenistan, Georgia and Venezuela

AREAS OF SPECIALIZATION:

neurology, psychiatry, endocrinology, ophthalmology and gynecology

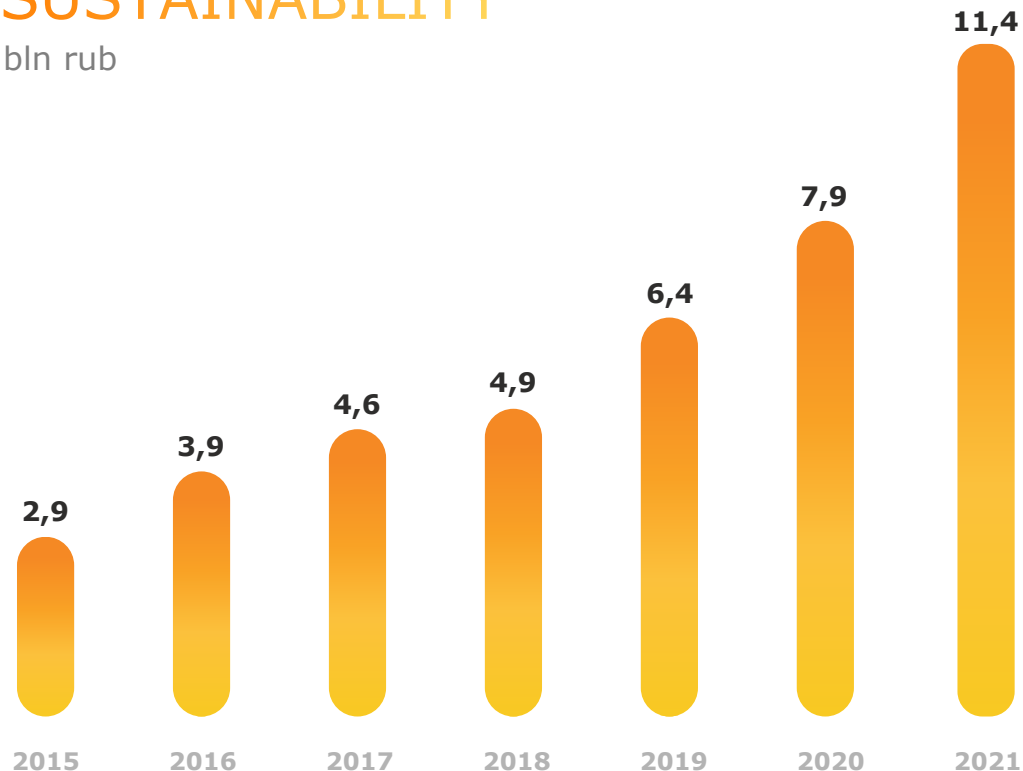
GEROPHARM AT A GLANCE



REVENUE VOLUME

IN 2021, GEROPHARM PROVED THE BUSINESS SUSTAINABILITY

