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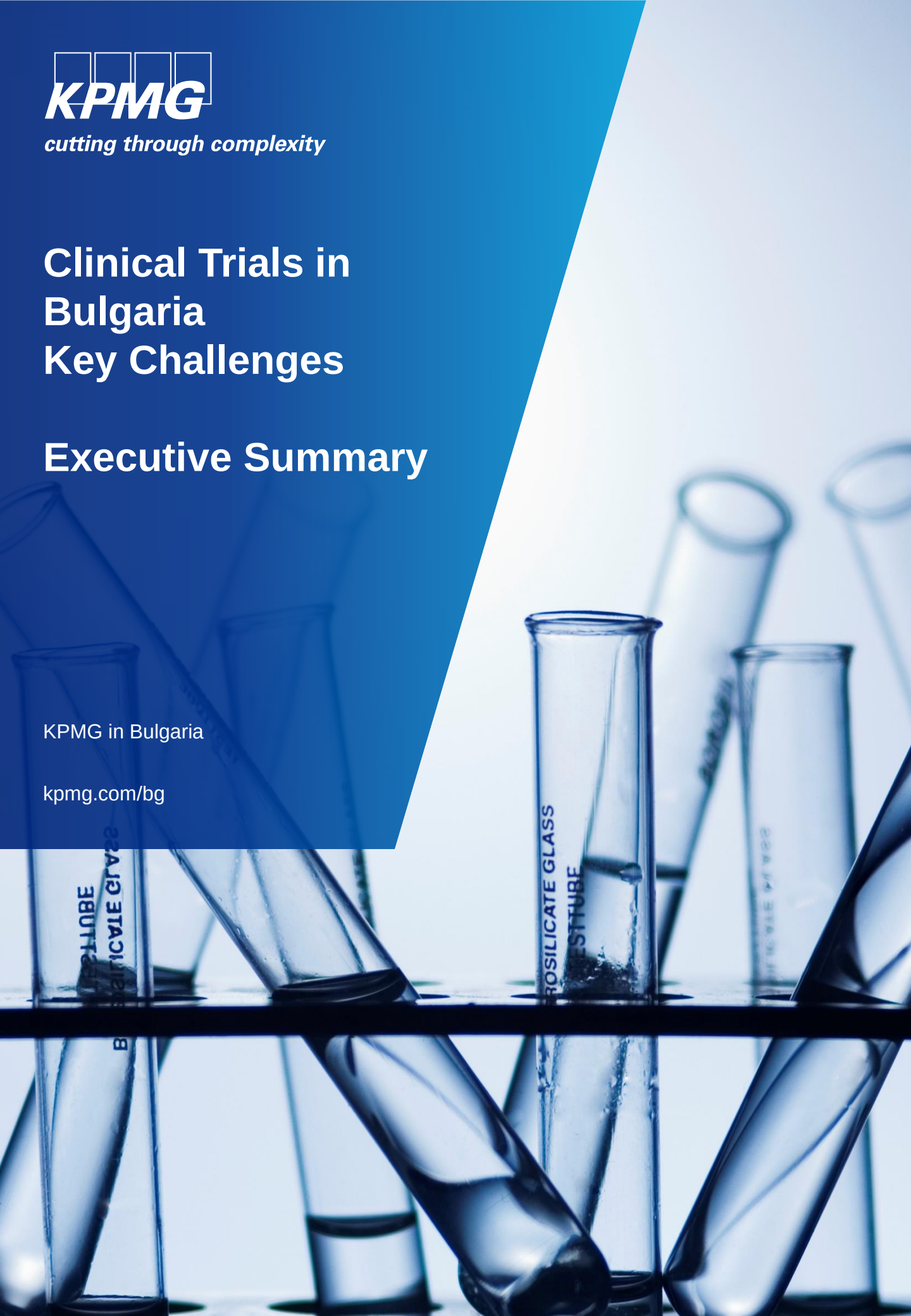
Clinical Trials in Bulgaria
Key Challenges

