Clinical Trials in Russia
Orange Paper
1st Quarter 2009

11, 4-Magistralnaya Ul., 123007 Moscow, Russia

www.synrg-pharm.com

Contents

11, 4-Magistralnaya Ul., 123007 Moscow, Russia

www.synrg-pharm.com

Executive Summary

The Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation (alias RosZdravNadzor, RZN) approved 113 new clinical trials during Q1 2009, a 13% decrease over the corresponding period of last year.

Clinical trials in Russia in Q1 2009 were sponsored by companies from 28 countries. The maximum number of trials (31) was initiated by Russian sponsors, American sponsors with 20 studies took the runner-up place, they are followed by the German sponsors with 12 trials, the same number of 8 new trials was instigated by the Swiss and Japan companies, and the top six is concluded by the UK sponsors with 7 new studies in Q1 2009.

Four new Phase I studies were launched in the first quarter of 2009; three trials less than in the corresponding quarter of last year. The number of the Phase II trials notably decreased from 41 trials in the first quarter of 2008 to 26 in the first quarter of 2009. Despite the overall trend, the number of Phase III trials demonstrated slight increase over last year number, up from 54 to 59 studies. The number of Phase IV trials slightly decreased from twelve in Q1 2008 to nine new studies in Q1 2009.

The number of patients which are planned to be enrolled in the Phase II-IV trials launched in the first quarter of 2009 stood at 9,784 patients, nearly the same as the last year number.

The German *Boehringer Ingelheim* sponsoring seven new studies is on the top of the heap in the first quarter of 2009. The Swiss *Novartis* with seven new trials in Q1 2009, but fewer number of patients, took the runner-up place, it is followed by American *Pfizer* with six new studies, and *Merck & Co.* with four new. The top five is concluded by German *Hexal Biotech* with three new studies in Q1 2009.

The Russian pharmaceutical company OOO *Pharmaclon* sponsoring two new clinical trials enrolling 140 patients in two sites, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in the first quarter 2009. OAO *Valenta Pharmaceutica* with two new trials and 105 subjects in four sites, took the runner-up place. It is followed by FGU *Russian Cardiologic Center* and ZAO *Biocad*. The fifth position is shared between OAO *Biosyntez* and ZAO *Vector-Medica*.

Seventy per cent of the new studies in Q1 2009 were conducted in six therapeutic areas. The maximum number of trials (17) were initiated in Cardiovascular diseases; 16 clinical trials in Neurology and Oncology; 14 studies were targeted at Infectious diseases; 12 – in Respiratory diseases and 11 endocrinological studies were initiated in Q1 2009.

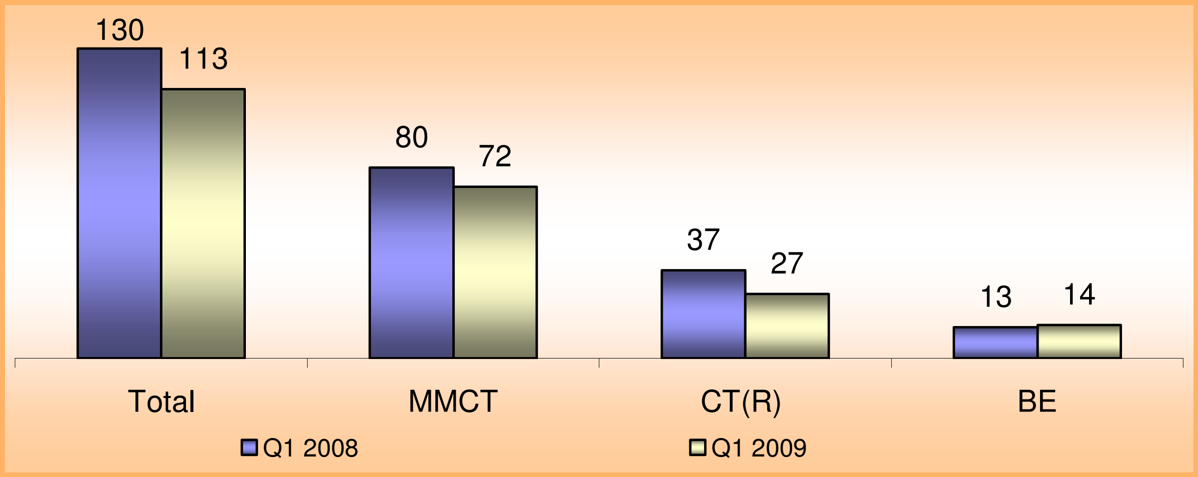
Clinical Trials by Type and Manufacturing Country

