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Cancer Therapeutics Gaining Ground in APAC

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Cancer, the leading cause of death in most parts of the world, is a veritable Achilles heel for the pharma industry. Not surprising that pharma companies continue to dedicate a significant part of their R&D budget for Oncology. Cancer medicine spending rose to $185 billion globally in 2021 and is expected to reach more than $300 billion by 2026, as per IQVIA.

An estimated 8.7 million Asians were afflicted with cancer in 2020. That's nearly half of all new global cancer cases. It’s no wonder then that the Asia-Pacific region has seen a 138 per cent increase in the number of oncology trials taking place over the past decade, the largest increase for any region worldwide, according to GlobalData.

"Cancer research in Asia Pacific is contributing significantly to the global knowledge base. Based on the data from ClinicalTrials.gov, the largest public clinical research database in the world, more than a quarter of the global cancer research is taking place in APAC. In addition, there are specific cancer types that are more prevalent in Asia. For instance, the frequency of epidermal growth factor receptor (EGFR) mutations was 50 per cent or higher for patients of East Asian ethnicities. While nasopharyngeal cancer (NPC) is rare in other parts of the world, it is quite commonly found in the southern region of China and many parts of Southeast Asia,” said **Choon-Peng Ng, Co-Founder and Chief Executive Officer, ImmunoScape, Singapore**. ImmunoScape, is developing T Cell Receptor-based (TCR) cell therapies across multiple HLA types, including A24 and A11 HLA types that are more prevalent in Asia, against solid tumours.

Immuno-oncology therapeutics

Immuno-oncology therapeutics have become the cornerstone of cancer treatment. They are classified into six broad drug categories, including Checkpoint Modulators, Cell therapies, Cancer vaccines, Cytokines, Bispecific antibodies and Oncolytic viruses. Currently, the Immuno-Checkpoint Modulators (ICMs) are the leading drug category and have been a mainstay of treatment for many different tumour types.

Asia Pacific has shown significant increase in Immuno-oncology (IO) trials between 2017 and 2021 and contributes to about 35 per cent of clinical development in IO globally. APAC has been the fastest growing region globally in IO trials. Phase II trials were the majority followed by phase I indicating a robust early and mid-stage IO drug development pipeline in the APAC

region, according to a report from Novotech. A plethora of companies, including Akeso Therapeutics, Junshi Biosciences, LG Chem and Noxopharm and others in the region are developing immune checkpoint inhibitors to improve the cancer treatment landscape.

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Akeso Biopharma's Ivonescimab is a first-in-class and the first to enter phase III clinical trial PD-1/VEGF bi-specific antibody. Currently, the firm is conducting a phase III clinical trial of AK112 monotherapy versus Pembrolizumab monotherapy as the first-line treatment for NSCLC patients with positive PD-L1 expression. In addition, a phase III clinical trial of AK112 plus chemotherapy versus chemotherapy in EGFR mutated advanced non-squamous NSCLC that failed in prior EGFR-TKI therapy is ongoing. The Chinese regulator granted Breakthrough Therapy Designation (BTD) for Ivonescimab, in October 2022.

Tifcemalimab is the world's first-in-human recombinant humanised anti-BTLA (B- and T-lymphocyte attenuator) monoclonal antibody independently developed by Junshi Biosciences. So far, tifcemalimab has entered phase Ib/II study, and several trials of tifcemalimab in combination with toripalimab in patients with different types of tumours are ongoing in China and the United States.

IBI110 is an IgG4? recombinant human anti-LAG-3 monoclonal antibody independently developed by Innovent Biologics, China. The firm presented positive phase 1b results in December 2022.

Korea's LGChem is developing CUE-101/LR19127 in collaboration with US-based Cue Biopharma for the treatment of HPV+ recurrent or metastatic head and neck cancer. This drug is currently in phase II development, and LGChem owns the Asia

rights to this checkpoint inhibitor drug.

Noxopharm's Veyonda is a first-in-class, dual-acting oncotoxic and immuno-oncology molecule known as idronoxil. Veyonda is currently being investigated in a phase 1 CEP-2 trial USA in combination with the chemotherapy drug doxorubicin, for first-line treatment of soft tissue sarcoma.? Veyonda received Orphan Drug Designation (ODD) from the USFDA in March 2022.

CAR-T Therapies

Chimeric antigen receptor therapy (CAR-T) is developing at a significant pace and is all set to revolutionise oncology. With Chinese companies undertaking the highest number of CAR-T cell therapy trials, GlobalData anticipates the country is likely to dominate the treatment landscape in coming years. According to GlobalData, there are nearly 60 CAR-T therapies in the overall clinical pipeline in China which are being developed by domestic pharma companies. Of which, there are 25 CAR-T therapies in phase II pipeline. So far, eight CAR-T cell products have been approved worldwide, including six US FDA-approved and two NMPA (National Medical Products Administration) approved CAR-T cell products.

