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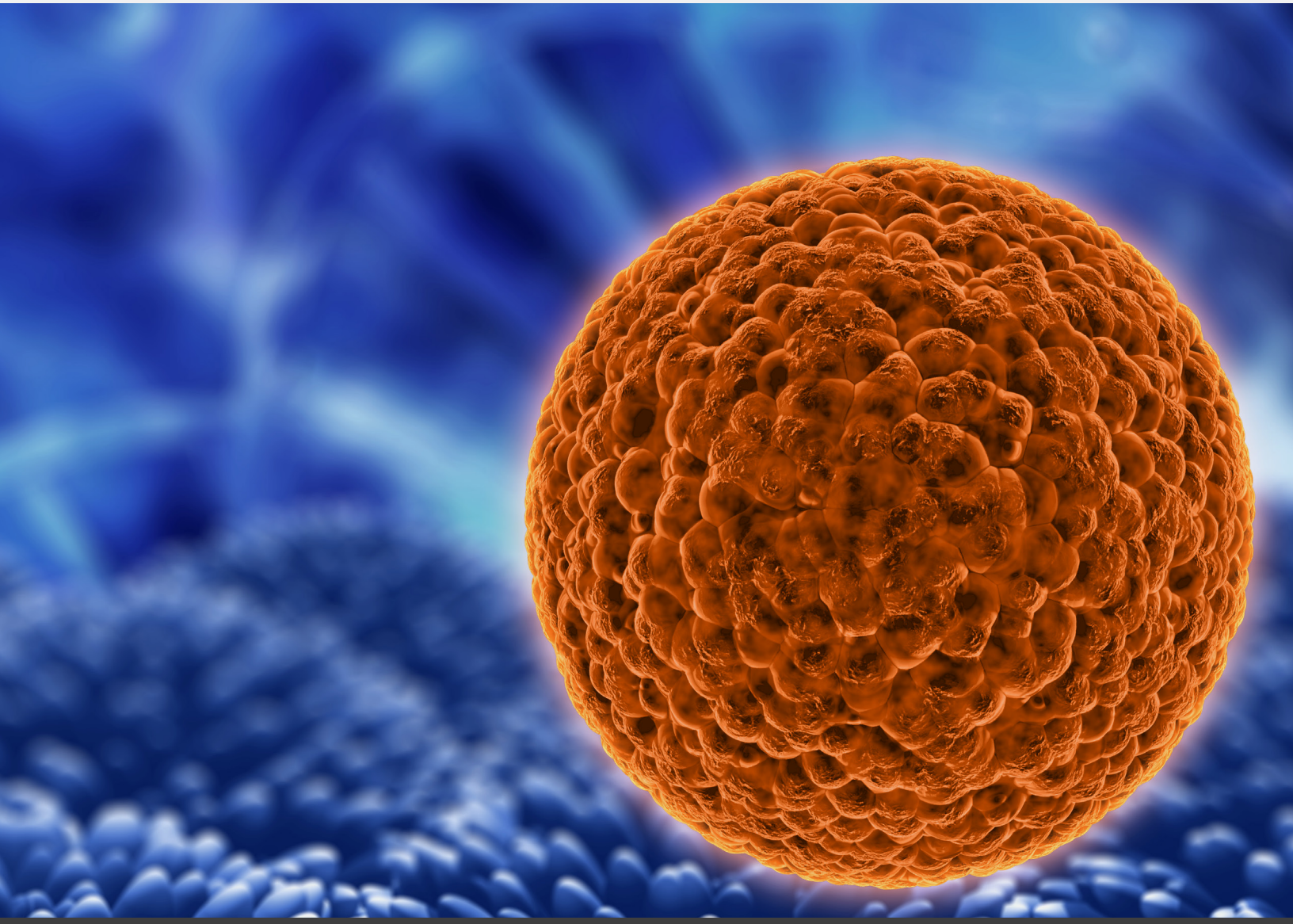
CAR T Cells: A New Weapon in the Armory for Battle against Cancer



