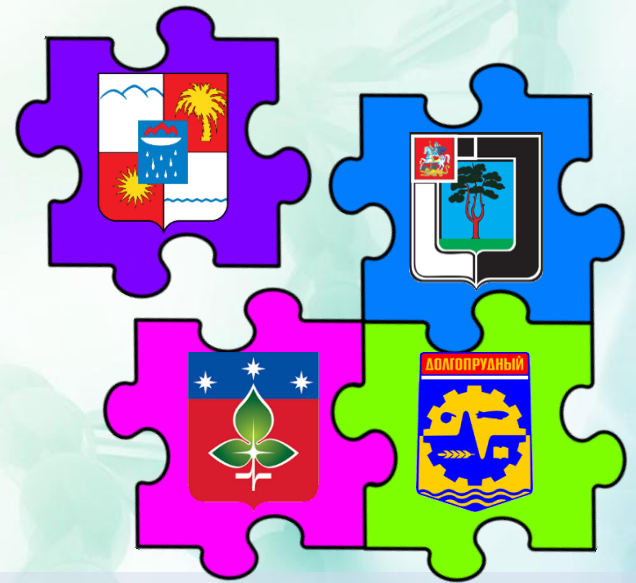


# “PharmValley” Cluster

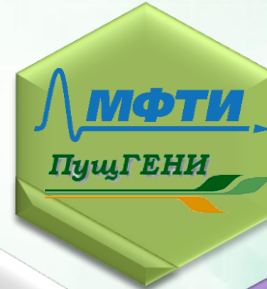


## *Development history:*

- *February 2017 - signing an agreement on the creation of the Cluster, 10 members*
- *September 2017 - the conclusion of the export contract, 13 members*
- *May 2018 - joining the international Biotox cluster*

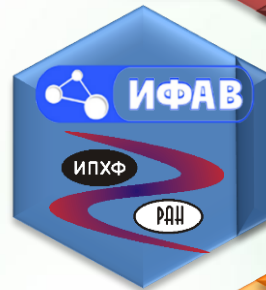
# Turn-key Medical Cluster

Branch of Institute of  
Bioorganic Chemistry  
Medical Primatology  
Research Center



Moscow Institute of Physics  
and Technology  
Pushchino State Natural  
Science Institute

Institute of Chemical  
Physics  
Institute of  
Physiologically Active  
Substances

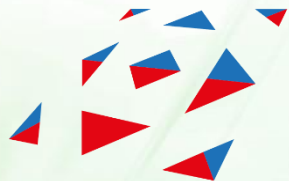


Hospital of Pushchino  
Hospital of  
Chernogolovka

Institute of Biochemistry and  
Physiology of Microorganisms  
Institute of Theoretical and  
Experimental Biophysics



Test Pushchino LLC  
ESMAR LLC  
PCSC LLC



RUSSIAN  
EXPORT CENTER



AGENCY  
FOR STRATEGIC  
INITIATIVES



# Global Engagement



«BioTox Cluster: Cluster for toxicological and ecotoxicological services under GLP conditions for customers from pharmaceutical, biotechnological and chemical Industry»

*Est. May 01 2018*

- *SITNO PHARMA Bratislava, Slovakia*
- *hameln rds a.s., Modra, Slovakia*
- *Cluster “PharmValley”, Russia*
- *LAUS GmbH, Germany*
- *RX Holding & Management B.V., Sampigny, France*
- *Slovak Medical University in Bratislava, Slovakia*
- *Comenius University in Bratislava, Jessenius Medical Faculty in Martin, Slovakia*
- *University of Veterinary Medicine and Pharmacy in Košice, Slovakia*