One of the trailblazers in this space in China is Legend Biotech. Its lead product candidate Cilta-Cel was the first Chinese CAR-T therapy to be approved by the US FDA in February 2022. Then the European Commission and Japan's Ministry of Health, Labour and Welfare granted conditional marketing authorisation of Cilta-Cel. In January 2023, NMPA formally accepted its NDA for Cilta-Cel. It is the first Chinese company to achieve the overseas commercialisation of self-developed CAR-T products.

Another leading company in China is CARsgen Therapeutics, which received NDA (New Drug Application) acceptance of their BCMA (B-cell maturation antigen CAR-T products, making them the first company in this sub-category.

Apart from these, Singapore-based UTC Therapeutics and Tessa Therapeutics are also developing CAR-T therapies. Australian firm Carina Biotech is also at the forefront of CAR-T therapy development in the region. On January 24, 2023, the firm received a green signal to conduct a first-in-human phase 1/2a clinical trial of CNA3103, its LGR5-targeted CAR-T therapy candidate, in patients with advanced colorectal cancer (CRC) in the US.

Antibody Drug Conjugate

Another promising cancer therapy is Antibody Drug Conjugate (ADC). One of the leading ADC companies in Asia is China's RemeGen. Its lead product Disitamab Vedotin?RC48), is the first Chinese ADC drug created and developed by to receive breakthrough designations in both the United States and China, the treatment of gastric cancer had been granted approval by NMPA in 2021 and also been included in the National Reimbursement Drug List (NRDL), the indication of urothelial carcinoma had been granted approval by NMPA in the same year. The drug is currently awaiting US FDA approval. The firm's other ADCs are in various stages of development. Another Chinese firm, Kelun Pharmaceutical, has three ADCs in pipeline, out of which two are currently in phase 2 trials and the other one is in phase 1 trial.

Singapore is also catching up in this space. The country's drug discovery efforts reached a new milestone as EBC-129, the first made-in- Singapore antibody-drug conjugate, was cleared by the US FDA to progress into first-in-human studies, in January 2023. Also, Singapore-based Hummingbird Bioscience has two ADCs in pipeline both in phase 1 studies.

Over the last few years, antibody-drug conjugates have continued to deliver a steady flow of positive news and the market is set to reflect that. The APAC ADC market, which was valued at $1.96 billion in 2022, is set to swell to $6.86 billion by 2027, according to Market Data Forecast.

Vaccines

Cancer vaccines can be categorised as either therapeutic or preventative. The stupendous success of COVID-19 vaccines has spurred the development of mRNA vaccines for cancer. On January 20, 2023, Korea's Genexine, received Fast Track

Designation (FTD) from the Korean Ministry of Food and Drug Safety (MFDS) for GX-188E (tirvalimogene teraplasmid), its first-in-class proprietary therapeutic DNA vaccine for advanced cervical cancer. China's Stemirna is also developing mRNA-based personalised cancer vaccines. On January 24, 2023, the Serum Institute of India launched the first indigenously developed human papillomavirus vaccine (HPV)-- CERVAVAC, against cervical cancer in women.

Chinese firm YS biopharma, currently has two cancer vaccines in development, YS-ON-001, which received US FDA orphan drug designation and category I in China is expected to start phase 1 trial in 2023. The other candidate is still in preclinical evaluation.

Synthetic lethality

Synthetic lethality is a promising new area of cancer therapy. A couple of firms in Asia are exploiting this approach to develop new anti-cancer drugs. Leading among them is China's Insilico Medicine which has built a strong portfolio of synthetic lethality assets. The company announced its first synthetic lethality preclinical candidate, a potent and selective MAT2A inhibitor. Insilico is progressing the candidate in IND-enabling studies and anticipates IND filing in early 2023.

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China-based Anticancer Biosciences is another leading firm in this space. China's IMPACT Therapeutic, the leading clinical programme, PARP inhibitor (senaparib/ IMP4297), is in phase II/III studies for ovarian cancer, prostate cancer, small cell lung cancer and other indications worldwide, including China. Senaparib's preliminary clinical data demonstrated superior tolerability and wider therapeutic window compared with other PARPi.

Another innovative firm in this space is Korea's Avelos Therapeutics. It is currently developing a synthetic lethality platform called SMILOG (Small Molecules Inducing Lethality in OncoGenic cells) to find new and more reliable synthetic lethal targets. In August 2022, the firm raised $8 million in Series A funding round. Though still in its infancy, Avelos Therapeutics has established meaningful research partnerships, including a collaboration for a first-of-its-kind drug programme with the Research Institute of England. The company plans to select preclinical candidates in the first half of 2023.

Oncolytic viruses

In November 2021, Japan approved the world's first oncolytic virus therapy for brain cancer. Daiichi Sankyo's, DELYTACT (teserpaturev/G47?), an oncolytic virus developed by the company in collaboration with Professor Tomoki Todo of the Institute of Medical Science, The University of Tokyo.

