While the powerhouse pharmaceutical companies of old had extensive R&D departments embedded within their structures, the emergence of agile start-ups and a drive for efficiencies in the delivery of new therapeutic options has made this model less sustainable. Cash-strapped healthcare systems demand value and, to be fair, the pharmaceutical industry has responded with mixed results. This has forced the industry to evolve and adapt.

Strategic partnerships now play an increasing role in how medicines are developed and delivered to patients. Smaller biotechs and research organisations have been given the opportunity to hit the big time by capitalising on the clinical and commercial expertise of medium to large pharmaceutical company partners who, in turn, see an opportunity to reduce R&D costs by taking on candidates that are further along the pipeline. The life science R&D ecosystem that has evolved over the past decade is now driven primarily by partnerships.

The evolution of R&D

Research and development is, by definition, an extensive and expensive process with a high attrition rate for potential new candidates. New treatments can take upwards of 12 years to get to the point of marketing authorisation, with many investigational candidates not even getting past the preclinical phase. In the long-term the sustainability of a company rests on its ability to match R&D investment with revenues and this can be increasingly difficult given the huge range of medicines that are now available, including generic options and biosimilars. The days of the blockbuster drug are well and truly behind us, forcing a change in approach throughout the industry.

In 2010, Pfizer launched its Centers for Therapeutic Innovation (CTI), a model for academic industry collaboration designed to bridge the gap between early scientific discovery and its translation into new medicine. In essence, the centres brought together the research expertise of academics with the development expertise and resources of Pfizer scientists to validate a drug candidate so that it could be moved into further clinical testing. Around the same time, GlaxoSmithKline (GSK) adopted a more entrepreneurial approach to R&D, dividing its scientists into small Discovery Performance Units (DPUs) to encourage innovation. Each DPU was tasked with making a case for its share of the overall R&D budget, encouraging a change in mindset and a greater focus on return on investment.
The shift in Glaxo’s R&D structure was also evidenced by its creation of Centres of Excellence for Drug Discovery (CEDDs), each focused on a different research track. The company subsequently went on to establish a Centre of Excellence for External Drug Development (CEEDD), sharing some of its assets for development by others when more potential targets were generated than GSK had the internal resource to develop.

Where big pharma led, others followed and, alongside academic collaborations, a proliferation in the number of biotechs in the last decade has seen an increase in partnerships across the board and an array of licensing arrangements for new assets.

As a network of independent associated companies operating across 120 countries worldwide, Mundipharma was founded on a partnership working model. Entrepreneurial at its heart, Mundipharma has always sought out opportunities for long-term relationships with independent companies to foster innovation, meet the challenges of increasingly stretched healthcare systems and increase patient access to effective therapies. In short, we exist to meet our stated purpose: To Move Medicine Forward.

Sometimes this involves focusing on innovation by acquiring compounds with interesting new mechanisms of action and fast-tracking them to the point of investigational new drug (IND) status. This is the case with one of our oncology assets which is now entering Phase I research for the treatment of relapsed/refractory haematological malignancies and Phase II for the treatment of advanced solid tumours. At other times we might acquire something further along the clinical development pathway and use our specialist R&D knowledge in a disease area to identify the right indication or specific patient population.

Mundipharma partners with organisations that have already achieved marketing authorisation for their medicines in some markets but are looking to expand their reach with the support of our in-depth local knowledge and relationships. We have found the key is to be strategic in our choices, looking for the opportunities that others may miss.

Partnering to treat and prevent invasive fungal infections – a case study

A good example of the Mundipharma partnership approach in action is in the case of rezafungin, a novel molecule in the echinocandin class of antifungals, developed by Cidara Therapeutics – a clinical-stage biotechnology company focused on the discovery, development and commercialisation of novel anti-infectives.

Rezafungin is a novel, once-weekly echinocandin antifungal being developed for the first-line treatment of candidemia and invasive candidiasis as well as for the prophylaxis of invasive fungal infections in patients undergoing allogeneic blood and marrow transplantation.

Invasive fungal infections (IFIs) represent a serious threat to millions of patients worldwide,
Drug Development

resulting in more than 1.5 million deaths annually and mortality rates ranging from 15% to 65%. These infections continue to be a global health issue, especially for critically ill patients in hospitals and patients with compromised immune systems, including cancer and transplant patients. Approximately 90% of all reported fungal-related deaths are associated with Candida, Cryptococcus, Aspergillus and Pneumocystis.