**RUSSIAN  
EXPORT CENTER**

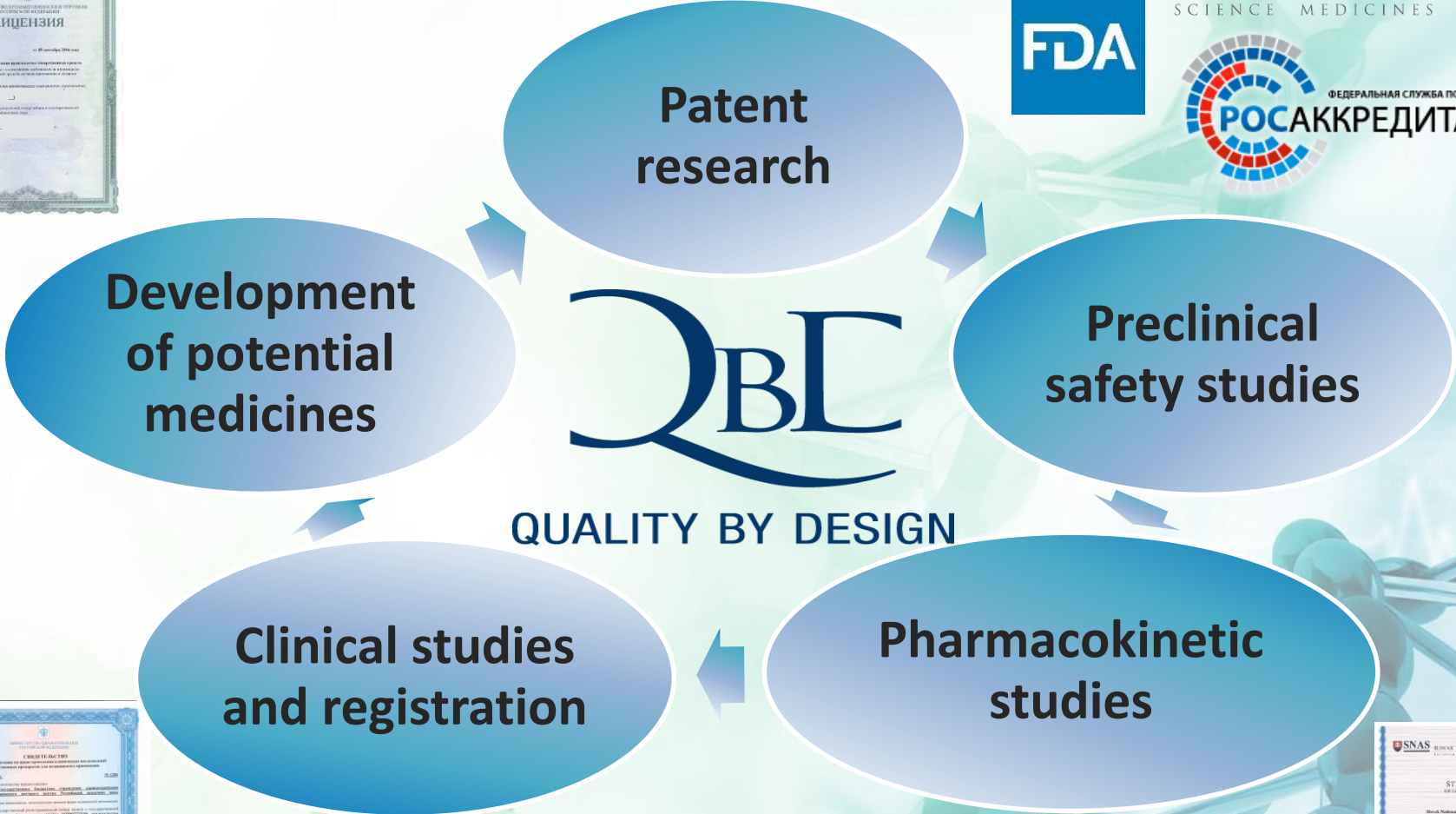
# CLUSTER CAPABILITIES



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH



ФЕДЕРАЛЬНАЯ СЛУЖБА ПО АККРЕДИТАЦИИ



**felasa**  
Federation of European Laboratory  
Animal Science Associations



# Center for Non-Clinical Studies



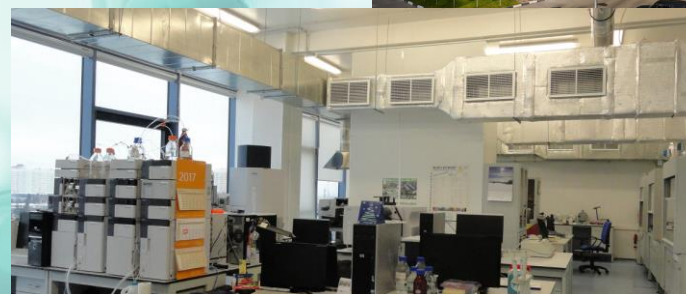
**AAALAC statement  
c 2005**



**Laboratory of Biological Testing**  
*Complete cycle of preclinical studies on  
SPF rodents and rabbits*

**Sochi Scientific Research Institute  
of Medical Primatology**  
*NHP studies*

**Moscow Institute of Physics  
and Technology**  
*Analytical and Clinical  
Chemistry testing*



**GLP OECD statement  
2013 - 2021**

# **OBJECTS OF NONCLINICAL RESEARCHES**

**Non-clinical studies on medical and environmental safety are conducted for objects contained in**

- ✓ **Medicines**
- ✓ **Pesticides**
- ✓ **Cosmetic products**
- ✓ **Veterinary drugs**
- ✓ **Food and feed additives**
- ✓ **Chemical substances for industrial use**