Executive Summary



KPMG in Bulgaria

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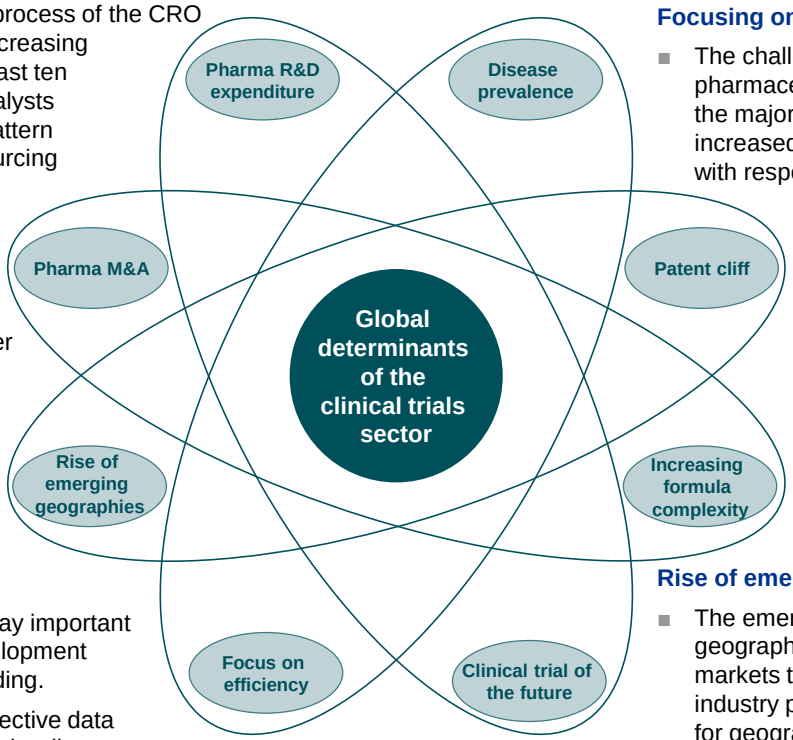
Executive summary

Global determinants of the clinical trials sector

- The Report explores a selection of factors which according to the performed analysis have substantial influence on the development of the clinical trials industry globally.

Prama R&D expenditure

- The Market study conclusions reveal that the Pharmaceutical industry maintained relatively constant drug development budget of approximately USD 100 billion.
- Nevertheless, it is clear that the penetration in the development process of the CRO industry has been increasing constantly over the last ten years and sector analysts anticipate that the pattern for increasing outsourcing would prevail in the foreseeable future.
- At the same time, the effectiveness of the R&D, if measured by cost per molecule brought to market declines constantly, forcing sponsors to seek optimization of Pharma R&D in general.



Disease prevalence

- Morbidity patterns play important role in the drug development strategies and spending.
- Statistical and prospective data provide evidence on the diseases which would influence drug development in the different countries.

Patent cliff

- Expiration of the patents of major medications generating substantial revenues for pharma companies resulted in the end of the so called blockbuster drug era.
- Sponsors are expected to intensify their efforts to rekindle innovation in R&D in search of new opportunities which would have positive effect on drug development, including clinical trials globally.

Increasing formula complexity

- Introduction of new complex formulas, increasing the share of poorly absorbed medications in R&D pipelines necessitates additional efforts in developing and trialing.

Clinical trials of the future

- Industry analysts conclude that drug development process would undergo numerous changes spanning from introduction of adaptive pathways through application of mobile technologies and “big data” to adoption of adaptive trial designs.
- The changes could present numerous opportunities for development of the clinical trials sector globally but would also present challenges to stakeholders to modernize and manage much more complex processes.

Focusing on efficiency

- The challenges facing the pharmaceutical industry forces the major players to pursue increased efficiency, particularly with respect to R&D.
- Outsourcing backed by the forming of new, long-term strategic partnerships between Pharma and CROs is expected to have strong positive effect on clinical trials globally.

Rise of emerging geographies

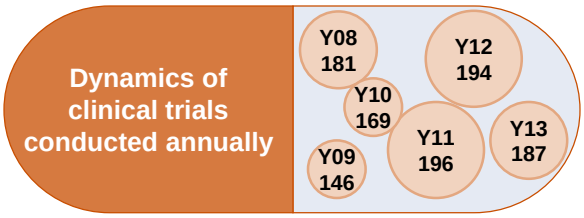
- The emergence of new geographies as potential lucrative markets to the pharmaceutical industry provides a strong drive for geographical diversification of clinical trials.
- The process is having a positive effect on the conducting of clinical trials in the emerging markets, including CEE.

