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cynata therapeutics

CYNATA THERAPEUTIC'S PARALLEL APPROACHES TO MARKET

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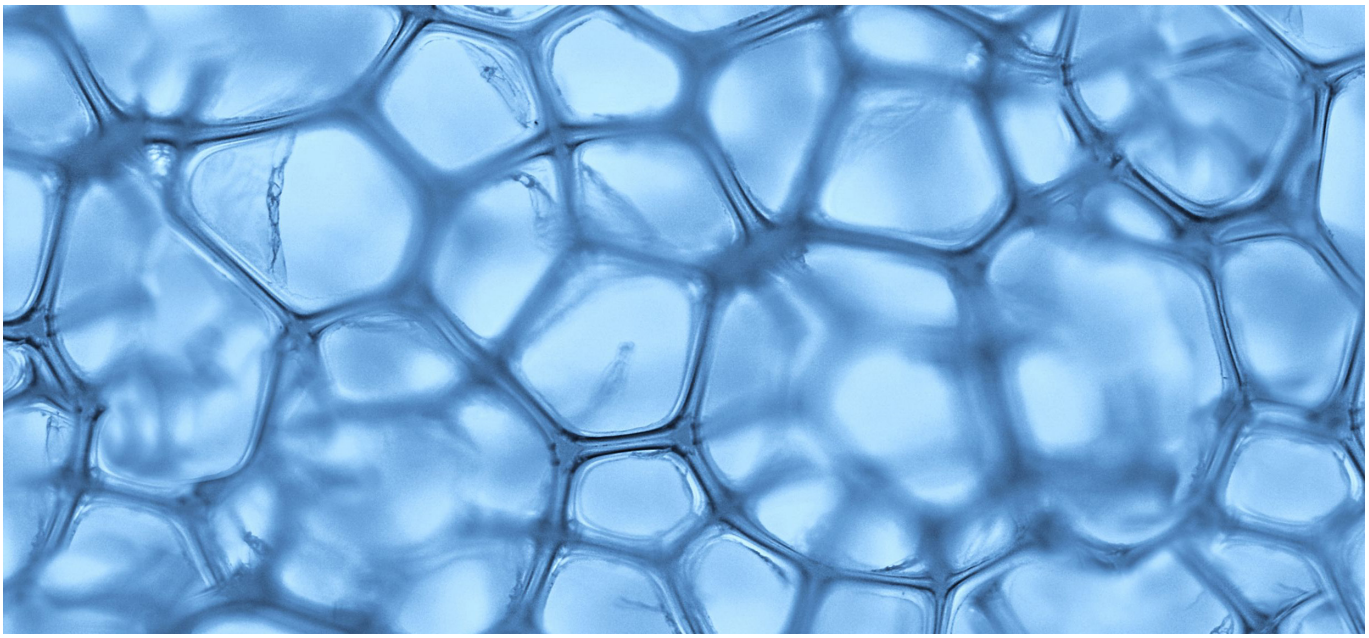


In 2014, Cynata Therapeutics commenced technology transfer and product development, and simultaneously commenced consultation with regulatory authorities regarding the approval pathways for its cellular therapy products.

Despite a lack of guidance because the field was emerging, Cynata Therapeutics Limited (Cynata) was able to secure regulatory approval for a world-first clinical trial, based on a sound scientific rationale. The clinical trial was completed and showed remarkable outcomes for the patients enrolled in the clinical trial. Throughout this period, Cynata's product development generated new intellectual property (IP), which is covered by a portfolio of patent applications wholly-owned by Cynata, in addition to the IP in-licensed in 2014. In short, Cynata has demonstrated significant efficiency in successfully co-developing its product, the IP covering it, and its regulatory pathway to market.

Background

Cynata is a publicly traded clinical-stage biotechnology company. Cynata is focussed on the development of its Cymerus™ platform, which is a scalable technology utilising induced pluripotent stem cells (iPSCs) to mass produce allogeneic (i.e. non-self) cell-based therapies.

iPSCs are mature cells that have been reprogrammed to behave like embryonic stem cells (ESCs), including the capacity to differentiate into any cell type and an effectively limitless replication capacity. This contrasts with stem cells isolated directly from adult tissues, which have a much more limited capacity for differentiation and replication. Further, because iPSCs are sourced from adult cells, they avoid the ethical controversy associated with ESCs. Therefore, iPSCs represent an ideal starting material for cellular production processes, for a wide range of applications, especially those requiring a large scale and consistent end product.

Cynata's lead product candidate is CYP-001, which consists of Cymerus allogeneic iPSC-derived mesenchymal stem cells (MSCs), administered by intravenous infusion. CYP-001 is indicated for treatment of graft versus host disease (GvHD), which is an often fatal complication of bone marrow transplantation.

Parallel approaches to market

The Cymerus development program commenced in early 2014 and comprised parallel strands in preparing for market.

In the first strand, Cynata commenced its technology transfer, with a suite of patents licensed from the University of Wisconsin – Madison, "the home of stem cells". Coupled with the technology transfer was development of the Cymerus platform, which in due course generated new IP wholly owned by Cynata.