**Studies are conducted under GLP OECD standard and**

**Reports are valuable within EMA and FDA submissions**

# LIST OF AVAILABLE METHODS OF TESTING THE IMPACT OF CHEMICAL PRODUCTS ON THE HUMAN ORGANISM (RED FONT)

| Test Guide Name   | TG OECD | REACH  | GOST RF                                |
|---|---------|--------|--|
| Acute Oral Toxicity - Fixed Dose Procedure              | 420     | 1 bis  | 32296-2013                             |
| Acute Oral toxicity - Acute Toxic Class Method          | 423     | 1 tris | 32644-2014                             |
| Acute Oral Toxicity: Up-and-Down Procedure (UDP)        | 425     |        |  |
| Acute Dermal Toxicity                                   | 402     | 3      | 32373-2013                             |
| Acute Inhalation Toxicity                               | 403     | 2      | 32542-2013                             |
| Acute Inhalation Toxicity – Acute Toxic Class Method    | 436     |        | 32646-2014                             |
| Repeated Dose 28-day Oral Toxicity Study in Rodents     | 407     | 7      | 32641-2014                             |
| Repeated Dose 90-Day Oral Toxicity Study in Rodents     | 408     | 26     | 32637-2014                             |
| Repeated Dose 90-Day Oral Toxicity Study in Non-Rodents | 409     | 27     | 56697-2015                             |
| Repeated Dose Dermal Toxicity: 21/28-day Study          | 410     | 9      | 32642-2014                             |
| Subchronic Dermal Toxicity: 90-day Study                | 411     | 28     | 32639-2014                             |
| Subacute Inhalation Toxicity: 28-Day Study              | 412     | 8      | 32643-2014                             |
| Subchronic Inhalation Toxicity: 90-day Study            | 413     | 29     | 32636-2014                             |
| Chronic Toxicity Studies                                | 452     | 30     | 32383-2013<br>32437-2013<br>32519-2013 |

# LIST OF AVAILABLE METHODS OF TESTING THE IMPACT OF CHEMICAL PRODUCTS ON THE HUMAN ORGANISM (RED FONT)

| Test Guide Name  | TG OECD    | REACH     | GOST RF           |
|--|------------|-----------|-------------------|
| <b>Prenatal Development Toxicity Study</b>   | <b>414</b> | <b>31</b> | <b>32380-2013</b> |
| <b>One-Generation Reproduction Toxicity Study</b>  | <b>415</b> | <b>34</b> | <b>32378-2013</b> |
| <b>Two-Generation Reproduction Toxicity</b>  | <b>416</b> | <b>35</b> | <b>56698-2015</b> |
| <b>Reproduction/Developmental Toxicity Screening Test</b>  | <b>421</b> |           | <b>32379-2013</b> |
| <b>Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test</b> | <b>422</b> |           |                   |
| <b>Extended One-Generation Reproductive Toxicity Study</b>   | <b>443</b> |           |                   |
|  |            |           |                   |
| <b>Carcinogenicity Studies</b>   | <b>451</b> | <b>32</b> | <b>32377-2013</b> |
| <b>Combined Chronic Toxicity/Carcinogenicity Studies</b>   | <b>453</b> | <b>33</b> | <b>32647-2014</b> |