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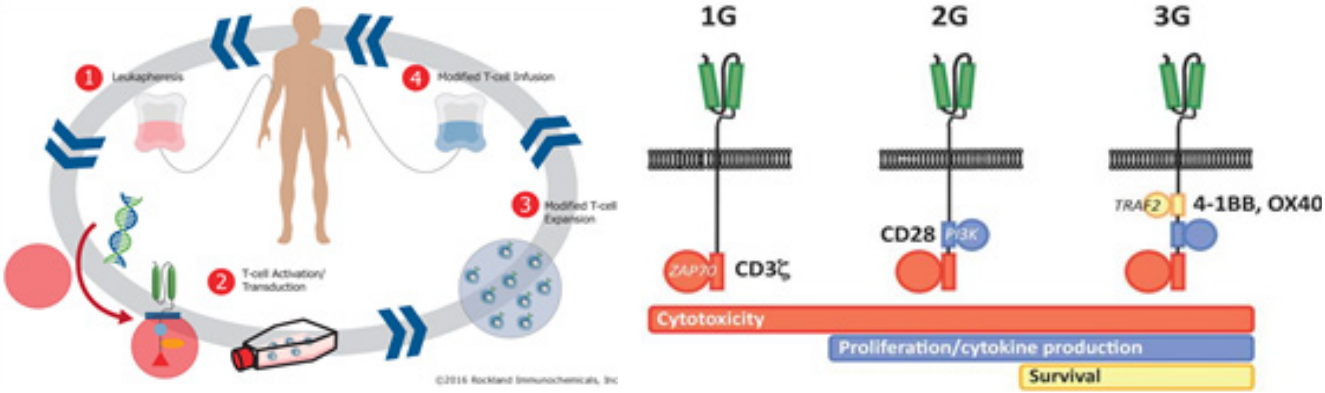
In the year 2012, Emily Whitehead at 6, was suffering from pre-B acute lymphoblastic leukemia and undergoing treatment at Children's Hospital of Philadelphia. Her parent's almost lost the hope after several cancer remissions and side effect associated with the chemotherapy. In April 2012, she enrolled for the phase 1 clinical trial of CART-19 or CTL019, a CD-19 targeting chimeric antigen receptor T cell (CAR-T) CAR developed by Novartis. She became the first child ever to receive engineered T cell therapy. She is now cancer free and not a single cancer cell has been traced in her body since last 5 years.

Consequently, in a historic decision last month (July 2017), US FDA's Oncologic Drugs Advisory Committee (ODAC) unanimously (10-0) voted in favor of approving CTL019 (tisagenlecleucel) which may prompt the accessibility of commercial products in upcoming years.

How does this "Miracle Cure" work for sustained remissions in cancer therapy?

CAR T cell based therapy involves isolation of T cells from patient, which are then genetically modified and expanded in vitro. The altered T cells are re infused into the patient body that expresses a Chimeric Antigen Receptor (CAR) on their cell membrane. This receptor checks with an outer target-binding domain intended to perceive a specific tumor antigen and an internal activation domain in charge of actuating the T-cell when the CAR-T binds to its target. Second generation CARs include intracellular flagging spaces from different co-stimulatory protein receptors (e.g., CD28, 41BB, ICOS) to the cytoplasmic tail of the CAR to give extra flags to the T cell. Preclinical examinations demonstrated that

the second generation enhances the antitumor action of T cells. Later on, third generation CARs join different flagging spaces, for example, CD3z-CD28-41BB or CD3z-CD28-OX40, to augment potency.



How has CAR-T altered the Scenario of immuno-oncology?

Expanding interest for genetically engineered treatment approach for high success rate in cancer treatment along with growing cancer incidence rate are scratch factors driving interest for CAR T cell treatment. Checkpoint inhibitors have just been amazingly fruitful as they hinder the mechanism that tumor cells use to repress T-cell action and overcome the immune system. CAR T goes one step above and engineers the T-cell itself to upgrade the immune reaction against a particular tumor antigen.

Who's leading the race?

There are a few companies contending to be the first to showcase. Rivalry is tight and the after effects of a clinical trial can change everything. Juno Therapeutics, which used to lead the race, reported the end of its lead CAR-T program after a sum of 5 patients kicked the bucket of cerebral

edema caused by the treatment. The company had huge aspirations, and its market top came to over €2.5 Billion just 3 years after its inception. Presently, in any case, it has returned to Phase I.

As far as clinical advancement, Novartis is by all accounts driving now — a FDA panel consistently voted for its CAR-T treatment CTL019. CAR T clinical trials have demonstrated huge reduction rates, of up to 94% in severe forms of cancer, which is especially amazing considering a large portion of the trials, enlist patients that have not reacted to all other accessible medications for their type of disease.