Pharma M&A

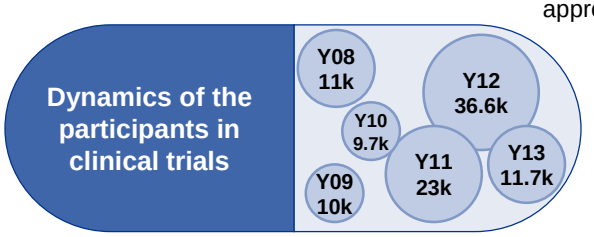
- Large merger and acquisitions in the Pharmaceutical industry have significant effect on R&D pipelines.
- The effects of the recently intensified M&A activity in the sector is yet to be seen. Nevertheless, industry analysts expect that new trends evident in recent transactions would lead to more focused, efficient and innovative drug development process.

Executive summary

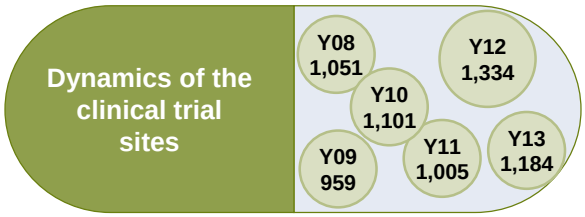
Clinical trials in Bulgaria



- As of 2013, the number of new clinical trial approvals in Bulgaria decreased if compared to 2012 reversing the upward trend in the approvals over the previous periods.
- Survey respondents point out that this negative trend is observed globally. Nevertheless, the decrease is partially due to the relatively slow approval procedure in Bulgaria, while Sponsors are increasing demands for swifter review and approval.

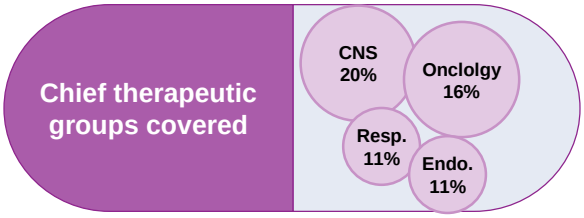


- After the record in year 2012, the number of trial participants decreased in 2013. Major reason is a change in the profile of the trials conducted in the country.
- During 2012 certain trials in the field of cardiovascular diseases were conducted in the country and these involved a high number of participants.



- Similarly to the number of clinical trials, the number of sites decreased in 2013.
- The number of newly opened sites with respect to active trials fluctuated significantly over the period 2008 – 2013, before decreased in 2013, which, according to respondents, is due to the difficult site contracting during the application stage.

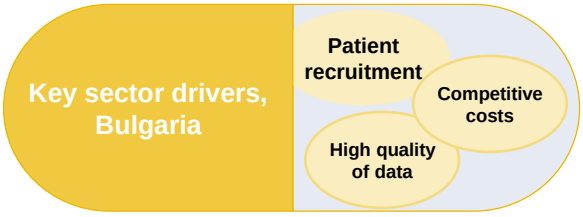
- There is a clear trend for increase in the number of new trials in CNS, oncology and respiratory diseases which account for approximately 50% of all trials.



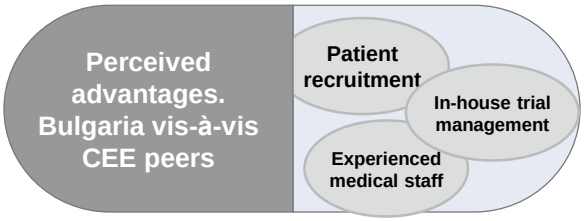
- Respondents point out that the sites' capacity to conduct trials in the major and growing fields (e.g. Oncology) is beyond optimal which may impede future growth in the sector.

- The number of CRA has been decreasing along with the falling number of clinical trials conducted.
- Nevertheless, the ratio of clinical trials per CRA increases as an illustration of the ongoing surge for increased efficiency in the sector.

- Almost all Survey participants are pointing efficient patient recruitment as one of the strongest drivers for the development of the clinical trials sector in Bulgaria.
- Other significant factors, apart from the quality data and competitive costs are inefficient healthcare system attracting patients to CTs and the availability of medical equipment.



- The perceived advantages of Bulgaria for conducting of clinical trials vis-à-vis CEE peers are similar to the identified sector drivers. Efficient patient recruitment, the experienced medical staff and in-house trial management are highly priced by respondents.

