GEORGIA – HIDDEN GEM FOR CLINICAL RESEARCH

Would you like to go from regulatory submission to study initiation in less than 2 months? If so, welcome to Georgia.

Not to be confused with America's Southern Peach State, this country, with population of 3.75 million and a unique location at the crossroads of Eastern Europe and West Asia, is becoming a very attractive location for clinical trials. In addition to lightning-fast startup times, robust enrollment and full compliance with the ICH-GCP you will also be pleasantly surprised by the high quality of the study data evidenced by 12 recent 100% NAI (No Action Indicated) reports from FDA inspections.

Georgia's ethnically diverse patient population, with many treatment-naïve patients in a wide range of therapeutic indications coupled with highly professional medical staff, make the country a great location for both de-novo and rescue studies.

COUNTRY OVERVIEW

Population – 3,720,400 (2016, Source: Geostat). Located between Western Asia and Eastern Europe in the Caucasus region of Eurasia, Georgia is bordered by the Black Sea to the West, Russia to the North, Turkey and Armenia to the South and Azerbaijan to the Southeast. Tbilisi is the capital city and home to 20% of the country's population. Georgian is the official language (but many doctors speak English as well). Georgia is a member of the Council of Europe and the GUAM Organization for Democracy and Economic Development. The largest cities are Tbilisi, Kutaisi, Batumi and Rustavi.

HEALTHCARE SYSTEM

Historical Highlights

- **up until 1991** – part of the Soviet "Semashko" healthcare model
- **1991** – Georgia gained independence, initiating social and economic reforms
- **1999** – national Health Policy was developed
- **2004** – private health insurance replaced social health insurance
- **2007** – replacement of the existing hospital infrastructure (from the state to the private sector)
- **2008 –** ICH-GCP compliance in clinical trials was adopted
- **2008** – distribution of primary healthcare "toolkits" to providers in 900 rural communities
- **2011** – "Georgia: National Healthcare Strategy 2011-2015" introduced patient-centric approach to healthcare infrastructure

Current Status

A significant effort has been made to improve Georgia's healthcare policy and system in recent years. The government of Georgia had implemented a comprehensive program aimed at a reduction of disease burden and mortality by 2015. Today there are 259 hospitals, clinics and medical centers in Georgia, with the largest

number located in Tbilisi (country capital). There are around 12,000 hospital beds. Additional information is provided below in Table 1 and Table 2.

Table 1. Main Characteristics of Georgia's Public Health Sector*

	2011	2012	2013	2014	2015
Number of physicians	21,800	19,400	22,500	22,900	24,300
Number of paramedical personnel	17,900	14,100	15,500	15,600	16,400
Number of hospitals	245	221	237	245	259
Number of hospital beds	12,800	11,300	11,600	11,700	12,800
Utilization of one hospital bed	7 days	7 days	5,4 days	5,2 days	5,3 days
Number of medical facilities rendering out-patient services	1812 units	1901 units	1990 units	2124 units	2385 units
Number of out-patient visits	7,705,900	9,494,700	10,974,500	11,881,100	13,243,900
** Source: Geostat, the National Statistics Office of Georgia*					