The RZN approved 113 new clinical trials of all types including local and bioequivalence studies during the first quarter of 2009; demonstrating a 13% decrease over the corresponding period of last year. As shown in the Figure 1, the main contribution into the total number of studies is still made by multinational multi-center clinical trials (presented as MMCT in Figure 1), even though the number of these studies decreased by 10% over Q1 2008 and stood at 72 new studies in Q1 2009.

The number of the local clinical trials conducted in Russia by domestic and foreign sponsors (the CT(R) bar in the Figure 1) is also down from 37 to 27 clinical trials demonstrating a notable 27% fall over the same point in 2008.

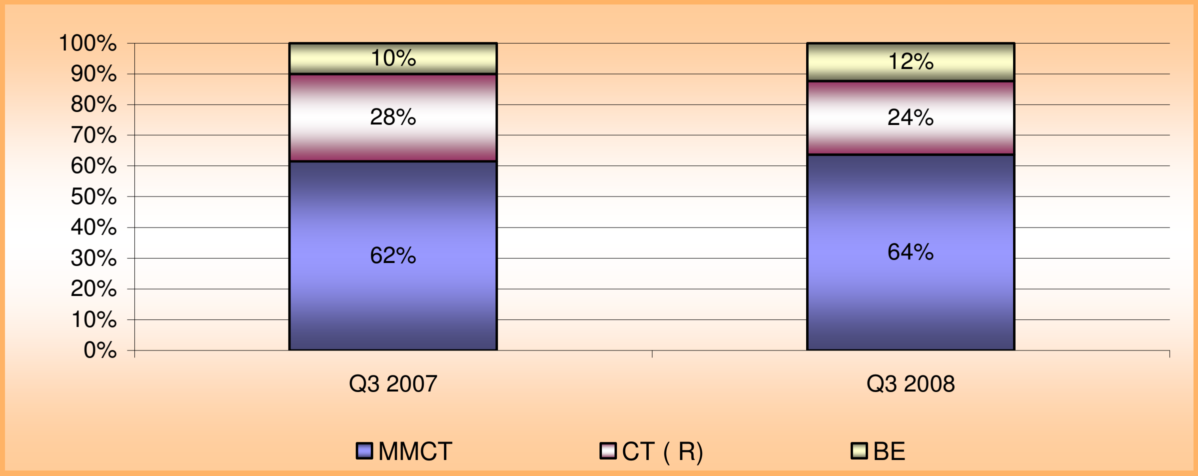
The number of bioequivalence studies (BE in Figure 1) in the first quarter of 2009 stood at 14 new trials, one study up over last year's figure.

Figure 1. Clinical trials approved by RZN in Q1 2009



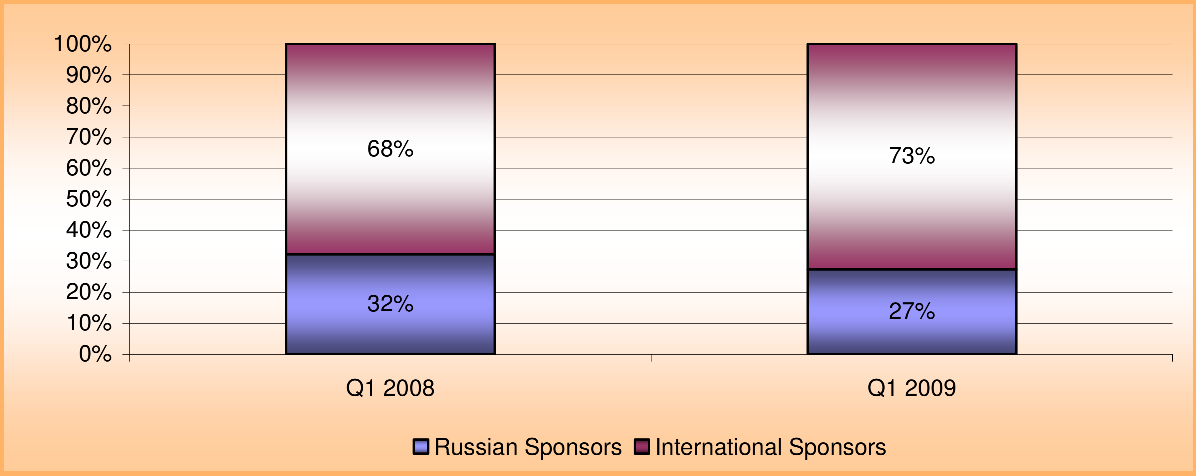
The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) did not change significantly over the same point in 2008. The share of multinational multi-center clinical trials slightly increased from last year's figure and stood at 64% of the total number of clinical trials approved by RZN in the first quarter of 2009. The shares of the local trials and bioequivalence studies in Q1 2009 stood at 24% and 12% of the total number of studies, respectively, while they accounted to 28% and 10% in Q1 2008.