Rezafungin is a novel, once-weekly echinocandin antifungal being developed for the first-line treatment of candidemia and invasive candidiasis as well as for the prophylaxis of invasive fungal infections in patients undergoing allogeneic blood and marrow transplantation, for which there have been limited advances in the last 13 years. It has a characteristic pharmacokinetic profile with a prolonged half-life and front-loaded plasma exposure which, in contrast to all other echinocandin antifungals, we believe allows rezafungin to be developed for once-weekly intravenous therapy for inpatient and outpatient use.

The US Food and Drug Administration (FDA) has designated rezafungin as a Qualified Infectious Disease Product (QIDP) with Fast Track status related to its use in the treatment of candidemia and invasive candidiasis and for prophylactic use, and has granted orphan drug designation for the treatment of candidemia and invasive candidiasis.

Tuznue® is a trastuzumab biosimilar treatment to Roche’s Herceptin® which is used to treat patients with HER2-overexpressing breast cancer, HER2-overexpressing metastatic gastric cancer or gastroesophageal junction adenocarcinoma.
Given the clear unmet patient need and the potential for rezafungin, Mundipharma entered into a strategic partnership in September 2019 to develop and commercialise intravenous rezafungin for the treatment and prevention of invasive fungal infections in all markets outside of the US and Japan. Our intention is to use our structured approach to development, global reach and knowledge of haematology/oncology to fully leverage the clinical and commercial potential of rezafungin, which has already shown promise in the STRIVE Phase II trial.

The Mundipharma research team will be working closely with Cidara on the ongoing global Phase III trials for the treatment and prevention of fungal infections – supporting these both financially and with our knowledge and experience.

As with all the best pharmaceutical partnerships, the potential to improve the lives of patients is clear and both companies are committed to making a difference in this area of major unmet medical need.

**Improving access to medicines**

Alongside the benefits to drug development offered by working in partnerships, the Mundipharma model also affords the potential to improve patient access to existing medications through expanded territorial coverage.

A successful example of this has been our partnership with Janssen Pharmaceutica NV on the Type 2 diabetes treatment Invokana® (canagliflozin), an SGLT2 inhibitor. Diabetes is a global epidemic with significant morbidity and mortality. Thanks to our partnership with Janssen we have been able to help increase patient access to this innovative class of Type 2 diabetes medication by marketing it in several European countries. Alongside the education and engagement of healthcare professionals, we have been able to make canagliflozin available to approximately 200,000 European patients.

Biosimilars have also been a key focus for us in recent years, and we excelled as a provider of high-quality biosimilars in the fields of haematology, oncology, rheumatology and gastroenterology.

Truxima® is a rituximab biosimilar treatment to Roche’s MabThera® which is used to treat patients for follicular lymphoma and diffuse large B cell non-Hodgkin’s lymphoma, chronic lymphocytic leukaemia, severe rheumatoid arthritis, granulomatosis with polyangiitis, microscopic polyangiitis and moderate to severe pemphigus vulgaris.
Drug Development

through consistently excellent launches of Remsima® (infliximab), Truxima® (rituximab), and Herzuma® (trastuzumab). The acquisition of Cinfa Biotech’s Pelmeg® (Pegfilgrastim) in 2018 is yet another enhancement to Mundipharma’s portfolio of biosimilars and, to date, we have contributed to an estimated one billion Euros saving to the European healthcare systems.

Our strategy has been to identify opportunities to expand into European markets where there is unmet patient need and a demand for cost-effective treatment options. The Central and Eastern Europe (CEE) region has been particularly important for us recently and in June 2019 we agreed an exclusive outsourcing distribution arrangement with Egis Pharmaceuticals for it to launch our pegfilgrastim biosimilar treatment, Pelmeg®, in Hungary, Romania, Latvia and Lithuania – countries where we do not have a commercial presence.

Pelmeg (pegfilgrastim), approved in the European Union in November 2018 as a biosimilar of Neulasta®, was developed to reduce the duration of neutropenia and the incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes). Neutropenia refers to an abnormally low number of neutrophils (a type of white blood cell) which can increase the risk of life-threatening infections and is a common side-effect of some chemotherapeutic regimes. Setting this long-term partnership in place means that more patients will now be able to access this medicine.