Australian firm Imugene is also developing oncolytic virotherapy. In January 2023, the firm received green signal to commence a phase I clinical trial of its oncolytic virotherapy candidate, VAXINIA in Australia.

There has been a flurry of activities and partnership in this space in Asia Pacific. In March 2020, Kissei Pharmaceutical (Japan) signed a licensing agreement with CG Oncology (US) to gain development and commercialisation rights to the US company's oncolytic viral therapy candidate CG0070 in 20 markets in Asia.

In August 2020, Chinese firms ImmVira and Shanghai Pharmaceuticals signed a clinical collaboration and exclusive licence agreement for ImmVira's MVR-T3011 intratumoral oncolytic virus programme.

"Asia offers huge opportunities in research, development and marketing of cancer drugs. There are some substantial hurdles for regulatory authorities but with this aside, it's a desirable region for development of cancer therapeutics," said **Leslie Chong, CEO, Imugene, Australia.**

Light activated drugs

Photoimmunotherapy is also being explored as a treatment for cancer. Japan's Rakuten Medical, is a pioneer in this space. The company's first drug developed on its Alluminox platform, ASP-1929, has received approval from the Japanese Ministry of Health, Labour, and Welfare, and is currently the subject of a global phase 3 clinical trial for recurrent head and neck cancer. In September 2022, the firm opened its India office.

In April 2022, Kansai Medical University established a new centre for research on photoimmunotherapy. The research centre in the western Japan city of Hirakata, Osaka Prefecture, is headed by Prof. Hisataka Kobayashi, who developed the treatment method.

Drugs launched in 2022

The US FDA approved 12 new therapeutics in 2022. It was the year of landmark approvals, the regulator approved the first T cell receptor (TCR) therapy, Immunocore's KIMMTRAK; the first radioligand therapy, Novartis' Locametz.

The year also saw the first approval of a LAG-3 therapy, BMS' Opdualag. Janssen marked first approval worldwide for Tecvayli, the first T-cell-engaging bispecific antibody for multiple myeloma. Ferring's Adstiladrin is the first gene therapy approved to treat bladder cancer.

Drugs in the pipeline

In June 2022, Gamida Cell completed its submission to the US FDA for omidubicel's biologics licence application, with a final decision expected on May 1, 2023. Omidubicel is the first stem cell transplant donor source to receive breakthrough therapy designation from the FDA and has also received ODD in the US and EU. If approved, omidubicel will be the first and only advanced cell therapy for patients with blood cancer in need of an allogeneic stem cell transplant.

In November 2022, Vertex and CRISPR therapeutics submitted regulatory filings for exa-cel (CTX001) in transfusion-dependent beta-thalassemia (TDT) and sickle cell disease. If successful, it will become the first CRISPR/Cas 9 based product ever approved, an important boost for gene editing technology. xa-cel has been granted multiple important regulatory

designations, including Regenerative Medicine Advanced Therapy (RMAT), Fast Track, Orphan Drug, and Rare Pediatric Disease Designations from the FDA for both SCD and TDT. Exa-cel has also been granted Orphan Drug Designation (ODD) from the European Commission, as well as Priority Medicines (PRIME) designation from the EMA, for both SCD and TDT.

AstraZeneca's breast cancer drug Capivasertib, a potential first-in-class AKT inhibitor, if approved, will become a new option for patients in this setting regardless of biomarker status. Another breast cancer drug awaiting approval is Gilead Trodelvy, an ADC.

On January 5, 2023, the US FDA granted priority review to Genentech's bispecific antibody Glofitamab for people with relapsed or refractory large B-Cell lymphoma. If approved, glofitamab would be the first fixed-duration CD20xCD3 T-cell engaging bispecific antibody approved to treat the most aggressive type of non-Hodgkin's lymphoma.

Crucial collaborations

There are 29 partnerships at present (from January 2022- 2023) between various pharma firms, research institutes and governments in Asia Pacific in a race to develop a cure for the deadly disease. China leads the way followed by Japan and South Korea.

Collaborations between pharmaceutical companies have varying focuses ranging from drug discovery and development, clinical trials, licensing and study combination therapies. Majority of the partnerships in the region is to develop immuno-oncology therapeutics. Almost all the big pharma firms have tied up with smaller firms in the region.

“The Asian region is very active in cancer drug therapy. China has the greatest number of immune therapies under trial including many CAR-T clinical trials and very active research in immune therapies including cell therapies. Having patents awarded in the Asia region is sound business and could lead to partnering and rights sales for developments for cancer therapies,” said **Professor Alan Trounson, CEO, Cartherics, Australia**. Cartherics is developing allogeneic and autologous CAR-T cell therapies. On January 9, 2023, Cartherics granted first patent in China for multiple development candidates

Asia Pacific is at the forefront of modern oncology drug development and the market is on the verge of a paradigm shift, with gene and cell therapy, targeted therapies and vaccines gaining much more ground. In the future, we may have an indigenously developed cure for this dreaded disease.

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