Figure 2. Clinical trials by type in Q1 2009



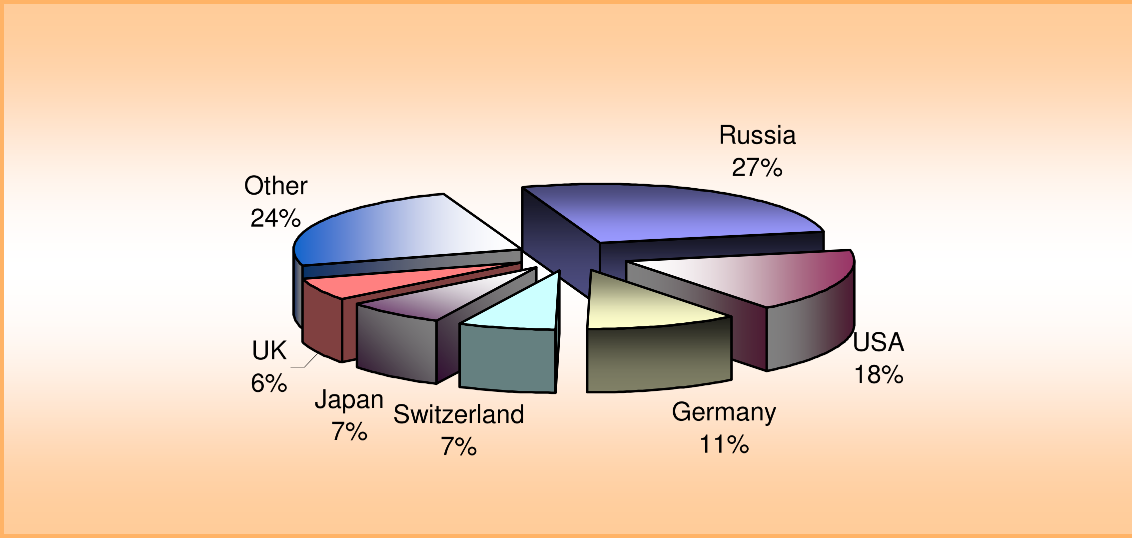
The lion's share of clinical trials in Russia is still being sponsored by foreign companies. Whilst their share increased from 68% to 73%, their number is up from 82 in Q1 2008 to 88 new studies in Q1 2009. Whilst the number of clinical trials initiated by the Russian sponsors, including bioequivalence studies, rose from 31 to 42, their share decreased from 32% to 27%.

Figure 3. Russian and International sponsors in Q1 2009



Clinical trials in Russia in Q1 2009 were sponsored by companies from 28 countries. Figure 4 demonstrates the input of the leading countries of sponsor's origin into the total number of clinical trials. The maximum number of trials (31) was initiated by Russian sponsors, American sponsors with 20 studies took the runner-up place, they are followed by the German sponsors with 12 trials, the same number of 8 new trials was instigated by the Swiss and Japan companies, and the top six is concluded by the UK sponsors with 7 new studies in Q1 2009.

