WHITE PAPER

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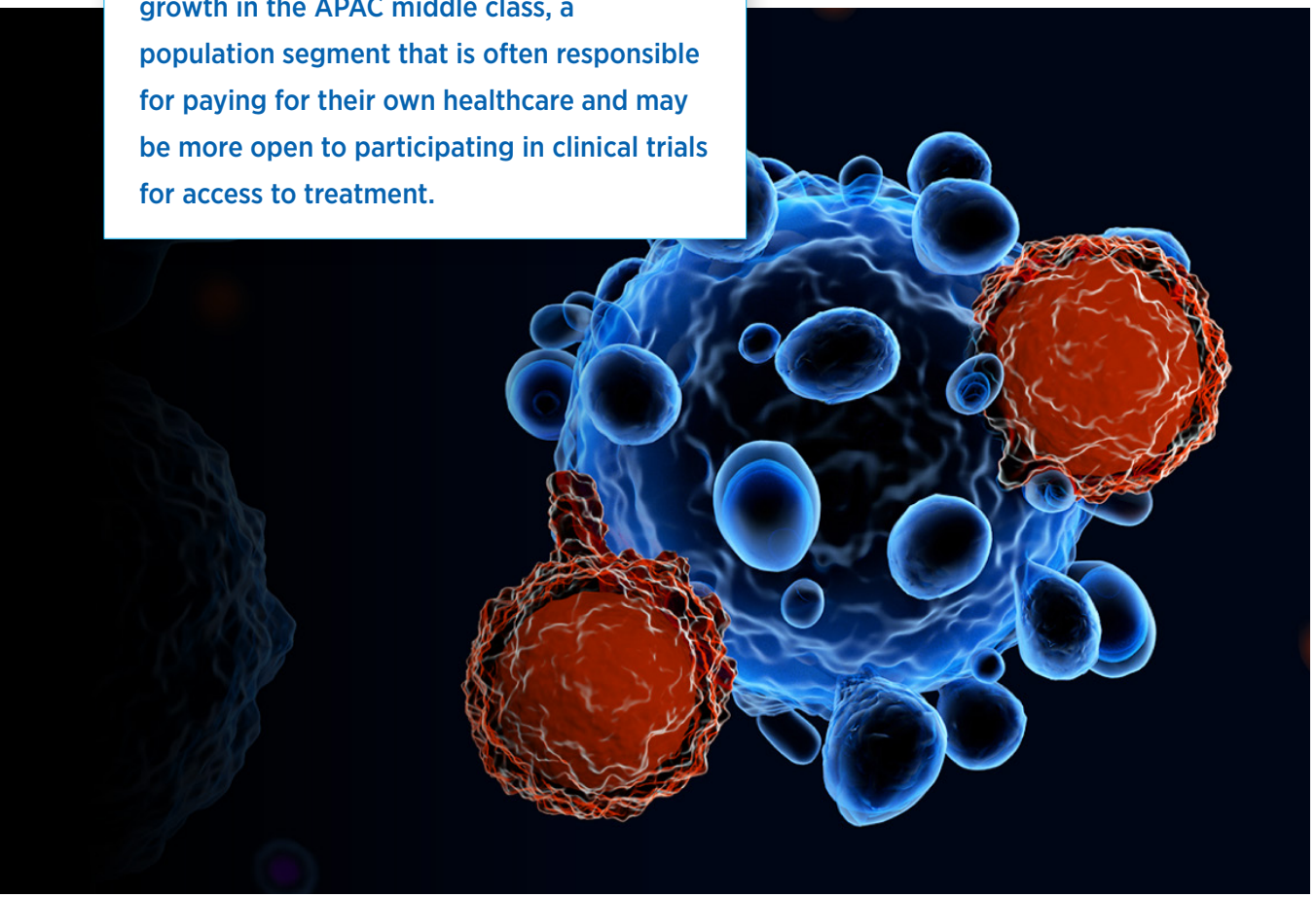
ONCOLOGY

Making the Asia-Pacific Region a Destination of Choice for Oncology Clinical Trials

ABSTRACT

Significant patient populations, top clinical institutions, and ease of regulatory compliance combine to support oncology trial success in this dynamic region.