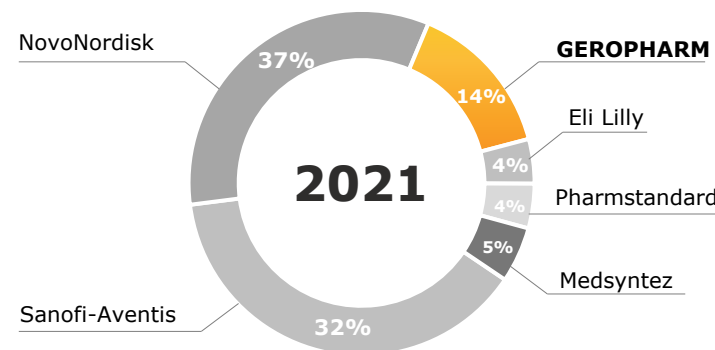
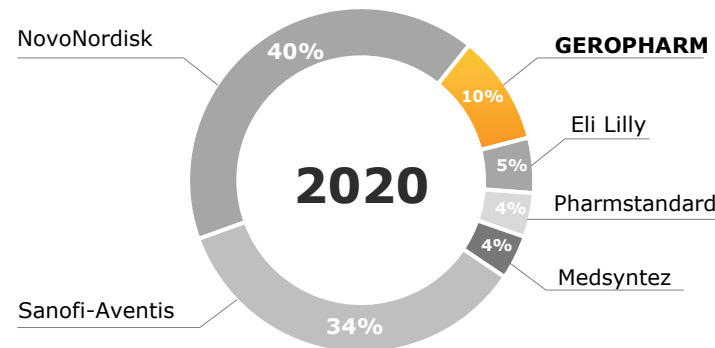
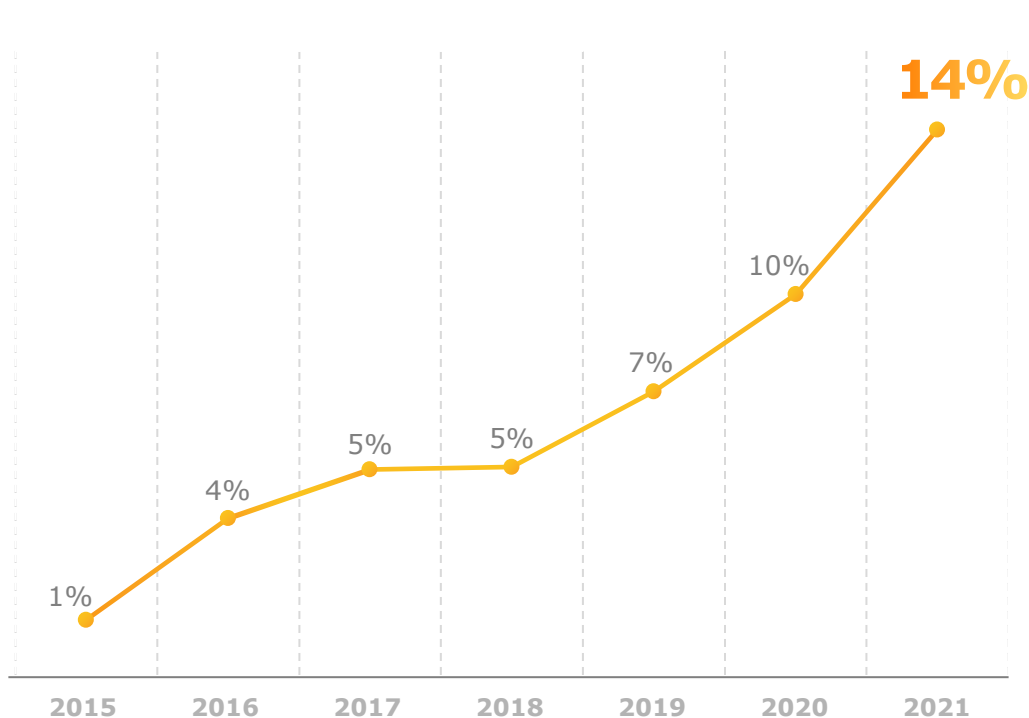
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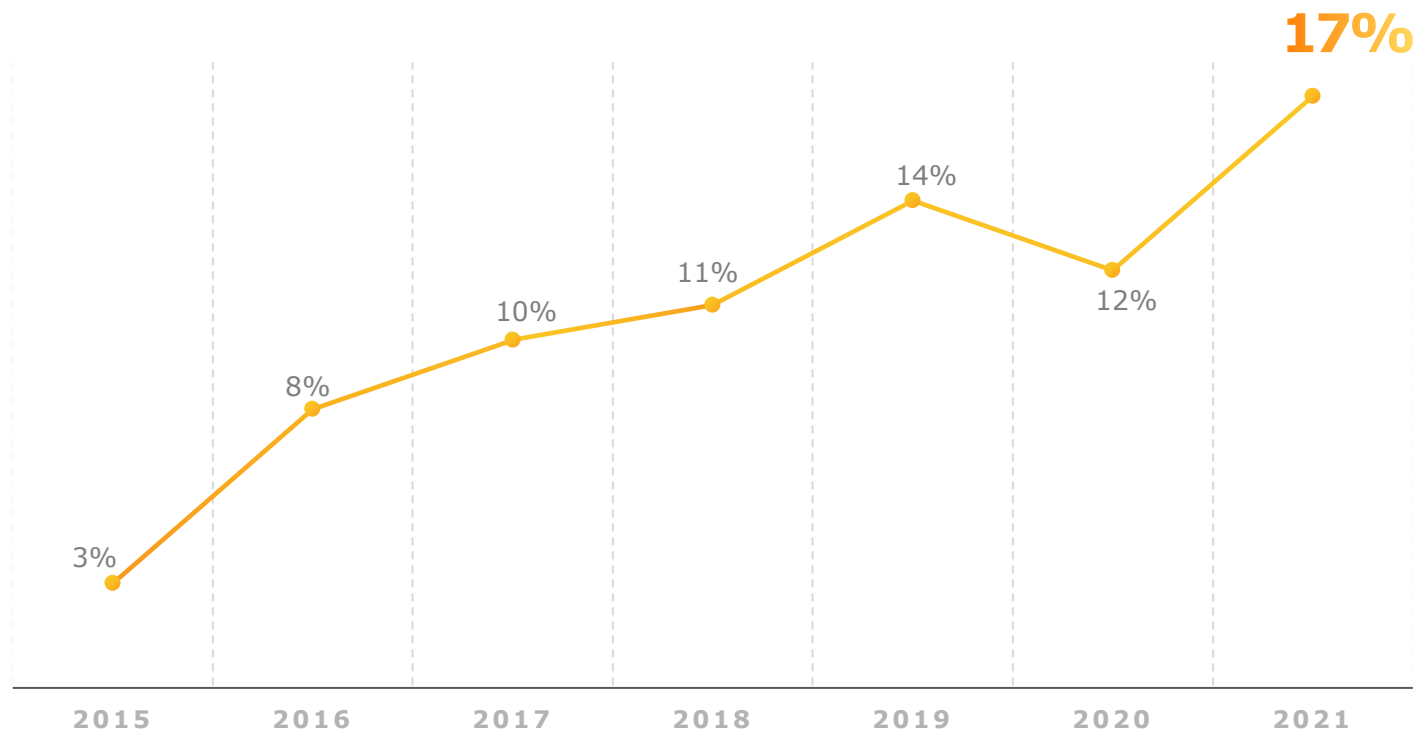
+44%

