

The importance of dealmaking in AstraZeneca's pursuit of transformational cancer outcomes

Rapidly responding to the needs of the evolving oncology landscape, AstraZeneca is focused on sourcing transformational programs and technologies, whilst nurturing mutually beneficial partnerships to deliver innovative treatment strategies to patients.

AstraZeneca has a single, ambitious goal in oncology: eliminating cancer as a cause of death. Its focus on developing transformative treatment regimens that increase the chance of cures has led the company to build one of the strongest portfolios and pipelines in the industry. Partnering is critical to the execution of the strategy.

Science and treatments are progressing faster in oncology now than at any other time in history. Given the pace of innovation, and the need to improve on current and potential near-term standards of care, AstraZeneca is laser focused on programs and technologies that have the potential to be transformational.

"If you're investing in something today, you've got to believe it's going to be substantially better than what will be available when the development program reads out in three to five years' time," said Craig Maxwell, VP, Oncology R&D Strategy, Business Development & Alliances at AstraZeneca. "You have to anticipate how the treatment landscape is changing and believe that it will still have transformational potential when it comes to market."

In pursuit of cures

AstraZeneca's pursuit of cures has led it to prioritize developing combinations of medicines that attack cancer from multiple angles. Spanning seven

scientific platforms, its portfolio encompasses a range of modalities and mechanisms that are designed to directly kill cancer cells or to activate the immune system against cancer (Fig. 1).

AstraZeneca views immuno-oncology (IO) and tumor-targeted therapies as complementary and fundamental to creating potentially curative regimens of the future. Rather than improving on just one aspect of a combination, the drug developer is committed to transforming whole regimens across six key tumor types: lung, breast, gastrointestinal, genitourinary, gynecological and hematological.

"Our focus on cure is a major driver that has shaped our portfolio," Maxwell said. "We need a breadth of drug modalities to kill the tumor using targeted therapies, and next-generation IO agents such as T cell engagers and cell therapies to activate

an immune response to ensure they are fully eradicated including micro-metastatic disease."

The drug developer has built its portfolio with this in mind, through ongoing investment in tumor-targeted cell-killing treatments such as antibody-drug conjugates (ADCs) and radio-conjugates that have the potential to replace chemotherapy and radiotherapy, and next-generation IO agents that overcome mechanisms used by the tumor to evade the immune system, or that activate the body's natural immune response against cancer.

The focus on developing novel combinations of internal and external assets is underpinned by the knowledge that it will be necessary to engage multiple targets to achieve transformational efficacy.

"AstraZeneca is focused on building the transformative oncology regimens of the future," said Polly Brown, VP, Head of Business Development, Oncology R&D. "We're one of the few companies that has a broad enough oncology portfolio and pipeline to attempt this, and we are looking for external partnerships that enable us to do that together. We're very serious about external innovation that's exploding across the world. It's everywhere. It's not just the US. It's China. It's across the world, and we are agnostic to the source of innovation."

Business development is vital to AstraZeneca's strategy because it helps the drug developer access

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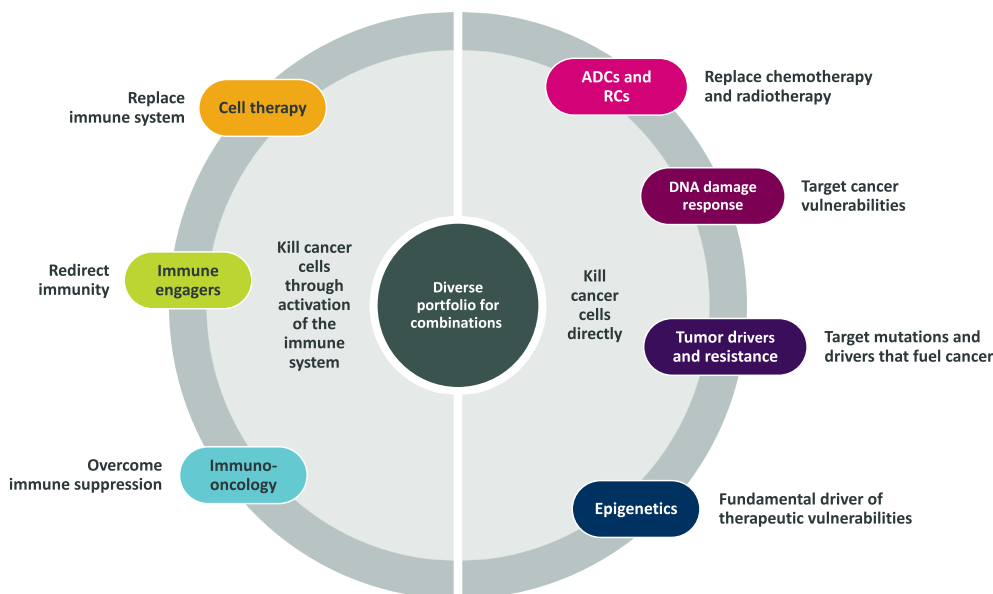