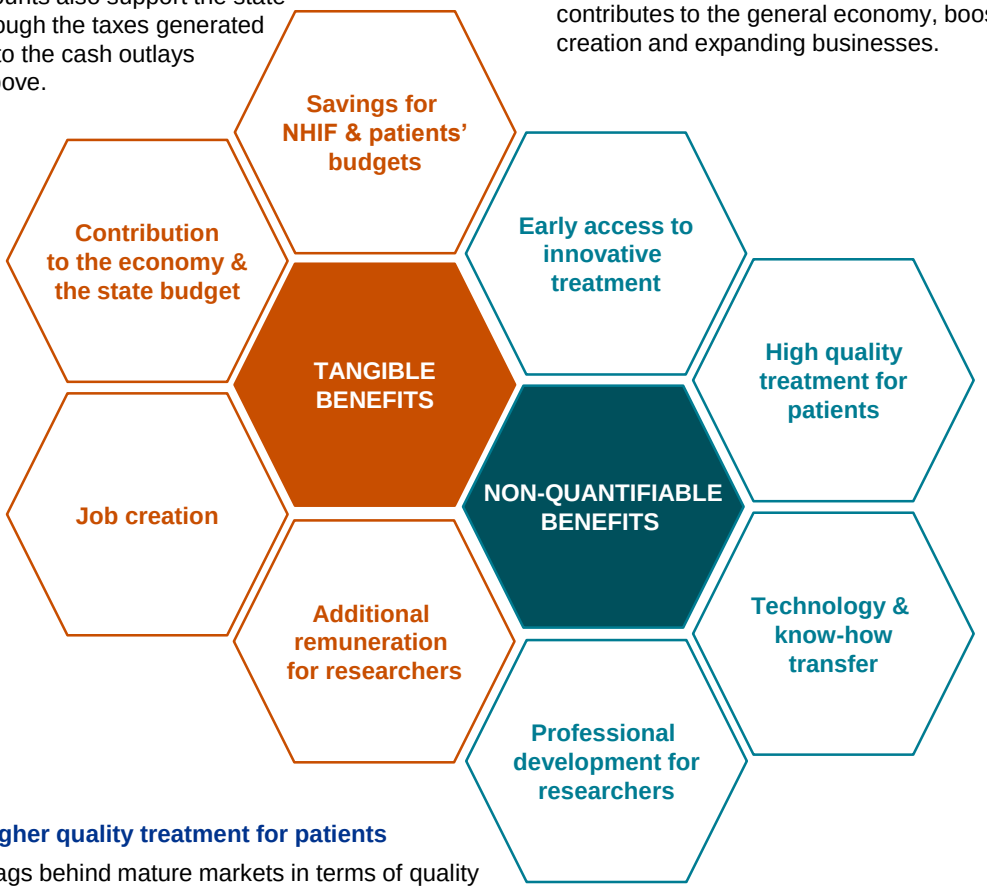


Risk-benefit analysis of clinical trials sector

- The conducting of clinical trials brings a number of benefits, both monetary and non-quantifiable to the countries which host this activity.

The analysis performed in this Market study suggests that the clinical trials sector brings in the Bulgarian economy BGN 151.5 million per annum in the form of direct costs such as salaries, sites and investigators remuneration, statutory fees and others.

- These amounts also support the state budget through the taxes generated in relation to the cash outlays outlined above.
- In addition, the sector generates a number of monetary benefits which quantification is highly subjective but are nevertheless substantial.
- These include the realized savings for the NHIF and patients' out-of-pocket payments for treatment.
- The effect from the retaining of medical specialists in the country because of the opportunity to generate additional income related to conducting clinical trials is also an important benefit.
- Finally, the clinical trials sector and its ecosystem of non-medical contractors and suppliers of services contributes to the general economy, boosting job creation and expanding businesses.



Access to higher quality treatment for patients

- Bulgaria lags behind mature markets in terms of quality of healthcare service. Participation in clinical trials is seen to provide higher quality treatment and increased availability of medically advanced drugs.
- Interviewees agree that treatment which is rather standard in WE can turn out to be very costly or even unavailable in Bulgaria during standard treatment procedures. Participation in clinical trial would make it accessible.

Professional development for researchers

- Clinical trials provide opportunity to upgrade the quality standards of the day-to-day work of the medical professionals conducting trials.
- Local medical staff and the healthcare system in general benefit from skills earned during the research process.
- However, interview feedback suggests that not all medical staff believe that this is a significant asset.

Technology transfer and know-how sharing

- Given the fact that the clinical trials are per se an innovation driven process, oftentimes involving the application of cutting edge treatment, conducting of trials inevitably leads to know-how transfer from sponsors, CROs to sites and researchers.