profit growth in 2021

GEROPHARM IN THE TOP-3 AMONG INSULIN MANUFACTURERS IN RUSSIA



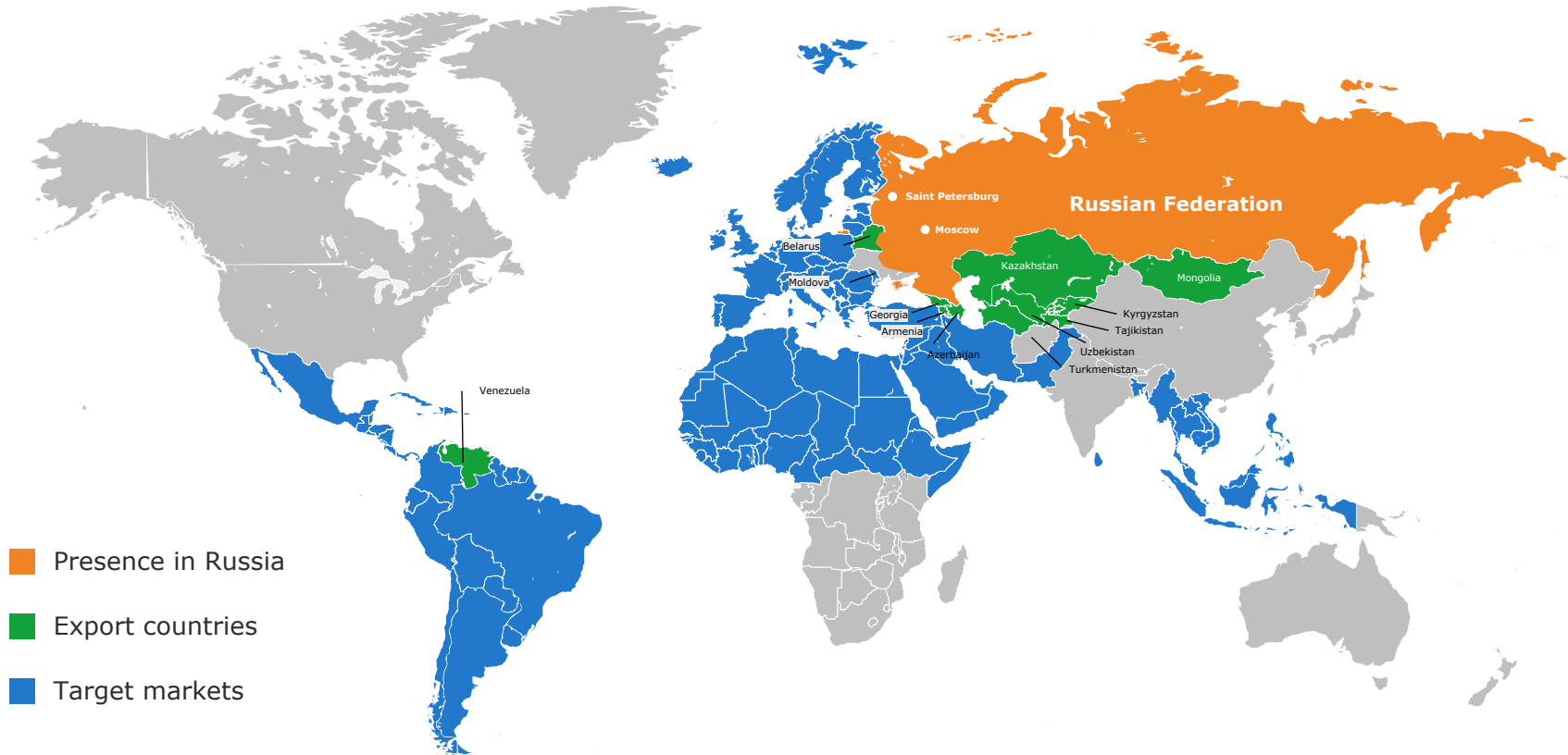
SHARE OF GEROPHARM IN INSULIN CONSUMPTION IN RUSSIA



OVER 20 YEARS OF CREATING A HEALTHY FUTURE



GLOBAL BUSINESS





RESEARCH AND DEVELOPMENT

OVER 10 YEARS OF INNOVATIONS

R&D CENTER



Full development cycle in accordance with GLP, GCP, GVP standards



Product development by methods of genetic engineering, molecular and cellular biology



More than 100 highly skilled specialists



Comprehensive approach to clinical trials — in-house expertise



SPECIAL ECONOMIC ZONE "ST. PETERSBURG"
(NEUDORF MANUFACTURING SITE)