Fig. 1 | AstraZeneca's seven scientific platforms. These platforms enable them to attack cancer from multiple angles and create novel combination regimens. ADC, antibody-drug conjugate; RC, radioconjugate.

new components of combination therapies and thereby maximizes its chances of creating regimens that have breakthrough efficacy. Deals for pipeline programs are more effective when paired with other capabilities.

"We need a really strong translational medicine platform to drive biomarker development and patient identification," Brown said. "We have strategic alliances with other companies that enable us to be at the cutting edge of those. All of these things are complementary and business development is a fundamental building block."

Another core feature of AstraZeneca's strategy is its focus on identifying and treating patients earlier when there is the greatest chance of cure, and real-time disease monitoring to inform treatment decisions. With emphasis on bringing the right treatment to the right patient at the right time, the drug developer is pioneering screening and diagnostic tools like circulating tumor DNA (ctDNA) through strategic collaborations. Beyond this, AstraZeneca's drive to advance research and development and improve cancer care has led to a focus on harnessing transformational technologies such as data science, artificial intelligence (AI) and digital healthcare, which includes a strategic collaboration with AI-enabled precision-medicine leader, Tempus.

"If we want to make a real difference to patients it's not just through the drugs we develop, but also where those drugs are going to have the most impact," Brown said.

I think a fundamental change in cancer treatment will be cell therapy

Craig Maxwell, VP, Oncology R&D Strategy, Business Development & Alliances, AstraZeneca

A history of dealmaking success

AstraZeneca's approach to using business development to grow its portfolio is exemplified by two ADC deals with Daiichi Sankyo. The deals, which were collectively worth \$2.35 billion upfront, have positioned the companies to replace chemotherapy with more targeted, more effective alternatives.

Since the start of 2022, AstraZeneca has entered into a series of deals to access other candidates that could form part of future transformational cancer regimens. As an ongoing area of growth, the company has built on its leadership in ADCs, securing global rights to KYM Biosciences' claudin-18.2 program, while expanding into T cell engagers through the acquisition of TeneoTwo's cluster of differentiation 19 (CD19)-targeting molecule and licensing of a claudin-18.2 asset from Harbour BioMed.

The recent acquisition of Neogene Therapeutics, pioneers of T cell receptor therapies, illustrates how AstraZeneca has used business development to expand its cell-therapy capabilities beyond chimeric antigen receptor T cells (CAR-Ts) and move into new areas.

"I think a fundamental change in cancer treatment will be cell therapy," Maxwell said, "and we are continuing to build our capabilities through internal and external investment. The field is moving at an incredible pace and bringing in experts from Neogene has been

