CLINICAL STUDY RESCUE: WHERE TO FIND PEACE OF MIND

PROBLEM

Conducting an effective and high quality clinical trial as part of a drug development process is a monumental undertaking. The complexity of this task easily surpasses the development of almost any new product in any field. Each study starts with a meticulous design, very thorough analysis of inclusion and exclusion criteria, and selection of the best suited vendors, investigators and sites. Diligent and extensive preparation for study launch is a must and every possible scenario should be dissected. However, even the most painstaking prelaunch readiness activity does not always translate into smooth study conduct and on-time delivery. Recent analysis of all pivotal clinical programs revealed that close to one-half ended up missing the anticipated timelines. These delays translate into late submissions to the FDA, late approvals of the NDAs and late market entry. Not only does this cause loss of profitability due to shortened patent life, but also loss of market share in the event that such delays translate into a competitor's product being first to market. For Pharma and biotech companies of any size, these issues have serious consequences with a price tag of up to $1 million in lost revenue for every day of delay.

While imperfections in study design and inadequacies on the part of vendors are a significant impediment to effective study conduct, the most serious delaying factor is a very straightforward one: Not enough patients are being recruited. Even if the company has conducted a very diligent assessment of recruitment feasibility, it is not at all a guarantee that selected sites in chosen countries will accrue enough patients and do so on time.
Unfortunately, the situation with missed targets continues to worsen for a number of reasons.
Firstly, the number of competing clinical programs is significant and recent focus on observational studies and registries has addeded to this problem. It is more difficult to find patients in a medical center that conducts several parallel trial programs, which target the same patient population. Secondly, introduction of personalized medicine and more stringent patient selection reduces the total available pool of study subjects at an ever increasing rate. The best example of such differentiation can be found in oncology studies, where absence of a certain genetic marker excludes a patient from the trial.
The logistics of finding another CRO, switching to a more efficient data capturing system and to electronic CRF format, while being important aspects of any study rescue process, are not being covered in this white paper. The purpose is to show how the addition of a certain, specified geographic region can help in accelerating study recruitment and meeting the timelines that were set forth at a study's inception.

SITUATION

In a hypothetical late stage trial that a company is currently running, the recruitment is not on target and certain decisions regarding its "rescue" need to be made. Assuming all logistical aspects of the study have been buttoned up, the issue at hand is identifying countries and sites that can bring study recruitment back on target.

While many countries can and should be considered, we will limit our discussion to the ones that we know and understand. This doesn't mean that described region is a perfect match for every study. There will be certain studies that are logistically too complex or require such a level of special care which cannot be delivered in our geographies.

We, at Cromos Pharma, strongly believe that acceleration of patient accrual should not compromise study quality and would be the first to warn you if your study would be best served by going to other locales.

However, in an overwhelming number of cases we can and will deliver both patients and quality data.

PROPOSED SOLUTION

We recommend the following deployment plan of additional sites in the following countries.

As there is usually a need to start "rescuing" the study instantly, you should look at the countries that have the most streamlined regulatory approval process. In our region such countries, in order of speediness of approval timelines are Georgia, followed by Latvia and Estonia and then by Russia and Ukraine.

STEP 1: Georgia

Georgia is a former Soviet republic that is located at the crossroads of Western Asia and Eastern Europe. It is bounded to the west by the Black Sea, to the north by Russia, to the south by Turkey and Armenia, and to the southeast by Azerbaijan. Its capital is Tbilisi and its population is around 4.7 million. Georgia's healthcare system combines the remnants of the old Soviet system with high hospital capacity and primary care that by its design acts as a referral base for specialized, disease-specific medical centers with active development of private sector and modernization of medical care as a whole.

Georgia has recently adopted a very efficient regulatory submission algorithm that allows receiving a full trial approval within 4-6 weeks. Georgian physicians are very eager to participate in clinical trials and to date have been providing very high quality data. Despite its small population, Georgia delivers very robust recruitment while maintaining high retention and low screen failure rates.

STEP 2: Latvia and Estonia

Being members of the European Union, Latvia and Estonia conduct clinical trials in full compliance with EU legislation and directives. Both countries have small patient populations, which does not preclude substantial recruitment rates, largely because of a very positive outlook on clinical research by both patients and physicians as well as due to relatively low reimbursement rates of health care workers. Approval timelines are also very favorable – the complete process takes on average around 3 months in both countries.

Latvia is is a former Soviet Republic located in the Baltic region of Northern Europe. It is bordered to the north by Estonia, to the south by Lithuania, to the east by Russia, and to the southeast by Belarus, and it shares a maritime border to the west with Sweden. It has a population of 2,070,371 inhabitants and its capital is Riga. Latvia once again became one of the fastest growing economies of the EU in 2011 and is a member of the United Nations, European Union, Council of Europe, NATO, Organization for Security and Co-operation in Europe, International Monetary Fund and World Trade Organization, and is part of the Schengen Area. The United Nations lists Latvia as a country with a "Very High" Human Development Index. It has a high and continuously improving level of medical care.

Estonia is a former Soviet Republic that is located in Northern Europe and is bordered to the north by the Gulf of Finland, to the west by the Baltic Sea, to the south by Latvia, to the east by Russia and Finland in the north. Its population is 1.29 million and its capital and largest city is Tallinn. Estonia is a member of the European Union, Eurozone and the NATO. Estonia has the highest gross domestic product per person among the former Soviet republics. It is listed as a "high-income economy" by the World Bank and the United Nations classifies Estonia as a developed country. Recent health care reform has significantly improved the quality of care, which is now on par with other developed European countries

STEP 3: Russia and Ukraine

While the study is being launched in the aforementioned countries, we propose to concentrate on obtaining a study approval status in Russia and in Ukraine. It is a slightly lengthier process – somewhere between 4 and 5 months. Usually such a wait is well compensated by a very vigorous recruitment that almost universally surpasses other countries, including such high recruiters as China and India. With Russian and Ukrainian populations of 142 million and 46 million respectively, the patient pool is more than sufficient for a study in almost any indication. Both the approval processes and the standards of care are quite similar between the two countries and have been improving. The centralized healthcare system with large, specialized medical centers is very conducive to clinical research as it allows for a rapid patient recruitment. Also, the presence of a common language (Russian) makes international communication significantly easier. This same concept applies to Georgia and, to a lesser degree, to Latvia and Estonia.

In conclusion, addition of the 5 countries that have been discussed will rapidly accelerate recruitment. The proposed algorithm of focusing simultaneously on regulatory submissions in all 5 countries and then launching trial sites in Georgia, Latvia and Estonia, Russia and Ukraine in 1, 3 and 4.5 months respectively is, in our view, a valid and logical approach to the challenges of slow patient accrual.

We are confident that with the inclusion of Russia, Ukraine, Georgia, Latvia and Estonia, your recruitment targets will be met and surpassed.