With globalization, there has been rapid growth in the APAC middle class, a population segment that is often responsible for paying for their own healthcare and may be more open to participating in clinical trials for access to treatment.



Introduction

Over the past decade, the Asia-Pacific (APAC) region has seen the most robust growth in oncology clinical trial activity, with a 138 percent increase over the period from 2010 to 2020.[1] In fact, APAC now ranks first in the world for total number of ongoing oncology clinical trials, with China accounting for more than half of those studies.[1] A number of factors are contributing to this flurry of activity, including relative ease of regulatory compliance, lower cost of study conduct, access to large patient populations, and presence of top clinical institutions and investigators.

In this white paper, we explore the growth of oncology clinical trials in APAC countries and discuss strategies to support global study success in this dynamic and complex region of the world.

Factors influencing the growth of APAC oncology clinical trials

A variety of factors are driving oncology clinical trial activity in the APAC region:

- **High patient population.** The APAC region is densely populated and includes the two most populous countries – China and India. APAC accounts for 60 percent of the global population, with an urban population of over 2.3 billion people.[2] Among this population are many treatment-naïve patients who may be eligible to enroll in clinical trials. Moreover, with globalization, there has been rapid growth in the middle class, a population segment that is often responsible for paying for their own healthcare and may be more open to participating in clinical trials for access to treatment.

- **Increase in skilled personnel.** As clinical trial activity increases in the APAC region, the number of overseas returnees with drug development expertise and personnel with global study training and knowledge of International Conference on Harmonization good clinical practice (IHC-GCP) is growing. The APAC contract research organization (CRO) market, including both global and regional CROs, was valued at $8 billion in 2020 and is projected to exceed $18 billion by 2028.[3]
- **Availability of world-renowned key opinion leaders and specialized clinical trial centers.** There are more than 50,000 active principal investigators supporting clinical trials in the APAC region. These key opinion leaders are often members of international expert groups, published authors in reputable medical journals, and affiliates of sites with advanced equipment and technology. Many APAC countries have also invested heavily in increasing clinical trial competitiveness with large, specialized centers boasting the latest equipment, technology, and infrastructure. Some hospitals in South Korea and Japan even have de-identified patient databases that can be used to help assess study design and feasibility and accelerate recruitment.[4]
- **Improvements in data quality.** In the past, sponsors may have been concerned about data quality in the APAC region. This perception is changing, with more stringent regulations and more rigorous oversight. Data from clinical trials in Asia have been accepted as part of U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) submissions.[4] In fact, the rate of EMA and FDA inspections is lower in the APAC region than in North America and the number of FDA designations for therapies originating in China has proliferated since January 2020.[5]
- **Rising incidence of cancer.** Globally, an estimated 19.3 million new cancer cases and nearly 10 million cancer deaths occurred in 2020. Half of these cancer diagnoses and 58.3 percent of these cancer deaths occurred in the APAC region.[6] China alone accounted for 24 percent of all new cancer diagnoses and 30 percent of cancer deaths worldwide.[7]
- **Prevalence of certain cancers.** Certain cancers such as gastric cancer and hepatocellular carcinomas are much more common in APAC countries than in Western countries. Four of the five highest prevalence countries for gastric cancer are in the APAC region, which would facilitate enrollment for studies targeting this therapeutic area.[8]
- **Faster enrollment.** Compared to studies in the U.S., studies in APAC countries often enroll more quickly.[9] As per capita government spending on healthcare is lower in the APAC region than in the U.S. or Western Europe, clinical trials offer an opportunity for patients in these countries to access treatment. According to GlobalData, from 2018 to 2019, the median number of patients recruited in oncology studies involving APAC sites was more than 40 percent higher than the global median.[10] Recruitment is also competitive, with state-of-the-art medical institutions serving as clinical sites.[7]
- **Shift from generics to novel drug development.** Maturing innovation ecosystems and evolving regulatory frameworks have spurred a shift from generics-focused development to new biopharmaceutical development. In China, the market value of publicly listed biopharmaceutical companies increased from $3 billion in 2016 to more than $380 billion in 2021.[5] As drug discovery and development increases in the APAC region, the number of APAC companies interested in conducting clinical trials in the U.S. and entering the global marketplace is increasing as well.