Figure 4. Countries presented on the Russian clinical trials market in Q1 2009

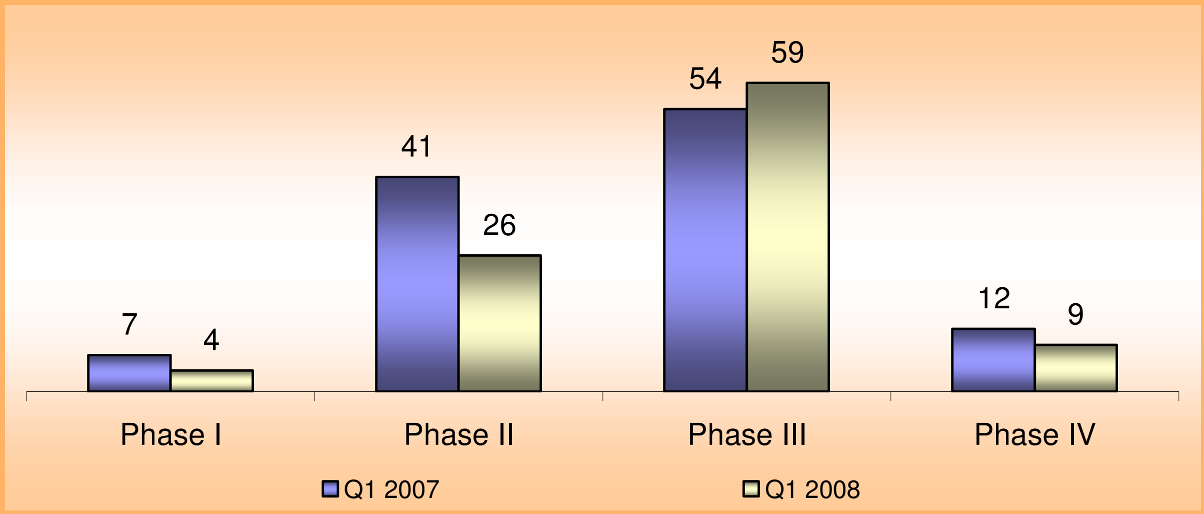


Austria, Denmark, Israel, Spain, Italy, Canada, the Netherlands, Norway, Pakistan, Poland, Portugal, Slovenia, Ukraine and Sweden are represented among others.

Clinical trials by Phase

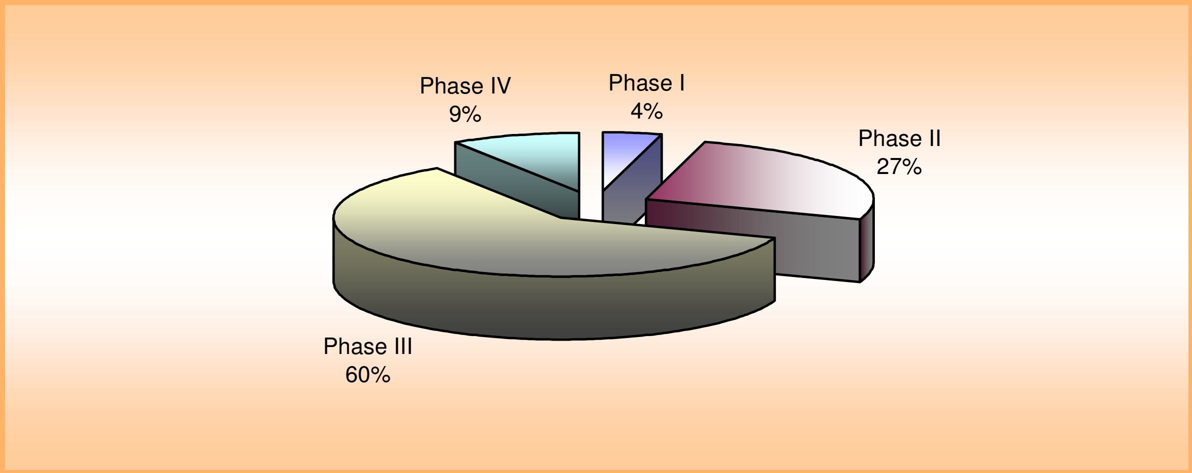
Four new Phase I clinical trials were launched in the first quarter of 2009; three trials less than in the corresponding quarter of last year. The number of the Phase II trials notably decreased from 41 trials in the first quarter of 2008 to 26 in the first quarter of 2009. Despite the overall trend, the number of Phase III trials demonstrated slight increase over last year number, up from 54 to 59 studies. The number of Phase IV trials slightly decreased from 12 in Q1 2008 to 9 in Q1 2009.