Table 2. Number of physicians in Georgia by specialty*

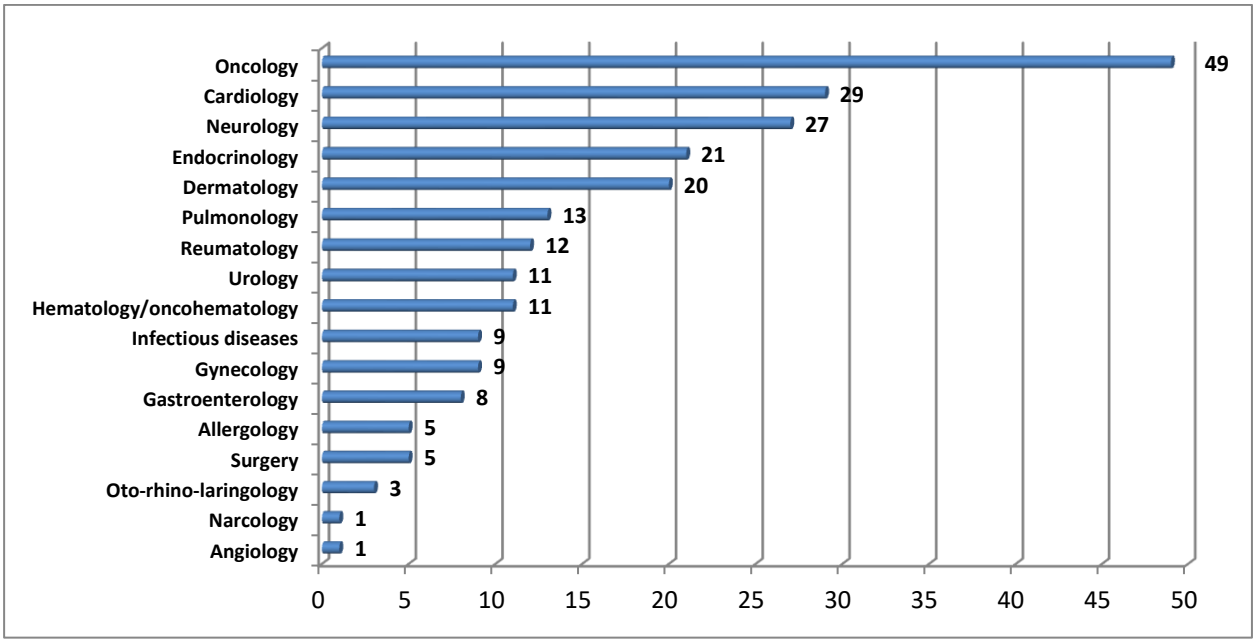
	2011	2012	2013	2014	2015
Internal medicine	1249	1238	1222	1131	1075
Surgeons	1110	1470	1634	1771	1998
OBGYN	1411	1453	1561	1649	1681
Pediatricians	1129	1440	1444	1367	1634
Ophtalmologists	369	381	486	500	548
Otolaryngologists	349	350	430	452	434
Neurologists	619	669	801	809	855
Psychiatrists	251	398	416	377	427
Pulmonologists	176	216	199	186	205
Dermatologists	276	323	356	352	373
Radiologists	520	1019	1212	1278	1409
Rehabilitation and sports medicine physicians	50	50	57	59	74
Dentists	1296	1701	1926	1846	2140
Other specialties	12968	8696	10746	11148	11454
In 2012 the health care human resources definitions were revised and classified in accordance with International Standard Classification of Occupations (ISCO-08). ** Source: Ministry of Labor, Health and Social Affairs of Georgia*					

CLINICAL TRIALS

Here are the reasons for why Georgia is an attractive destination for clinical trials:

- Large number of medical institutions with past experience in clinical trials
- Very short start-up timelines (< 2 months)
- High quality of data that is accepted by the FDA and proved by FDA inspections
- Clear regulatory requirements
- Fast and smooth import/ export of study materials (no separate import/export license is required)
- International medical standards in management of many diseases
- Reasonable investigator fees
- Motivated patients and sites
- Political and social climate welcoming and supportive of clinical trials

Figure 1. Number of Clinical Trials in Georgia by therapeutic area (2011-2015)



Specific features of study start-up in Georgia

- Very short start-up timelines (see Figure 2)
- Approval by local Ethics Committees (local ECs) precedes approval by the Regulatory Authority (RA = State Regulation Agency for Medical Activities)
- No import-export license is needed for study drug or for lab kits / bio samples
- Insurance for clinical trial should be obtained from local insurer

Figure 2. Average Start-up Period Duration in Georgia

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GEORGIA

Average Start-Up Period Duration

	Days	Weeks	Months
INDIVIDUAL STAGES			
Translation of docs and submission dossier preparation	35	5	1,2
Review & approval by by RA	21	3	0,7
Review & approval by the Central EC*	0	0	0,0
Review & approval by local ECs	14	2	0,5
Negotiating & signing study agreements	14	2	0,5
Obtaining import/export licenses, importation & distribution of IMP**	21	3	0,7
SUMMARY			
From submission till study approval	35	5	1,2
From submission till first site initiation	56	8	1,8
From start of work till first site initiation	91	13	3,0

week 1 week 2 week 3 week 4 week 5 week 6 week 7 week 8 week 9 week 10 week 11 week 12 week 13 week 14 week 15 week 16 week 17 week 18 week 19 week 20 week 21 week 22 week 23 week 24 week 25