# LIST OF AVAILABLE METHODS OF TESTING THE IMPACT OF CHEMICAL PRODUCTS ON THE HUMAN ORGANISM (RED FONT)

| Test Guide Name  | TG OECD | REACH | GOST RF    |
|--|---------|-------|------------|
| Delayed Neurotoxicity of Organophosphorus Substances Following Acute Exposure  | 418     | 37    |            |
| Delayed Neurotoxicity of Organophosphorus Substances: 28-day Repeated Dose Study   | 419     | 37    |            |
| <b>Neurotoxicity Study in Rodents</b>  | 424     | 43    | 32645-2014 |
| <b>Developmental Neurotoxicity Study</b>   | 426     |       |            |
|  |         |       |            |
| <b>Uterotrophic Bioassay in Rodents</b>  | 440     |       |            |
| <b>Hershberger Bioassay in Rats</b>  | 441     |       |            |
| Performance-Based Test Guideline for Stably Transfected Transactivation In Vitro Assays to Detect Estrogen Receptor Agonists | 455     |       |            |
| H295R Steroidogenesis Assay  | 456     |       |            |
| BG1Luc Estrogen Receptor Transactivation Test Method for Identifying Estrogen Receptor Agonists and Antagonists              | 457     |       |            |
|  |         |       |            |
| In Vitro 3T3 NRU Phototoxicity Test  | 432     | 41    | 32372-2013 |
|  |         |       |            |
| <b>Toxicokinetics</b>  | 417     | 36    |            |

# LIST OF AVAILABLE METHODS OF TESTING THE IMPACT OF CHEMICAL PRODUCTS ON THE HUMAN ORGANISM (RED FONT)

| Test Guide Name  | TG OECD | REACH | GOST RF    |
|--|---------|-------|------------|
| Bacterial Reverse Mutation Test  | 471     | 13/14 | 32376-2013 |
| <b>In vitro Mammalian Chromosome Aberration Test</b>   | 473     | 10    |            |
| <b>Mammalian Erythrocyte Micronucleus Test</b>   | 474     | 12    |            |
| Mammalian Bone Marrow Chromosome Aberration Test   | 475     | 11    |            |
| <b>In vitro Mammalian Cell Gene Mutation Test</b>  | 476     | 17    | 32638-2014 |
| Genetic Toxicology: Sex-Linked Recessive Lethal Test in Drosophila melanogaster                  | 477     | 20    | 32648-2014 |
| Genetic Toxicology: Rodent Dominant Lethal Test  | 478     | 22    |            |
| Genetic Toxicology: In vitro Sister Chromatid Exchange Assay in Mammalian Cells                  | 479     | 19    |            |
| Genetic Toxicology: Saccharomyces cerevisiae, Gene Mutation Assay                                | 480     | 15    |            |
| Genetic Toxicology: Saacharomyces cerevisiae, Miotic Recombination Assay                         | 481     | 16    |            |
| Genetic Toxicology: DNA Damage and Repair, Unscheduled DNA Synthesis in Mammalian Cells in vitro | 482     | 18    |            |
| Mammalian Spermatogonial Chromosome Aberration Test  | 483     | 23    |            |
| Genetic Toxicology: Mouse Spot Test  | 484     | 24    |            |
| Genetic toxicology, Mouse Heritable Translocation Assay  | 485     | 25    |            |
| Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells in vivo                          | 486     | 39    |            |
| <b>In Vitro Mammalian Cell Micronucleus Test</b>   | 487     |       | 32635-2014 |
| Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays                                     | 488     |       |            |
| <b>In vivo mammalian alkaline comet assay</b>  | 489     |       |            |
| <b>IN VITRO MAMMALIAN CELL TRANSFORMATION TESTS</b>  |         | 21    |            |

# LIST OF AVAILABLE METHODS OF TESTING THE IMPACT OF CHEMICAL PRODUCTS ON THE HUMAN ORGANISM (RED FONT)

| Test Guide Name  | TG OECD | REACH  | GOST RF    |
|--|---------|--------|------------|
| <b>Acute Dermal Irritation/Corrosion</b>   | 404     | 4      | 32436-2013 |
| <b>Skin Sensitisation</b>  | 406     | 6      | 32375-2013 |
| Skin Absorption: In Vivo Method  | 427     | 44     | 32371-2013 |
| Skin Absorption: In Vitro Method   | 428     | 45     | 32435-2013 |
| Skin Sensitisation   | 429     |        |            |
| In Vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER)                                   | 430     | 40     |            |
| In Vitro Skin Corrosion: Human Skin Model Test   | 431     | 40 bis | 32634-2014 |
| In Vitro Membrane Barrier Test Method for Skin Corrosion   | 435     |        |            |
| In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method  | 439     |        |            |
| Skin Sensitization Local Lymph Node Assay: DA  | 442A    | 42     |            |
| Skin Sensitization - Local Lymph Node Assay: BrdU-ELISA  | 442B    |        |            |
|  |         |        |            |
| <b>Acute Eye Irritation/Corrosion</b>  | 405     | 5      | 32374-2013 |
| Bovine Corneal Opacity and Permeability Test Method for Identifying Ocular Corrosives and Severe Irritants | 437     |        |            |
| Isolated Chicken Eye Test Method for Identifying Ocular Corrosives and Severe Irritants                    | 438     |        |            |
| Fluorescein Leakage Test Method for Identifying Ocular Corrosives and Severe Irritants                     | 460     |        |            |