Figure 5. Clinical trials in Russia in Q1 2009 by phase



As shown in Figure 6, the share of Phase III trials in Q1 2009 stood at 60% of the total number of studies, the share of Phase II trials accounted at 27%, Phase IV trials stood at 9%, and the share of Phase I studies amounted to four per cent.

Figure 6. The proportions between study phases in Russia in Q1 2009



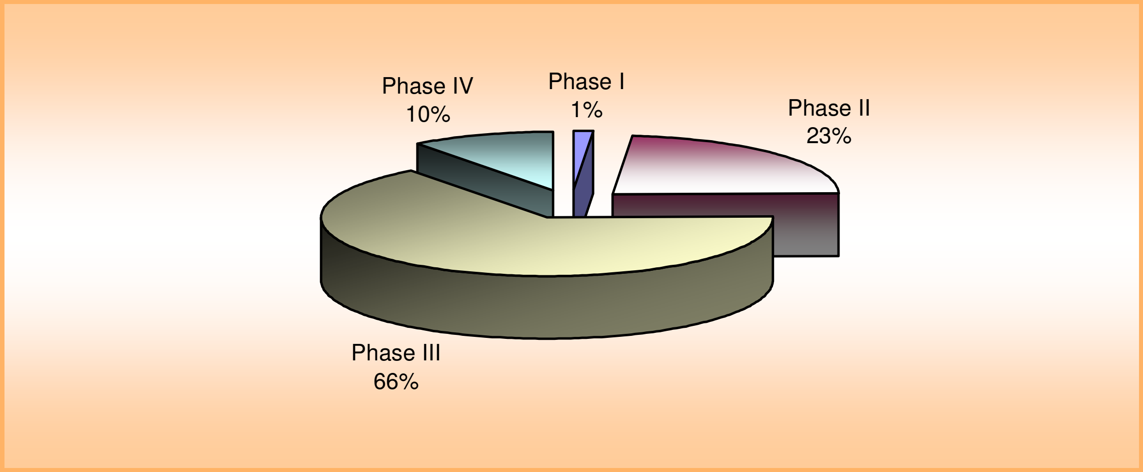
The number of patients which are planned to be enrolled in the Phase II-IV trials launched in the first quarter of 2009 stood at 9,784 patients, nearly the same as the last year number. It's worth mentioning that the number of Phase III subjects rose by 30% from last year's figure.

One hundred and twenty five subjects will be recruited in Phase I trials; 2,283 patients – in Phase II trials; 6,380 subjects – in Phase III studies and 996 patients will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is ten, the maximum number is 1,186.

The proportions of the number of patients between different Phases is shown on the Figure 7.

Figure 7. The number of patients in Q1 2009 by study phase



The duration of the shortest trial is three month; of the longest one will last six years.

Rating of international sponsors

The German *Boehringer Ingelheim* sponsoring seven new studies is on the top of the heap in the first quarter of 2009. The Swiss *Novartis* with seven new trials in Q1 2009, but fewer number of patients, took the runner-up place, it is followed by American *Pfizer* with six new studies, and *Merck & Co.* with four new. The top five is concluded by German *Hexal Biotech* with three new studies in Q1 2009.

Top five international sponsors by the number of new studies in Q1 2009 are presented in Table 1.

Table 1. Top-5 international study sponsors in Q1 2009

№	Sponsor	No. of trials	No. of patients	No. of sites
1	Boehringer Ingelheim	7	695	63
2	Novartis	7	397	54
3	Pfizer	6	100	16
4	Merck & Co.	4	210	15
5	Hexal Biotech	3	406	27

Rating of Russian sponsors

The Russian pharmaceutical company OOO *Pharmaclon* sponsoring two new clinical trials enrolling 140 patients in two sites, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in the first quarter 2009.

OAO *Valenta Pharmaceutica* with two new trials and 105 subjects in four sites, took the runner-up place. It is followed by FGU *Russian Cardiologic Center* and ZAO *Biocad*. The fifth position is shared between OAO *Biosyntez* and ZAO *Vector-Medica*.