WORK STREAM

R&D CENTER



Medicinal products development



Technology testing and
implementation to the
industrial-scale manufacturing



Full range of pre-licensure studies



Pharmacovigilance



Registration activities

STRUCTURE

R&D CENTER



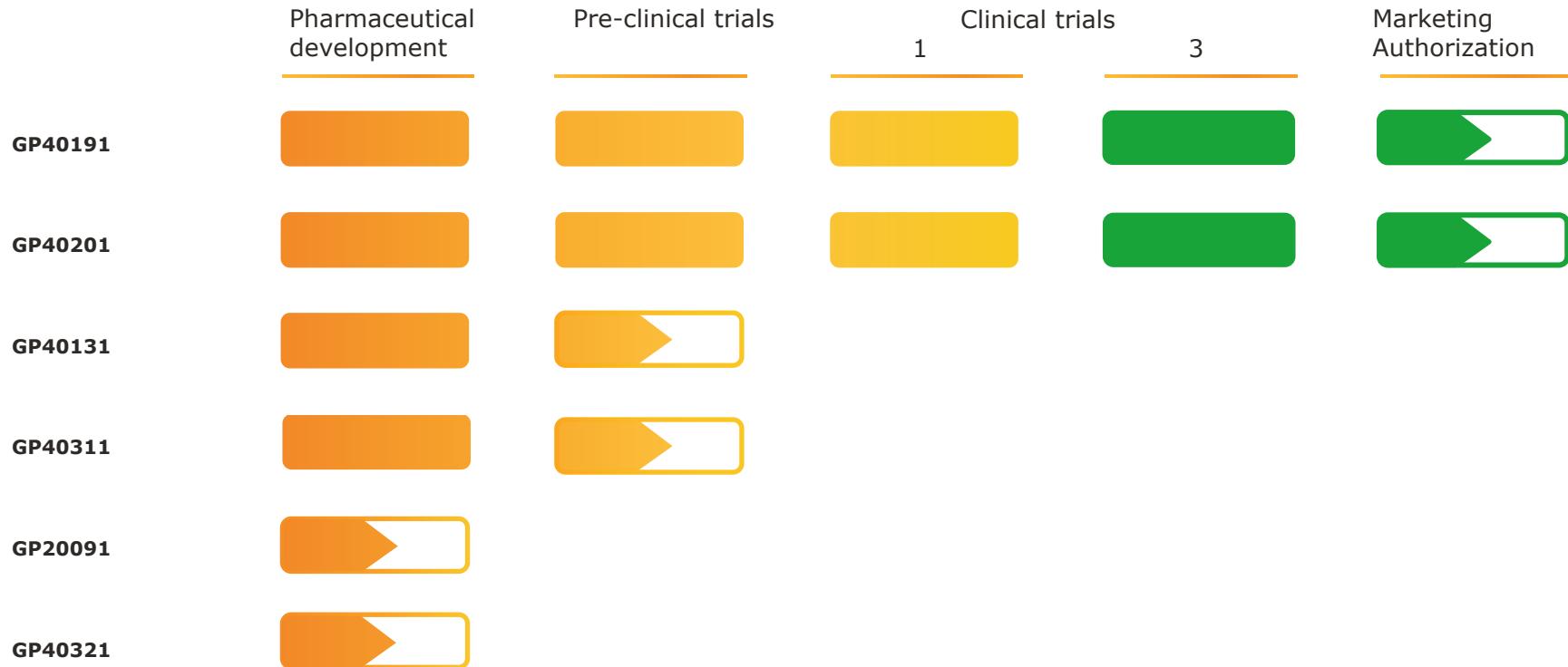
Laboratories

- Drug Development Laboratory
- Bioprocess Development Laboratory
- Analytical Testing Laboratory
- Pharmacological Laboratory
- Laboratory Support Department

In-House Specialisation

- Department of Early Drug Development
- Research Department
- Medical Department
- Department of Early Phase Clinical Trials
- Clinical Operations Department
- Data Collection and Processing Department
- Pharmacovigilance
- Project Management Department
- Quality Assurance Department
- Regulatory Department

PORTFOLIO OF INSULIN FORMULATION



A detailed view of an industrial robotic assembly line. In the foreground, a robotic arm with a gripper is positioned over a work area. Various blue and white cables are connected to the machinery. The background shows a blurred view of the factory floor with other equipment and a worker in a blue uniform. The overall scene is dimly lit, emphasizing the mechanical components.

PORTFOLIO

INTEGRATED APPROACH TO THE DIABETES MELLITUS SEGMENT



BIOSIMILARS OF INSULIN ANALOGUES HAVE BEEN SUCCESSFULLY TESTED IN ALL THE NECESSARY CLINICAL TRIALS

In accordance with the requirements of Russian laws and regulations and international guidelines of the EMA (European Medicines Agency).

THE GOAL IS TO PROVE:



high degree of
molecular similarity
of the reference and
investigational
products



the same way of
molecule getting into
the central circulation
(i.e., equivalent
bioavailability)

If identical molecules are delivered to their place of action in the same way,
their effects should be identical as well.



ENDOCRINOLOGY

GEROPHARM INSULIN STUDIES

COMPARATIVE STUDIES OF GEROPHARM BIOSIMILAR INSULIN ANALOGUES VS. REFERENCE PRODUCT HAD 3 PHASES:



- 1 A study of physical and chemical properties:** to prove the equivalence (similarity) of the composition of the reference insulin and GEROPHARM insulin
- 2 In vitro pharmacodynamic studies:** to prove the equivalence of the mechanism of action on cell lines