Cellectis initially created UCART19, now licensed by Servier and Pfizer. It's a CAR-T treatment with a switch control framework that exclusive enacts the built cells when rapamycin is available. The treatment is in Phase I and has officially spared two children with recurring, late stage types of leukemia. Bellicum Pharmaceuticals, in the US, is building up a comparative innovation called GoCAR-T that requires rimiducid for CAR-T cell actuation.

Kite Pharma has likewise announced outcomes from a Phase II clinical trial with its lead applicant, axicabtagene ciloleucel, already KTE-C19. The treatment figured out how to keep 36% of patients with lymphoma clear of the infection following a half year, which made Kite's offers bounce by 16%. Be that as it may, this progressing trial has effectively revealed three deaths, two of them connected to the CAR-T treatment. The company has just documented a FDA application and is expecting an official choice in November.

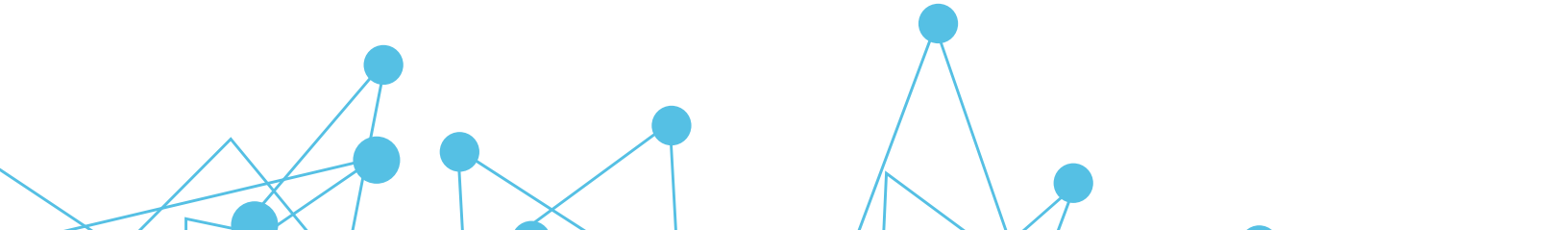
Industry Movement: CAR T-Cell Deals

In the course of recent years, the industry has been a hive of action, with about six companies forging deals valued at more than a half billion dollars altogether. Notwithstanding the apparent money related capability of these treatments, the sustaining craze may partially be inferable from the way that administrative experts are giving CAR T-cell medicines need audit for filling neglected restorative needs. A large number of these treatments are accepting vagrant or leap forward status from the US

Food and Drug Administration (FDA), bringing assisted administrative survey, which converts into prior acknowledgment of money related advantages from more fast market passage. In November 2014, for instance, the FDA conceded vagrant status to Juno's JCAR015. Kite's KTE-C19 for unmanageable forceful non-Hodgkin's lymphoma additionally as of late got the assignment from both the FDA and the European Medicines Agency. Also, the University of Pennsylvania/Novartis' CTL019 for ALL got leap forward status last July.

Institution/Company	Date	Partner	Terms
Universty of Pennsylvania	August 2012	Novartis	Undisclosed
Celgene	March 2013	Bluebird Bio, Baylor College of Medicine	Unspecified upfront payment plus up to $225 million per product in option fees and milestone payments
Cellectis	June 2014	Pfizer	$80 million upfront plus up to $185 million per product and royalties
Cellectis	January 2015	Ohio State University	Undisclosed
Kite Pharma	January 2015	Amgen	$60 million upfront and up to $525 million per product in milestone payments, plus royalties on sales and IP licensing
Md Anderson	January 2015	Ziopharm, Intrexon	$100 million in stock and $15–20 million/year for 3 years