COVID-19 spurred a revolution in digital technologies, contributing to an increase in outsourcing of pharmaceutical activities to CROs. Pandemic-related site closures and travel restrictions also gave rise to greater adoption of decentralized trial approaches.

- **Local innovation**. APAC countries such as Korea and China are actively developing novel oncology molecules, with strong government support. In recent years, China has tripled its share of the global innovation pipeline, from 4.1 percent in 2015 to 13.9 percent in 2020.[11] This robust research and development activity is reflected in the increase of clinical trial applications submitted to the National Medical Products Administration (NMPA) by local biotech companies. Since 2016, local applications have increased at an average rate of 32 percent per year and, in 2020, local biotechs accounted for more than half of the new molecules under development in China.[5]

As the fastest growing global market for pharmaceutical sales, the APAC region also represents a significant commercialization opportunity as disposable incomes and health awareness increase.

Advantages of conducting oncology clinical trials in APAC

Historically, most of the clinical trials conducted in the APAC region were later-phase studies. More recently though, there has been an increase in the number of Phase 1 trials. For sponsors, focusing on the APAC region for clinical trials comes with numerous advantages:

- **Lower cost.** The cost per patient across all clinical trial phases and therapeutic areas is often lower in Asian countries.[1] It is estimated that studies conducted in the APAC region cost 30-40 percent less than in developed markets.[12] While the cost differential is not as pronounced in Australia, the Australian government's Research & Development Tax Incentive offers generous tax offsets of up to 45 percent for eligible companies.
- **Less competition.** Given the large patient population and the relatively lower volume of studies, there is lower trial density across the APAC region and, thus, less competition for eligible patients. This may be particularly important for rare cancers and biomarker-driven clinical trials.
- **Diverse ethnicities and geographies.** Regulatory agencies are placing increased emphasis on clinical trial diversity. In the APAC region, sponsors have access to cross-genealogical populations, enabling the collection of a broad spectrum of data. This includes rural residents and people from traditionally underrepresented groups.[7]
- **Bridging the gap in genomic data among Asian populations.** A 2009 analysis showed that 96 percent of participants in genome-wide association studies were of European descent, revealing a significant diversity gap.[13] In 2016, the Genome Asia 100K Project was launched, with the aim of addressing the underrepresentation of non-European populations in published studies by sequencing the genomes of 100,000 Asian individuals. Many APAC countries, including China, Japan, and South Korea, have established genomic screening projects or even large-scale platforms to identify oncogenic drivers and advance the development of new molecular targeted drugs and diagnostics.
- **Future-proofing with diversification and decentralized trials.** As the COVID-19 pandemic unveiled, planning for the unexpected is essential for ensuring study continuity. Consequently, diversification of clinical research sites may be an effective risk management strategy.

In addition, COVID-19 spurred a revolution in digital technologies, contributing to an increase in outsourcing of pharmaceutical activities to CROs. Pandemic-related site closures and travel restrictions also gave rise to greater adoption of decentralized trial approaches. Decentralized clinical trials (DCTs) bring clinical research studies to patients, using digital technologies and off-site visits to collect study data and reduce participation burden. DCTs offer a patient-centric approach to clinical trial management and empower participants to take an active role in not only improving their own health, but also contributing to the body of scientific knowledge. By engaging patients where they are, DCT approaches may help accelerate enrollment, increase compliance, improve retention, and even produce higher quality, real-time data.

Given the high rates of mobile phone use, internet availability, and technology adoption in many APAC countries, this region is poised to be at the forefront of DCTs. Already, many APAC countries are well-versed in digital health and health technologies such as electronic medical records, electronic data capture (EDC), and telehealth.

While DCTs hold great promise, sponsors may face challenges with implementation in APAC countries due to evolving regulations. While regulatory agencies are open to DCT approaches, they are seeking data and expertise to ensure that patient safety remains paramount.

The APAC region may be particularly attractive for immuno-oncology trials, as lack of reimbursement for immunotherapies may motivate patients to participate in clinical trials for access to innovative treatments.