Table 2. Top-5 Russian study sponsors in Q1 2009

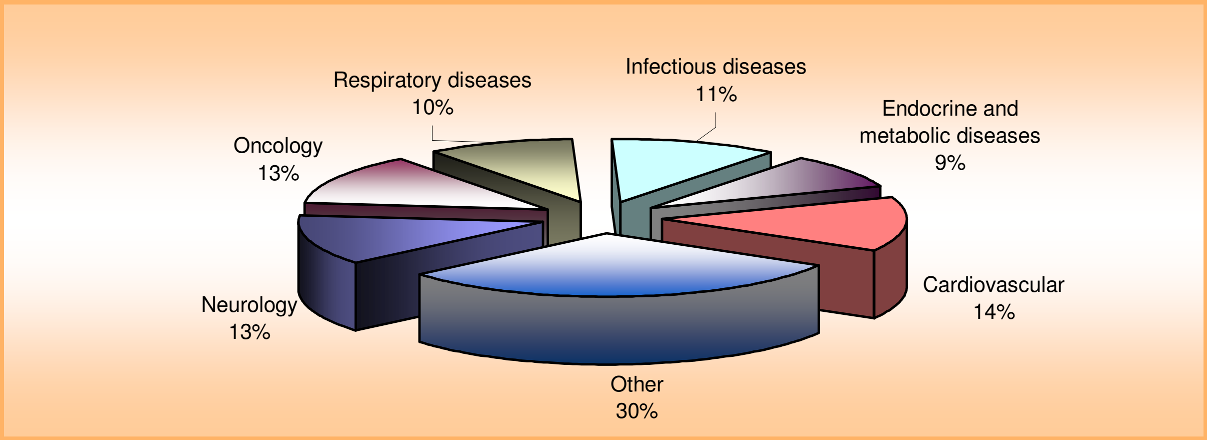
№	Sponsor	No. of trials	No. of patients	No. of sites
1	Pharmaclon	2	140	2

2	Valenta	2	105	4
3	Russian Cardiologic Center	1	126	9
4	Biocad	1	100	3
5	Biosyntez Vector	1	100	1

Therapeutic areas of clinical trials in Russia in Q1 2009

Seventy per cent of the new studies in Q1 2009 were conducted in six therapeutic areas. The maximum number of trials (17) were initiated in Cardiovascular diseases; 16 clinical trials in Neurology and Oncology; 14 studies were targeted at Infectious diseases; 12 – in Respiratory diseases and 11 endocrinological studies were initiated in Q1 2009. The proportions between different therapeutic areas are shown in Figure 8.

Figure 8. Clinical trials in Russia in Q1 2009 by therapeutic area



Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 12[1] new drugs during Q1 2009; only three of them are new molecular entities; others are the new dosages, manufacturers or indications of the already marketed drugs. The Table 3 represents those five of them which were, or are being tested in clinical trials in Russia.

Table 3. New Drugs approved by FDA in Q1 2009 and tested in Russian sites

Approval date	Drug	Manufacturer
01/23/2009	Savella (Milnacipran Hydrochloride)	Cypress Bioscience
01/30/2009	Kapidex (Dexlansoprazole)	Takeda
02/27/2009	Temodar (Temozolomide)	Schering
02/27/2009	Stavudine; Lamivudine; Nevirapine	Pharmacare Ltd
03/30/2009	Afinitor (Everolimus)	Novartis
		Source: CDER FDA http://www.fda.gov/cder

[1] CDER FDA http://www.fda.gov/cder

During the period from January 1 to March 31 2009 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) reviewed 16[1] applications to market drugs in the EU. Negative opinion was adopted for three of the drugs which had been approved earlier. Seven of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia (see Table 4).

Table 4. New Drugs approved by EMEA in Q1 2009 and tested in Russian sites

Approval date	Drug	Manufacturer
22/01/09	Protopic (tacrolimus)	Astellas
19/02/09	Avastin (bevacizumab)	Roche
19/03/09	Renvela (sevelamer carbonate)	Genzyme Europe B.V.
19/03/09	Modigraf (tacrolimus)	Astellas
19/03/09	Qutenza (capsaicin)	NeurogesX, Inc.
19/03/09	Nimvastid (Rivastigmine)	Krka, d.d., Novo mesto
19/03/09	Glivec (imatinib)	Novartis
Source: CHMP EMEA http://www.emea.europa.eu/index/indexh1.htm		

FDA inspections

According to the FDA data, as of 17 April 2009 there were no FDA inspections conducted in the Russian investigative sites during Q1 2009.

[1] CHMP EMEA http://www.emea.europa.eu/index/indexh1.htm