Barriers to market development

Perceived roadblocks hampering sector development

Systematic obstacles

- Attitude of key stakeholders
- Timing of administrative procedures
- Lack of predictable approval date
- Administrative burden stemming from high number of documents included in a CT application
- Cumbersome dual supervisory mechanism
- Limited patient awareness

Site-related obstacles

- Insufficient site capacity
- Sub-optimal medical equipment
- Discriminatory fees for medical procedures charged in relation to clinical trials
- Ununiformed fee policy across sites
- Insufficient transparency of site rules
- Ununiformed site contracting process
- Limited number of study coordinators at sites

Remedies proposed by Survey participants

- Amend the applicable regulatory framework
- Eliminate redundant documents from applications for new clinical trials
- Enhance patient awareness
- Involve key stakeholders
- Strengthen the capacity of the relevant authorities with respect to enhance monitoring and improve approval times

- Improve/ standardise efficiency of the contracting process
- Introduce uniformed fees across sites
- Establish units dedicated to clinical trials management, employing qualified coordinators
- Enhance capacity management, particularly in overrepresented fields with growth potential such as Oncology, Rheumatology

- An important element of the performed Survey encompassed the perceived roadblocks before the successful development of the clinical trials sector in Bulgaria.
- The respondents concurred that the major factors impeding the sector growth are related to the overly rigorous and cumbersome regulatory framework, particularly in relation to approval of new trials.
- Further, the Survey participants point out that their work with sites and that the overall process of management of clinical trials by healthcare providers could be optimized.

- Based on the available information, it appears that the clinical trials sector in Bulgaria declines at a CAGR of 14%. Hence, all else kept unchanged, it could be assumed that the sector volume would decline to approximately BGN 102 million as at 2016 if the environment remains unchanged and the negative trend continues.
- On the other hand, it appears that if the proposed improvements are implemented and the main roadblocks impeding the sector growth are alleviated, the clinical trials in Bulgaria could grow with a CAGR of 15.8% and, hence, reach a volume of BGN 185.8 million.

SWOT analysis

Strengths

- Stable and predictable regulatory environment for the development of the clinical trials sector ensured by the country's EU membership and the harmonization of the national legislation with the EU acquis
- Highly efficient patient recruitment is one of the strongest positive descriptors of the local clinical trials sector pointed by Survey participants
- Competent medical personnel ensures the quality of the conducted trials
- High quality of data collected
- Relatively favorable cost base enjoyed by researchers conducting trials in Bulgaria

Weaknesses

- Small-sized population and pharmaceutical market limit the potential for expansion of the clinical trials sector particularly with respect to development of drugs for treatment of rare diseases
- Technological base of sites is oftentimes sub-optimal given industry trends for increasing formula and drug development complexity
- Limited site capacity in certain high-growth, high-impact therapeutic fields could impede sector expansion
- Cumbersome administrative procedures particularly with respect to approval of new trials as well as the complicated sector oversight results in longer development periods which may decrease the country's attractiveness as a destination for conducting of clinical trials for sponsors
- Lack of uniform policies by healthcare providers with respect to clinical trials management hinders and lengthens the development process, thus limiting sector's growth

Opportunities

- Global pharmaceutical industry is striving to rekindle R&D innovation through increased efficiency and focused research. The process provides growth opportunities to agile, emerging geographies
- Clinical trials sector penetration in the country is average vis-à-vis regional and less than mature-market peers, if measured by patients, sites and pivotal trials to population. Hence there might be a growth potential for the sector as part of a general convergence process
- Addressing certain relatively easy to comprehend issues impeding the industry development could lead to quick wins with respect to the future growth of the clinical trials sector
- Strengthening of the domestic research industry (as a result from government policy, EU funding, etc.) could nurture increased domestic capacity with respect to drug discovery and development

Threads

- Competition from larger and commercially attractive markets (i.e. Poland, Russia) could lead to a gradual decrease in the number of clinical trials conducted in Bulgaria
- Therapeutic concentration in several key areas (i.e. oncology) exposes the sector to technological and regulatory risks. A research breakthrough in that field or an unanticipated change in the applicable regulations in major markets could have an adverse effect on a large number of trials conducted in Bulgaria
- Failing to follow sector's technological changes could result in deteriorating competitive position of sponsors, CROs and sites which could undermine the country's appeal as a geography for conducting clinical trials
- Recent consolidations in the pharmaceutical industry could lead to optimisations of the R&D process with adverse effects on the number and breath of conducted clinical trials
- Healthcare reform both domestic or in large foreign markets could have negative impact on sites capabilities, study designs, etc.

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