# Phase I – IV Clinical Trials

CRO

Phase I-IV Clinical studies  
Pharmacovigilance  
Marketing Authorization  
Innovation's and Start-UP's



SMO

Geographically isolated and equipped  
early phase unit for 45 beds in Pushchino  
and a network of research centers in  
Russia, Ukraine, Belarus and Kazakhstan  
under centralized QbD management.



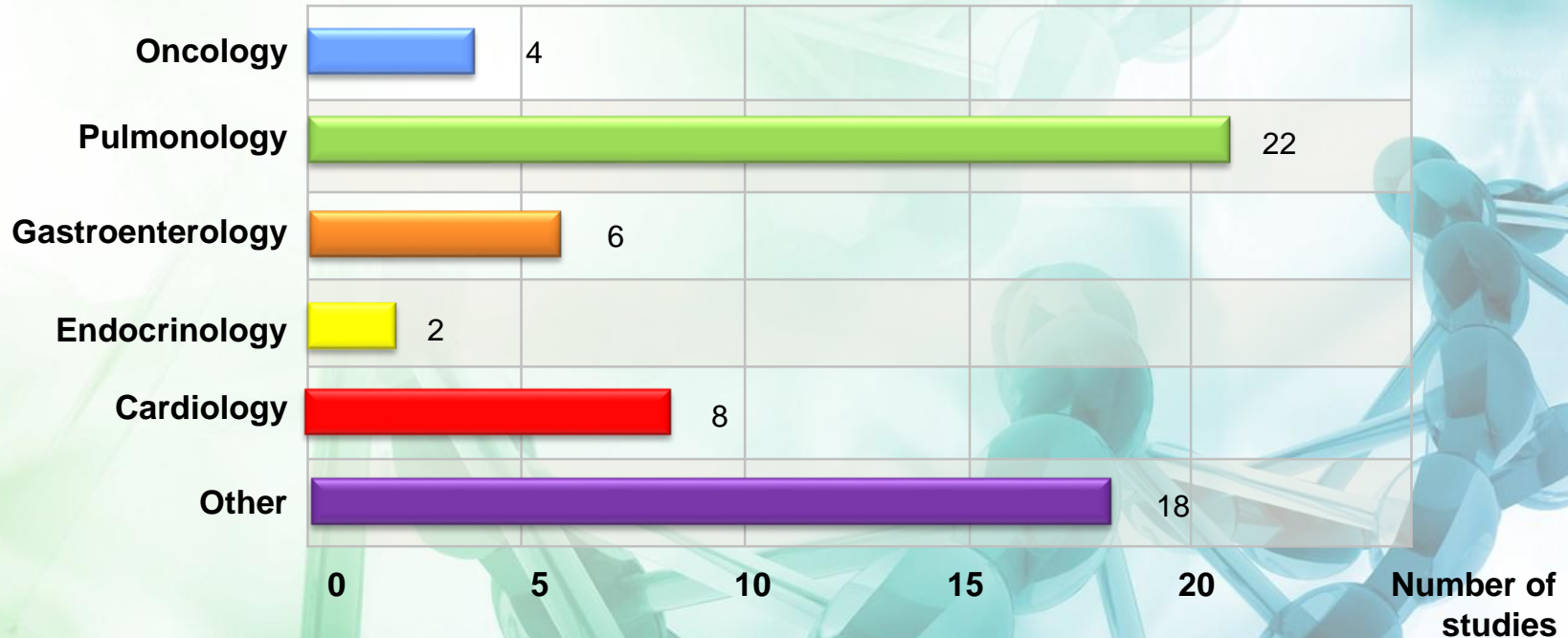
R&D

Scientific, Research and Medical Centers  
from early preclinical stage to post-  
registration and pharmacoeconomic  
research in EEU and CIS