* not applicable in Georgia

** no importation license needed in Georgia

REGULATORY AUTHORITIES AND SUMBMISSION/APPROVAL PROCESSES

Study agreements

- In most cases two separate agreements per site (with investigator and with institution) are required before study initiation
- Negotiation and signature process takes around 2-3 weeks and may be done in parallel with study approval process (there is no need to submit signed study agreements either to local ECs or to the RA)
- Study agreements should be signed before site initiation

Legal restrictions

It is prohibited to conduct clinical trials on:

- Orphans
- Military personnel
- Prisoners

Trials on pregnant women and children are only approved in cases where a drug will be used specifically in such groups of patients. In cases where drugs are planned to be used in both in adults and children, studies on adults should precede studies on children and pregnant women.

Country Specific Requirements / Timelines for Study Approval (see also Figure 2)

- Study dossiers should be first submitted to Local ECs, which are present in all sites. Local ECs usually provide approvals within 1 to 2 weeks.
- After obtaining approvals from all Local ECs, a Submission letter is sent to the State Regulation Agency for Medical Activities.
- The State Regulation Agency for Medical Activities approves the study in 3-5 weeks after receiving approvals from the Local ECs.
- All documents must be provided in both electronic and paper forms.
- All study-related documents provided as printouts should be submitted in English with a notarized Georgian translation.
- The applicant should be a local company or registered as individual entrepreneur (National Agency of Public Registry states that according to Georgian legislation, foreign company / company's branch office/ representation is not considered a legal entity and therefore cannot conduct legal activities on behalf of the company)
- Import/export licenses are not required.

  Note: The State Regulation Agency for Medical Activities provides an Approval Letter and a Clinical Trial Authorization Certificate. Import/Export process is based on these documents. In the case that other drugs (comparator, concomitant medications) are being provided and imported by the sponsor, but not mentioned in the protocol, a country specific Protocol Amendment regarding drug importation into Georgia must be issued by the sponsor.

Initial Dossier for Study Approval

Printouts and electronic versions of all documents should be submitted to Local ECs and the State Regulation Agency for Medical Activities. List of documents submitted to RA for study approval is provided below:

- A copy of an insurance certificate

  Note: Insurance Policy should be issued by a local insurance company. The amount of insurance compensation is not defined and depends on the study project and is subject to approval by the RA (State Regulation Agency for Medical Activities).

- A legalized Power of Attorney (PoA) and notarized translation of the PoA.

  Note: PoA must be legalized – there are two ways of legalization that are accepted in Georgia:

  1. Apostille: If the document emanates from a country that is party to the Hague Convention on Legalization (1961), an apostille should be attached to the document.
  2. Consular legalization: If the country from which the document emanates is not a party to the Hague Convention on Legalization, then a more formal process of consular legalization is usually required.

- Protocol – the latest version in English and notarized translation into Georgian.
- Investigator's Brochure –version in English/Russian (for RA) and translation into Georgian (for Local ECs).
- Printout of CRF – in English and notarized translation into Georgian.
- Informed Consent Form – in English and notarized translation into Georgian.
- Questionnaires, patients' cards, diaries and all documents provided to the trial subjects – notarized translation into Georgian.
- CVs of all Principle Investigators /Licenses of all institutions.
- Principle Investigators' GCP certificates.
- Approval letters from Local ECs of all participating medical institutions.
- GMP Certificate / Certificate of Analysis of the study drug
- Registration Certificate of the study drug (in case it has been registered for clinical use in Georgia for any indication).
- List of study sites.
- Information about comparators and concomitant medications.
- Document proving the payment of submission fee (for RA only).
- The formal business registration proof of Georgian legal status of the applicant (for RA only)
- Label template in Georgian.

CROMOS PHARMA IN GEORGIA

Cromos Pharma's office is situated in the very heart of Georgia, in the capital city of Tbilisi. There is good reason for such location as a large percentage of clinical trials in Georgia are conducted here. Our office provides full service support for Phase I-IV clinical trial management.

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If you would like to continue receiving the most up to date information on clinical trials in Georgia, please join our LinkedIn group "Clinical Trials in Georgia".