Another recent partnership in the biosimilars sphere is with Prestige Biopharma. In contrast to the previous example, our role in this partnership will be to distribute, market and sell the trastuzumab biosimilar Tuznue® in selected European countries following marketing authorisation, including France, Spain, Norway, Sweden, Denmark, Finland, Portugal, Switzerland and Austria. Tuznue® is a trastuzumab biosimilar treatment to Roche’s Herceptin® which is used to treat patients with HER2-overexpressing breast cancer, HER2-overexpressing metastatic gastric cancer or gastroesophageal junction adenocarcinoma.

Moving medicine forward

Partnerships are nothing new in the field of healthcare. Early stage innovation, clinical research, market access, medical education, advocacy – these have always required a degree of collaboration, with organisations and individuals working together to achieve the optimum outcome for patients. However, recent years have seen a more structured approach to partnerships with successful pharmaceutical companies taking steps to evolve their approach to R&D, licensing and distribution to stay commercially viable.

In the case of Mundipharma, this has played to our strengths as a global network and we have been able to embrace the new healthcare landscape in which we find ourselves thanks to the flexibility of our structure and our drive to uncover new opportunities. We are proud supporters of the Babraham Research Campus accelerator programme, through a financial grant and coaching, helping to provide opportunities for start-up companies in the field of life science. We have also found that being able to offer value from both sides of the equation, with our R&D capabilities to support in development and our commercialisation know-how to expand market access, has made us an attractive partner for many. Even given that, we have had to make our own adjustments in our approach to drug development and there has been considerable restructuring along the way. We have also had to learn which partnerships are the ones worth pursuing, understanding that the right partnerships are those that fit with our stated purpose as an organisation.

Just as some treatments do not make it to market, not every partnership we have explored has come to fruition, however those that have continue to yield considerable benefits, not only commercially, but also in terms of moving medicine forward.

Dr Brian Sheehan is Senior Vice President, Innovation at Mundipharma. He joined Mundipharma in 2015 as Director of Projects and held a number of R&D roles in Cambridge and in Tokyo from Executive Director of Projects to Executive Director of Innovation and new product development. Brian brings 20 years of experience in the pharmaceutical industry at companies such as Schering Plough and MSD with a track record of new product development and approvals in oncology and infectious diseases. He has successfully led R&D organisations and teams in Europe and in Asia (Japan and Singapore) and is a big advocate of teamwork, his motto being ‘great things happen when we work collaboratively together!’ Brian started his career in the academic sector, including research positions at the Institute Pasteur in Paris and the Imperial College in London and, immediately prior to joining Mundipharma, spent five years on the leadership team of the Cancer Research UK Centre for Drug
Development as Head of Project & Portfolio Management. Brian holds a PhD in molecular biology from Trinity College, Dublin.

Marco Cerato is Senior Vice-President, Business Development and Strategic Partnerships at Mundipharma. Marco joined the Mundipharma network of independent associated companies in 2018 to further enhance the external partnerships and medicine pipeline. Prior to joining Mundipharma, Marco was Head of Business Development and Licensing at Helsinn and previously served as Head of Licensing for late-stage assets since January 2016. Marco has significant commercial, development and strategic leadership expertise from an 11-year career in the pharmaceutical industry, with a specific focus on cancer supportive care and oncology. In his tenure at Helsinn he oversaw more than 50 licensing deals covering more than 190 countries around the world across cancer supportive care and oncology. Marco holds a degree in Biotechnologies and a specialisation in industrial biotechnologies completed by an executive made-to-measure Masters course in Business Administration from the Bocconi School of Management.

Invokana® is a registered trademark of Janssen-Cilag International NV.
Remsim®️, Truxima®, and Herzuma®️ are registered trademarks of Celltrion Inc.
Pelmeg®️ is a registered trademark of Mundipharma Biologics S.L.
Tuznue®️ is a registered trademark of Prestige BioPharma Pte Ltd.
Herceptin®️ is a registered trademark of Roche Registration GmbH.
Neulasta®️ is a registered trademark of Amgen Europe BV.