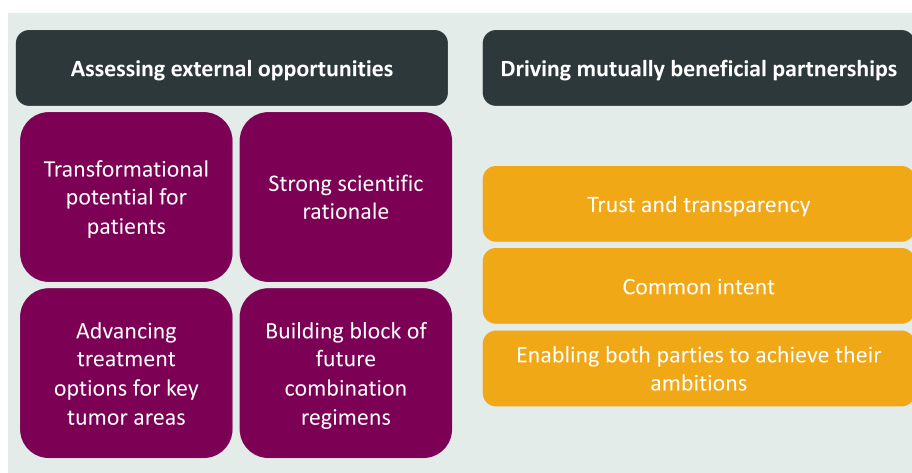


Fig. 2 | AstraZeneca's approach to partnering.

really important for building the T cell receptor-therapy strategy, so we can work towards our common goal of bringing cell therapies to patients with solid tumors."

Other deals include a collaboration with Scorpion Therapeutics focused on transcription factors, a class of proteins previously considered 'undruggable' using conventional drug discovery approaches, and collaborations with biotechs Accent Therapeutics and Proteros to accelerate AstraZeneca's efforts in epigenetics.

How AstraZeneca assesses opportunities

Internally, AstraZeneca has robust criteria for all its drugs and drug candidates, with a clear line of sight for their development early in a program. Its approach to dealmaking is no different: the drug developer focuses on the acquisition or in-licensing of therapies that have the potential to become a building block for future regimens to address medical unmet need across core tumor types.

The team is always looking for ways to stay ahead of the curve. As Maxwell explained, "the oncology team is super careful not to judge new innovation based on what the world looks like today. The candidates AstraZeneca invests in today will come to market years in the future—by then, barriers that look impenetrable today may no longer exist, and the standards of care will look very different."

"In a future where next-generation sequencing is becoming completely mainstream, new approaches to diagnostics, plus developments in AI and electronic patient-record keeping, may make it possible to do things that look impossible today. If we think an asset has a possibility of being part of a transformational regimen, we may take a risk and invest in it," Maxwell said.

AstraZeneca applies this thinking to all its decisions, looking beyond therapeutics to AI, diagnostics and other technologies that could transform healthcare to assess how the landscape may have changed by the time programs reach clinical readouts. As with all drug development, there is some risk because nobody can predict the future, but a bigger risk is failing to see that the future will be different.

Forming mutually beneficial partnerships

AstraZeneca's work with companies such as Daiichi Sankyo reflects its focus on creating mutually beneficial partnerships founded on trust and transparency. Brown explained how AstraZeneca tries to ensure its partnerships live up to that ideal.

"It's key that you establish a common intent between the two parties, for example transforming patient outcomes and advancing the science. It might be that AstraZeneca has an intent to address a gap in our portfolio and 'Company A' has an intent to become a next-generation company that develops their technology. We both understand those two things and we want to help each other do those two things," Brown said.

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Polly Brown, VP, Head of Business Development, Oncology R&D, AstraZeneca

"That requires both parties to be upfront about what they want," Brown said. "I am a strong believer in communicating quite straightforwardly. That, and being transparent, I think are the key for building trust. The best partnerships emerge from spending time face to face and having honest discussions about the data."

The time AstraZeneca commits to nurturing partnerships reflects the importance of external innovation to its ambitious oncology strategy (Fig. 2). By pairing the best external candidates in development with its broad internal pipeline and deep expertise in cancer and drug development, the company is positioning itself to deliver on its ultimate goal of eliminating cancer as a cause of death.

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CONTACT Polly Brown, VP Head of Business Development, Oncology R&D
AstraZeneca
Boston, MA, USA
Email: oncology-partnering@astrazeneca.com