- 3 Clinical trials:** to prove the equivalence of action in humans:



pharmacokinetics and pharmacodynamics studies: equivalent insulin absorption into the central circulation, metabolism and excretion



safety studies with particular attention to immunogenicity

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CLINICAL TRIALS

Pharmacokinetics and pharmacodynamics studies



hyperinsulinemic
(euglycemic) clamp
according to the standard
international procedure



equivalent insulin absorption
into the central circulation,
metabolism and excretion



DESIGN:

double-blind, randomised,
comparative, cross-over
pharmacokinetics and
pharmacodynamics study
on healthy subjects or type 1
diabetes mellitus patients.

CLINICAL PHASE:

- screening
- 2 stages of product
administration (clamps)
- “washout”
- final visit



During the clamp procedure, blood samples are collected
for pharmacokinetics study and pharmacodynamics evaluation

N^o1

GEROPHARM is the first company in the Russian Federation to conduct clamp studies for the purpose of getting the approval of medicinal products (insulins).

ENDOCRINOLOGY

RECOMBINANT HUMAN INSULINS (RHIs)



standard multicenter,
parallel-group studies



as close as possible
to real-life clinical practice



include patients with type 1
or type 2 diabetes mellitus

ENDOCRINOLOGY

RECOMBINANT HUMAN INSULINS (RHIs)

**Rinsulin® R,
Rinsulin® NPH,
Rinsulin® Mix 30/70**

- full cycle: to the finished dosage form
- independence from foreign suppliers of raw materials
- dosage forms: vials, cartridges, injection pens



ENDOCRINOLOGY

INSULIN ANALOGUES



RinLis®

INN: insulin lispro

- widely used ultra-rapid-acting prandial human insulin analog
- notable for the reverse sequence of proline and lysine in the amino acid chain of insulin
- rapid absorption from subcutaneous injection sites
- can be used in children and adolescents

in 15 min

onset of action after
SC injection

30–70 min

maximum effect

RinLis® Mix 25

INN: biphasic insulin lispro

- prandial component provides a faster and more predictable onset of action, as well as the rapid elimination specific to the physiological secretion of insulin
- prolonged-action component provides a smooth, peak-free profile of the basal insulin
- can be used from 12 years