An evolving regulatory and clinical trial landscape

When undertaking clinical trials in the APAC region, sponsors will need to incorporate regulatory heterogeneity into study planning and timelines. For example, in some countries, institutional review board approval, regulatory, import licensing, and contract negotiations can be undertaken simultaneously. In others, these activities may need to be carried out in sequence.

Although there are no harmonized regulatory standards, many APAC countries have implemented, or are working on, pathways that streamline the review and approval process. In our experience, there has been a seismic shift in the approach that regulatory bodies in the APAC region have been taking to drug development. The following is a sampling of the current regulatory and clinical trial climates in APAC countries.

Figure 1. Regulatory bodies in the APAC region

Country	Regulatory Body
Australia	Therapeutic Goods Administration
Bangladesh	Directorate General of Drug Administration
China	National Medical Products Administration Center of Drug Evaluation
Hong Kong	Department of Health – Drug Office
India	Central Drug Standards Control Organization Ministry of Health and Family Welfare
Japan	Pharmaceuticals and Medical Devices Agency Ministry of Health, Labor and Welfare
Malaysia	Ministry of Health
Philippines	Republic of the Philippines Department of Health Food and Drug Administration of the Philippines
Singapore	Health Sciences Authority
South Korea	Ministry of Food and Drug Safety
Thailand	Food and Drug Administration of Thailand
Taiwan	Taiwan Food and Drug Administration
Vietnam	Ministry of Health

China

China, for example, was long considered a challenging market to enter due to registration application backlogs, long review timeframes, and significant gaps in quality between locally and internationally manufactured products.[14] To address these challenges, the NMPA amended and reformed their regulatory framework in 2015 to promote increased transparency and encourage development of drugs on par with global standards. Key elements of this reform included increasing the number of drug reviewers and introducing a Conditional Approval Policy for drugs and medical devices targeted at serious life-threatening conditions, significant unmet medical needs, or rare diseases. These changes enabled the NMPA to clear a backlog of 20,000 applications in two years.[9] The NMPA also introduced priority review for certain innovative drugs, newly-launched generic drugs, and global clinical trial applications submitted in China in parallel with the U.S. or EU.[2]

According to NMPA data, the proportion of drugs under priority review was 77 percent in 2019, up from 14 percent in 2016. More recently, the NMPA adopted a policy to accept clinical trial data from studies conducted outside of China, if those data meet relevant requirements.[15] In July 2020, Chinese Drug Registration Regulations also introduced a new pathway for breakthrough therapies and over 70 drugs received this designation as of August 2021.[9]

India

In 2019, India's Ministry of Health and Family Welfare introduced New Drugs and Clinical Trials Rules (NDCT). These regulations provide for time-bound review of applications, greater predictability and transparency of the regulatory pathway, stricter rules on clinical trial conduct, and increased clarity on complex topics such as orphan drug designation, post-trial access, and pre- and post-submission meetings.[16] Changes enacted by the NDCT have made India a top destination for clinical trials, with over 100 studies approved in 2021.[17] Though these new rules have increased the cost of conducting studies in India, experts estimate that clinical trial costs are still 60 percent less than in the U.S.[16]

Japan

In April 2018, Japan established the Clinical Trials Act to ensure the reliability and scientific soundness of clinical research, improve study conduct, and revise regulations to support these changes. The Japanese government also published Ethical Guidelines for Medical and Biological Research Involving Human Subjects in March 2021.[18]

South Korea

Clinical trials in South Korea have demonstrated significant growth over the past decades, in part due to regulatory reforms such as the adoption of ICH-GCP in 2000 and the introduction of clinical trial authorization in 2002.[19] The government has also invested heavily in clinical trial capacity building through programs developed by the Korea National Enterprise for Clinical Trials (KoNECT), a non-profit organization affiliated with the Korean Ministry of Health and Welfare. According to an analysis by KoNECT, among all therapeutic areas, oncology represents the most robust clinical trial activity and the highest proportion of clinical trial approval by the Ministry of Food and Drug Safety.[17]

Key considerations for study success in APAC countries

For sponsors who are contemplating the APAC region for their clinical trials, below are a few key considerations.