# Clinical trial experience in Phase II, Phase III and Phase IV studies

Countries, in which, registration services are provided:



## Completed studies in Oncology

| Pathology  | Phase | Number of sites | Number of patients | Countries              |
|--|-------|-----------------|--------------------|------------------------|
| Prostate Cancer  | III   | 4               | 25                 | Russia                 |
| Rectal Carcinoma Dukes' B or C   | III   | 10              | 53                 | Russia                 |
| Hormone therapy refractory patients with HER-2/neu 1+ or 2+ expressing advanced or metastatic breast cancer. | II    | 2               | 8                  | Russia                 |
| Non-Small Cell Lung Cancer   | II    | 6               | 32                 | Russia/Ukraine         |
| Relapsed/Refractory Precursor T-Lymphoblastic  | II    | 8               | 20                 | Russia/Ukraine/Georgia |
| Leukemia/Lymphoma  |       |                 |                    |                        |
| Glioblastoma   | III   | 2               | 6                  | Ukraine                |
| HER2-negative high-risk breast cancer  | III   | 4               | 35                 | Russia                 |
| Study of neoadjuvant chemotherapy for triple negative locally advanced breast cancer                         | III   | 2               | 80                 | Russia                 |

## Completed study in Cardiology

| Pathology   | Phase | Number of sites | Number of patients |
|---|-------|-----------------|--------------------|
| Primary Pulmonary Arterial Hypertension           |       |                 |                    |
|   | III   | 4               | 4                  |
|   | III   | 2               | 2                  |
| Arterial Hypertension                             |       |                 |                    |
|   | III   | 8               | 100                |
|   | III   | 10              | 132                |
|   | IV    | 2               | 88                 |
| Others  |       |                 |                    |
|   |       |                 |                    |
|   |       |                 |                    |
| Chronic Stable Nitrate-Responsive Angina Pectoris | II    | 7               | 54                 |
| Congestive Heart Failure                          | III   | 6               | 168                |
| Severe Hypertriglyceridemia                       | III   | 13              | 155                |

## Completed study in other diseases

| Pathology  | Phase | Number of sites | Number of patients |
|--|-------|-----------------|--------------------|
| <b>Ulcerative Colitis</b>                          |       |                 |                    |
|  | III   | 7               | 58                 |
|  | III   | 14              | 154                |
|  | III   | 6               | 66                 |
| <b>Cistic Fibrosis</b>                             |       |                 |                    |
|  | II    | 8               | 48                 |
|  | II    | 4               | 32                 |
|  | II    | 12              | 56                 |
| <b>Others</b>                                      |       |                 |                    |
| <b>Crohn's Disease</b>                             | II    | 3               | 20                 |
| <b>Huntington's disease</b>                        | II    | 3               | 9                  |
| <b>Non-cystic fibrosis bronchiectasis</b>          | III   | 12              | 56                 |
| <b>Chorea Associated with Huntington's Disease</b> | II    | 4               | 7                  |
| <b>Immune thrombocytopenic purpura</b>             | II    | 2               | 5                  |



## Russia Our clinical trial experience in influenza

| No | Type of study         | Phase    | Number of sites | Number of subjects | Type of product                                 |
|----|-----------------------|----------|-----------------|--------------------|---|
| 1  | local clinical trials | III / IV | 2               | 120                | immunomodulatory drugs with an antiviral effect |
| 2  | local clinical trials | III      | 2               | 140                | influenza vaccine                               |
| 3  | local clinical trials | III      | 1               | 140                | drug based on interferon                        |
| 4  | local clinical trials | III      | 1               | 52                 | influenza vaccine                               |

## Ukraine

| No  | Type of study                 | Phase | Number of sites | Number of subjects | Type of product    |
|-----|-------------------------------|-------|-----------------|--------------------|--------------------|
| 1   | international clinical trials | III   | 1               | 10                 | antibacterial drug |
| 2 * | international clinical trials | III   | 1               | 8                  | antiviral drug     |

We have had experience in several local studies of drugs against influenza and influenza vaccines in Russia.

In Ukraine, we did not conduct research on influenza. We conducted studies in pulmonology and one study antibacterial drug which involved patients with rhinosinusitis.

\* Research Center of our medical center in Ukraine participated in an international clinical trial of the drug against influenza

# THANK YOU FOR ATTENTION!

[www.ruslasa.ru](http://www.ruslasa.ru)