2–5 h

insulin lispro
duration of action

up to 15 h

biphasic insulin lispro
duration of action

ENDOCRINOLOGY

INSULIN LISPRO TRIALS

MEDICINAL PRODUCTS

RinLis®

(insulin lispro)

RinLis® Mix 25

(biphasic insulin lispro)

REFERENCE PRODUCTS

Humalog®

Humalog® Mix 25

1ST STAGE

CLAMP-BASED STUDIES

 on the basis



28 

subjects
RinLis®

48 

subjects
RinLis® Mix 25

A high level of equivalence was demonstrated between pharmacokinetic and pharmacodynamic profiles of RinLis® / Humalog® and RinLis® Mix 25 / Humalog® Mix 25, confirming the biosimilarity between investigated insulin products and reference products.

2ND STAGE

MULTICENTER COMPARATIVE CLINICAL TRIALS OF IMMUNOGENICITY

RinLis® Mix 25/Humalog® Mix 25

18 
clinics

210 
subjects

TYPE 2 
diabetes mellitus

The following was proved: safety and immunogenicity characteristics of the biosimilar RinLis® Mix 25 were comparable to those of Humalog® Mix 25.

ENDOCRINOLOGY

INSULIN ANALOGUES



RinGlar®

INN: insulin glargine

- long-acting basal human insulin analog
- the most widely used basal insulin analogue in the world*
- available in U100 concentration
- can be used in children from 2 years

in 1 hour

onset of action after
SC injection

up to 29 h, average - 24 h

duration of action

ENDOCRINOLOGY

INSULIN GLARGINE TRIALS

MEDICINAL PRODUCT

RinGlar®

REFERENCE PRODUCTS

Lantus® SoloStar®

1ST STAGE

CLAMP-BASED STUDIES

 on the basis



42 
subjects

TYPE 1 
diabetes mellitus

This study showed high level of equivalence of pharmacokinetics and pharmacodynamics between RinGlar® and Lantus®. Thus, the biosimilarity of these products and the efficacy of the investigational insulin glargine made by GEROPHARM have been confirmed.

2ST STAGE

**MULTICENTER COMPARATIVE
CLINICAL TRIALS OF IMMUNOGENICITY**

14 
clinics

180 
subjects

TYPE 1 
diabetes mellitus

As a result, comparable safety and immunogenicity of RinGlar® versus original medicinal product Lantus® SoloStar® have been proven.

ENDOCRINOLOGY

INSULIN ANALOGUES



RinFast® INN: insulin aspart

- the most common prandial analogue of ultra-rapid-acting insulin in Russia*
- faster absorption rate compared to regular human insulin
- can be used in children from 1 year

in 10–20 min
onset of action after
SC injection

1–3 h
maximum effect

3–5 h
duration of action

ENDOCRINOLOGY

INSULIN ASPART TRIALS

MEDICINAL PRODUCT

RinFast®

REFERENCE PRODUCTS

NovoRapid®

1ST STAGE

CLAMP-BASED STUDIES

 on the basis



26 
subjects

TYPE - 
healthy volunteers

This study demonstrated high level of equivalence of pharmacokinetics and pharmacodynamics between RinFast® and NovoRapid®. Thus, the biosimilarity of these products and the efficacy of the investigational insulin aspart made by GEROPHARM have been confirmed.

2ST STAGE

**MULTICENTER COMPARATIVE
CLINICAL TRIALS OF IMMUNOGENICITY**

19 
clinics

264 
patients

TYPE 1 
diabetes mellitus

As a result, the comparable safety and immunogenicity of RinFast® versus original medicinal product NovoRapid® have been proven.

ENDOCRINOLOGY

INSULIN ANALOGUES



RinFast® Mix 30

INN: biphasic insulin aspart

- contains 30% ultra-rapid-acting soluble insulin aspart and 70% protamine-crystallized insulin aspart with medium-term hypoglycemic effect
- the first component acts mainly in the postprandial period, the second component controls the basal level of glycemia
- can be used in children from 6 year

in 10–20 min

onset of action after
SC injection

1–4 h

maximum effect

up to 24 h

duration of action

ENDOCRINOLOGY

BIPHASIC INSULIN ASPART TRIALS

MEDICINAL PRODUCT

RinFast® Mix 30

REFERENCE PRODUCTS

NovoMix® 30

1ST STAGE

CLAMP-BASED STUDIES

 on the basis



34 
subjects

TYPE - 
healthy volunteers

This study demonstrated high level of equivalence of pharmacokinetics and pharmacodynamics between RinFast® Mix 30 and NovoMix® 30. Thus, the biosimilarity of these products and the efficacy of the investigational insulin aspart made by GEROPHARM have been confirmed.