Cost of labor

Labor rates are generally lower but may vary widely across the APAC region. Australia and Japan typically have the highest labor rates, while Malaysia and the Philippines have the lowest.[1]

Understanding of the local market

Differences in language, culture, and belief systems may influence perceptions of clinical trials, nuances of study conduct, and even patient-reported outcomes. Clinical trial success will depend on localization and adaptation of study protocols based on standard of care and other norms. Translation of trial documentation, including patient-facing materials, may also be required.

Understanding of the local market also extends to insight on the differences in market access among the countries in this region. Differences in demographics and market maturities, and variations in cost and reimbursement structures contribute to a complex healthcare landscape and market-access environment.[20]

Reimbursement for standard of care

In the U.S., EU, and Australia, standard of care in clinical trials is generally reimbursed by the payer, whether it is a commercial insurer or the government. In the APAC region, however, the sponsor is typically expected to cover standard of care due to lack of systematic reimbursement, even in countries with nationalized health systems. Requirements will vary from country to country, for example:[21]

- In China, India, Japan, Malaysia, Singapore, and Taiwan sponsors are required to pay for standard of care, with very few exceptions. This is also true in South Korea, although the government is contemplating national insurance coverage to improve the competitiveness of the country's clinical trial capability.
- In the Philippines, access to national insurance for standard of care is available, but coverage is low, and sponsors will need to cover out-of-pocket costs.
- In Hong Kong and Thailand, payment for standard of care is usually a negotiation between the sponsor and the site.

Transportation and logistics

Transportation issues exist in many APAC countries, whether it is scarcity in the emerging markets or traffic congestion in metropolitan megacities.[4] These issues may impact not only transport of study materials and biospecimens, but also travel for study participants. If transport is time-sensitive or requires cold-chain logistics, sponsors will need to plan carefully for all scenarios to mitigate risk.

Local expertise

Having a partner on the ground with local knowledge and relationships with investigators, sites, and key opinion leaders is critical for operational success in APAC countries. Given the diversity of the APAC region, sponsors may need to engage multiple CROs to address the unique challenges of each country.

With our global footprint, Premier Research has a meaningful presence and strong capabilities in the APAC region, including extensive clinical trial experience, strong local relationships, and a deep understanding of regulatory requirements and cultural nuances. With our focus on biotech and specialty pharma, Premier is also well-equipped to help sponsors in the APAC region globalize their trials to the U.S. and other Western countries.

Contact us to learn more how we can help you globalize trials into – or out of – the APAC region.

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Rupa Doshi, Ph.D. | Vice President, Oncology Strategy

With more than 23 years in the industry, Dr. Rupa Doshi is an experienced professional with demonstrated leadership skills in clinical operations, global project/program management, customer management, and strategy development. Her experience spans the clinical development spectrum from pre-IND to NDA and she has also led global teams in the execution of full service complex clinical trials across all phases.

Dr. Doshi brings drug discovery and clinical development experience with biologics, small molecules as well as cell and gene therapy products over a range of indications. Her doctoral research focus was on breast cancer, her post-doctoral research was in site directed mutagenesis and she holds patents in the area of angiogenesis. Dr. Doshi has also supported three products resulting in agency approval.

Ashish Jain | Senior Vice President, Asia-Pacific

Ashish Jain has more than two decades of clinical research experience in India, Singapore, and the United States. Mr. Jain is responsible for Premier Research's business in the Asia-Pacific region and ensuring the company's continuous expansion, smooth project delivery, and customer satisfaction. He is also responsible for commercial opportunities in the Asian market and established a Premier Research corporate support services center in Asia.

Mr. Jain has vast experience in creating and implementing business strategies, effectively managing human resources, developing effective customer relationships, and managing financial plans. He has set up new clinical research units and built businesses across the Asia-Pacific, acquired companies, and integrated businesses across continents.

About Premier Research

Premier Research, a clinical research company, is dedicated to helping biotech, specialty pharma, and device innovators transform life-changing ideas and breakthrough science into new medical treatments. As a global company, Premier specializes in the use of innovative technologies for smart study design and trial management to deliver clean, conclusive data to sponsors. Whether it's developing product lifecycle strategies, reducing clinical development cycle times, securing access to patients, navigating global regulations, maximizing the impact of limited rare disease data, or providing expertise in specific therapeutic areas, Premier is committed to helping its customers answer the unmet needs of patients across a broad range of medical conditions.

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