Simultaneously, with respect to regulatory approval, Cynata designed a development plan based on scientific rationale, supported by relevant regulator guidelines/ precedents (to the extent that they existed), and engaged external consultants with appropriate expertise and experience. Having established this foundation, Cynata commenced extensive consultation with regulatory authorities:

- European Medicines Agency (EMA) – May 2014 / December 2014
- US Food & Drug Administration (FDA) – September 2015 / May 2017
- EU national authorities, including UK Medicines and Healthcare products Regulatory Agency (MHRA) January- February 2016
- Health Canada – January 2017
- Japanese Pharmaceuticals and Medical Devices Agency (PMDA) – August 2018

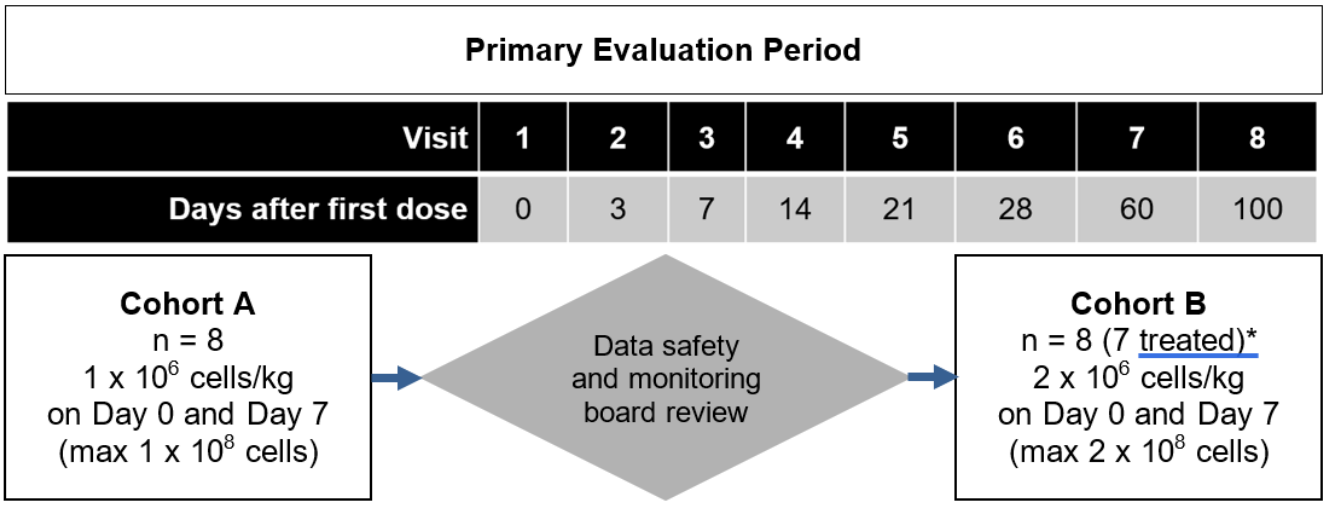
Regulatory approval for phase I clinical trial

As a reward for Cynata's foresight and organisation, MHRA granted approval in September 2016 for a clinical trial of Cymerus MSCs to treat GvHD. And in March 2018, Cymerus MSCs Received Orphan Drug Designation from the FDA.

The GvHD clinical trial was completed in August 2018. It represented the first regulatory clearance and first completed clinical trial worldwide for human use of an allogeneic iPSC-derived product. Moreover, the GvHD clinical trial was highly successful.

GvHD clinical trial

Protocol



* The clinical investigator determined that one patient was no longer a suitable candidate for treatment, due to a medical complication that occurred shortly after enrolment, but prior to treatment.

CyGvHD response by cohort

Endpoint	Cohort A (28 days)	Cohort B (28 days)	Pooled (28 days)	Cohort A (100 days)	Cohort B (100 days)	Pooled (100 days)
Safety	No safety issues / treatment related adverse events observed					
Complete Response	13%	57%	33%	50%	57%	53%
Overall Response	63%	86%	73%	88%	86%	87%
Overall Survival[1]	88%	≥86%	≥87%	88%	≥86%	≥87%

[1]. One patient in cohort A died of pneumonia (unrelated to treatment) and one patient in cohort B withdrew from the trial on Day 22 to commence palliative care.

As shown above, Cymerus MSCs elicited a remarkable outcome in this clinical trial, with a complete response achieved in 53% of patients and an overall response achieved in 87% of patients, without observation of any treatment-related serious adverse events.

Challenges and opportunities

In early 2014, when the Cymerus development program began, the lack of precedents and limited guidelines made obtaining regulatory approval for Cymerus MSCs challenging. The challenges included:

- no clinical grade allogeneic iPSC line (starting material) existed worldwide
- no iPSC-derived product had ever been administered to a human subject
- no clinical trial involving allogeneic iPSC-derived cells had received regulatory clearance anywhere in the world
- no other systemic clinical use of an iPSC-derived product had even been proposed (as far as was known)
- many regulatory guidelines have limited relevance to cell-based therapies
- conventional pharmacokinetic assessments cannot be performed
- standard toxicology studies may not be logical/ feasible
- laboratories that can establish specialised animal models required for cell-based therapies often cannot comply with GLP (and vice versa)
- may not be possible to administer human cells to animals, in particular large animals
- cell-based therapies may have potential risks that do not apply to small molecules/ antibodies

However, the absence of relevant precedents and guidelines represents an opportunity as well as a challenge, because one is not constrained by prejudice expressed as “that’s how it has always been done”, and new and unconventional approaches may be acceptable.

The impact on Cynata’s IP

Cynata was provided the opportunity to develop its patent portfolio in concert with its applications for regulatory approval and clinical trials. In fact, since 2014 when Cynata in-licensed its initial iPSC/ MSC technology, Cynata has developed its own technology and application of that technology such that Cynata now owns five International PCT applications, two of which have recently entered the national/ regional phase, and has another provisional application pending.

The consequence of these parallel approaches is that Cynata is now well placed in the market with both clinical trials underway and IP underpinning the technology used in those clinical trials, ultimately resulting in commercial interest from third parties.

If you have a question regarding the IP opportunities in the Life Sciences sector please contact our expert Malcolm Lyons.

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