2ST STAGE

**MULTICENTER COMPARATIVE
CLINICAL TRIALS OF IMMUNOGENICITY**

17 
clinics

264 
subjects

TYPE 2 
diabetes mellitus

As a result, the comparable safety and immunogenicity of RinFast® Mix 30 versus original medicinal product NovoMix® 30 have been proven.

ENDOCRINOLOGY

EVODIN®



INN: evogliptin

evogliptin is a hypoglycemic medicinal product of dipeptidyl peptidase-4 inhibitors (iDPP-4) class, which is prescribed to patients with type 2 diabetes mellitus.

- Evogliptin is the newest original molecule of the iDPP-4 group
- tasks of combining all clinically significant positive characteristics for this group acted as prerequisites for the development of evogliptin, resulting in reduction of the daily dose to 5 mg once a day while maintaining therapeutic effects
- product is associated with a lower risk of hypoglycemia compared to the oral hypoglycemic medicinal products of other groups
- product has no effect on body weight

ENDOCRINOLOGY

RINFORMIN® LONG



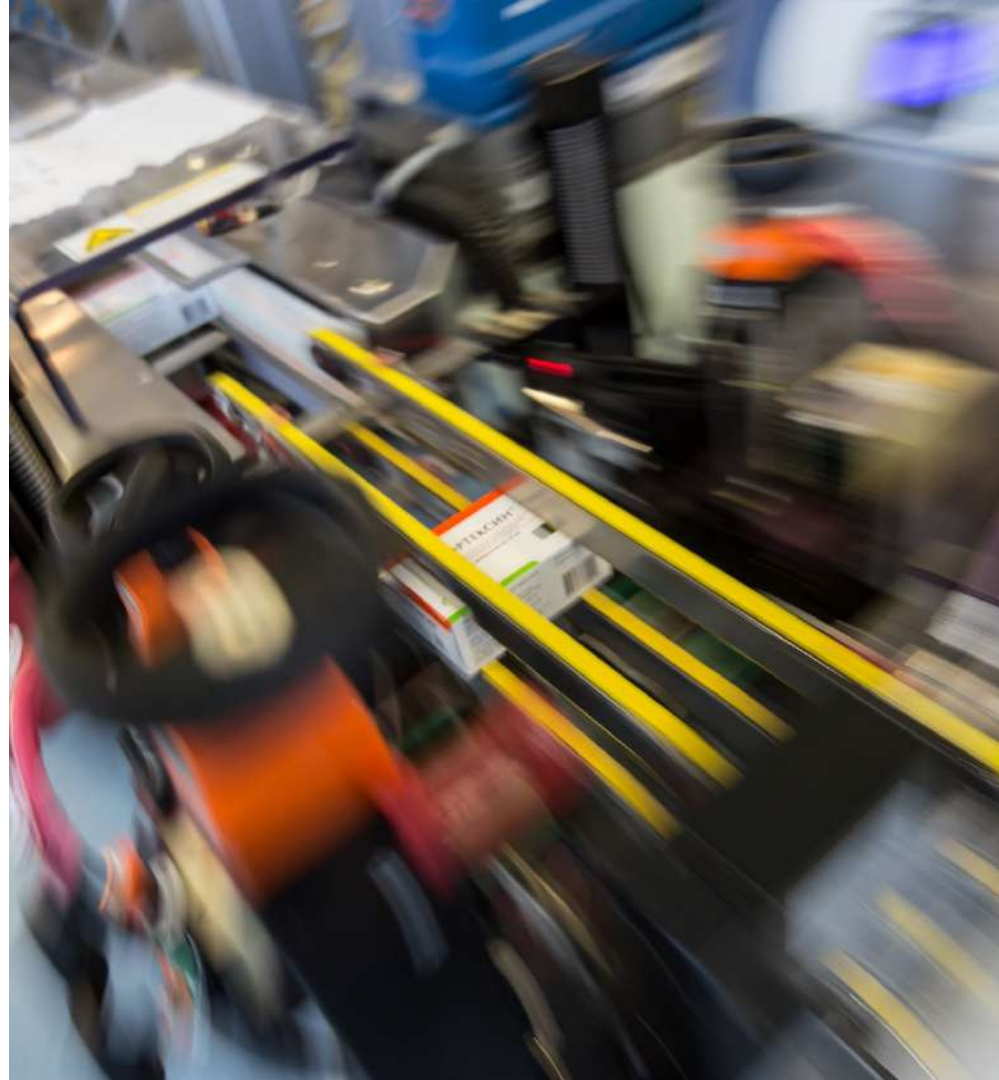
INN: metformin

Priority starting line product for type 2 diabetes mellitus

Clinical benefits:

- low risk of hypoglycemia
- no effect on body weight
- lipid profile improvement
- reduced risk of myocardial infarction in patients with type 2 diabetes mellitus and obesity
- reduced risk of type 2 diabetes mellitus in impaired glucose tolerance (IGT)

ORIGINAL MEDICINAL
PRODUCTS



NEUROLOGY

CORTEXIN®

Cortixin®, 10 mg
Cortixin®, 5 mg (for children)

neuropeptide, which provides protection and restoration of nervous tissue in various nervous system diseases.

The product is used as part of combined therapy for:

- epilepsy
- asthenic conditions (suprasegmental autonomic disorders)
- decreased learning ability
- delays in psychomotor and speech development in children
- various forms of cerebral palsy
- traumatic brain injury and its consequences
- encephalopathies of various origins
- cognitive impairments
- acute and chronic encephalitis and encephalomyelitis
- traumatic brain injury and its consequences



GYNECOLOGY

PINEAMIN®

the 1st exclusive injectable medicinal product with an innovative PPG (Polypeptides of Pineal Gland) class effect and anti-age effect for the treatment of the menopausal syndrome.

- high therapeutic activity
- high level of safety and tolerability
- long-term effect
- short injection courses



OPHTHALMOLOGY

RETINALAMIN®

a medicinal product that stimulates retinal regeneration

The product is used as part of combined therapy for:

- compensated primary open-angle glaucoma
- diabetic retinopathy
- inflammatory or traumatic central retinal degeneration
- central retinal degeneration
- myopia (as part of comprehensive treatment)
- central and peripheral tapetoretinal degeneration
- rhegmatogenous and traumatic retinal detachment (post-operative rehabilitation period, as part of comprehensive treatment)





MANUFACTURING

MANUFACTURING SITE OBOLENSK



Serpukhov city district, Obolensk work settlement,
Moscow region

Plant was launched in 2013



Full cycle of manufacture:
from substance synthesis to
dosage form



Proprietary
insulin manufacturing
process



Advanced technologies
and latest control methods,
GMP Pharmaceutical Quality
System

INSULIN MANUFACTURE

FROM SUBSTANCE TO DOSAGE FORM



Obtaining inclusion body paste

1



Fusion protein isolation and purification

2



Insulin substance preparation and purification

3



Solution preparation

4



Aseptic filling

5



Inspection

6



Packaging and labeling

7

PRODUCTION SITE PUSHKIN

Execution deadline:

2017

production start-up for the pharmaceutical substances for original medicinal products

2018

production start-up for the genetically engineered insulin substances and insulin analogs



100%

of the Russian population needs and export development can be provided with GEROPHARM capacities



High degree of automation



Advanced technologies

and latest control methods,
GMP Pharmaceutical Quality
System



**Production of active
pharmaceutical ingredients**



Saint Petersburg, Pushkin

WHY WE ARE LEADERS

- The first Russian producer of insulin which is manufactured on a full cycle basis: from substance to the finished dosage form
- Development of modern pharmaceutical infrastructure — R&D Center and high-tech full cycle manufacturing in compliance with GMP standard
- One of the priorities is production of active pharmaceutical substances
- Manufacturing of originator products that target for treatment of socially significant diseases as well as generic drugs that have a priority in terms of import substitution





SOCIAL PROJECTS



DIABETES IN PERSONS

The main goal is **TO TAKE CARE OF THE PATIENT**

Informational, social project about diabetes and life with it, which has existed for 10 years.

Since 2013, the project has implemented a series of unique social activities on the problem of diabetes, which included different photo projects.

Also GEROPHARM launched an information campaign about the symptoms of diabetes in children, which helped to reduce the time of diagnosis of the disease.

Later, the project has been carrying out activities aimed at practical assistance to patients with diabetes.

- Large-scale educational project for patients "Diabetes academy"
- The aid programme to children with T1D living in orphanages in Russia "Children also suffer from diabetes"
- Offline activities for kids: theater school course, dance workout, New Year's events, etc.





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