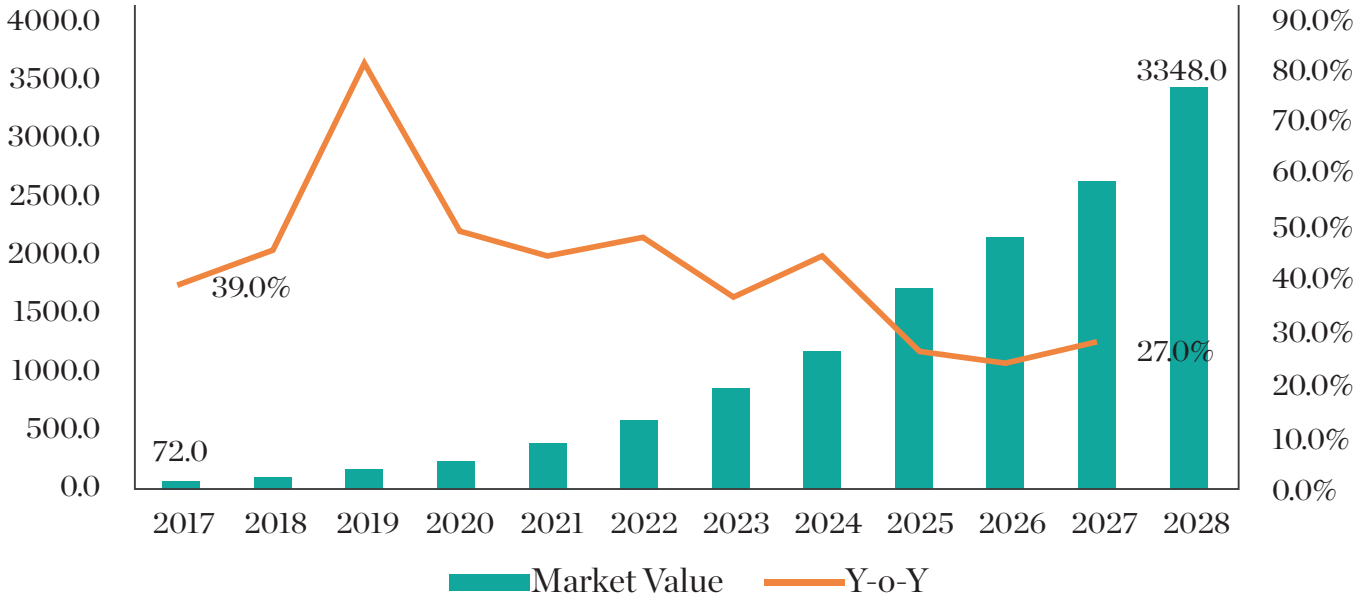
CAR T-Cell Biotech IPOs



In 2011, the Penn group portrayed the consequences of an early trial of its CTL019 CAR T-cell treatment in three progressed perpetual lymphocytic leukemia (CLL) patients (Sci Transl Med, 3:95ra73, 2011). The findings—including two patients who have now stayed going away 4.5 years after their treatment—filled in as an early showing that CAR T cells can effectively treat patients with late-organize sickness. The group has now tried CAR T-cell treatments in around 125 individuals, with six distinct trials in progress for pediatric and grown-up ALL, CLL, various myelomas, and non-Hodgkin's lymphoma. Other CAR T-cell treatments are in trials for strong tumors, including ovarian, bosom, and pancreatic growths, and mesothelioma and glioblastoma.

Company	Date	Value
Juno	December 2014	$264.6 million
Cellectis	March 2015	$228 million
Bellicum	December 2014	$160 million
Kite Pharma	June 2014	$134.1 million

CAR T-Cell Therapy Steer towards Market



Over the last few years, CAR T Cell therapy has gained wide recognition in the healthcare industry. CAR T cell is an innovative technique that includes expulsion of T Cells from patient's blood before reinsertion utilizing a genetically altered mechanism. The technology is still in the early stage; however, is required to develop at twofold digit development rate making multi-billion outright dollar open door for industry players soon. Starting at 2016, a little more than 40 companies are occupied with CAR T cell treatment showcase. Novartis International AG, Juno Therapeutics, and Kite Pharma Inc. are the main players that are relied upon to dispatch items by 2018. With long looming clinical trials and research exercises completed utilizing chimeric antigen receptor cells (CAR-T) cells, these players in the pharmaceuticals business are eager to launch their products in upcoming years in the market.

In 2015, Cellectis went into clinical organization together with MD Anderson for improvement of UCARTCS1 in MM, UCART22 taking all things together, UCART38 in T-cell ALL and UCART123 in an uncommon non-treatable disease. The worldwide CAR T cell treatment advertise is evaluated to be esteemed at US$ 72.0 million of every 2017 and is anticipated to extend exponentially at a CAGR of 46.1% amid 2019 – 2028.

Reference/Image Links

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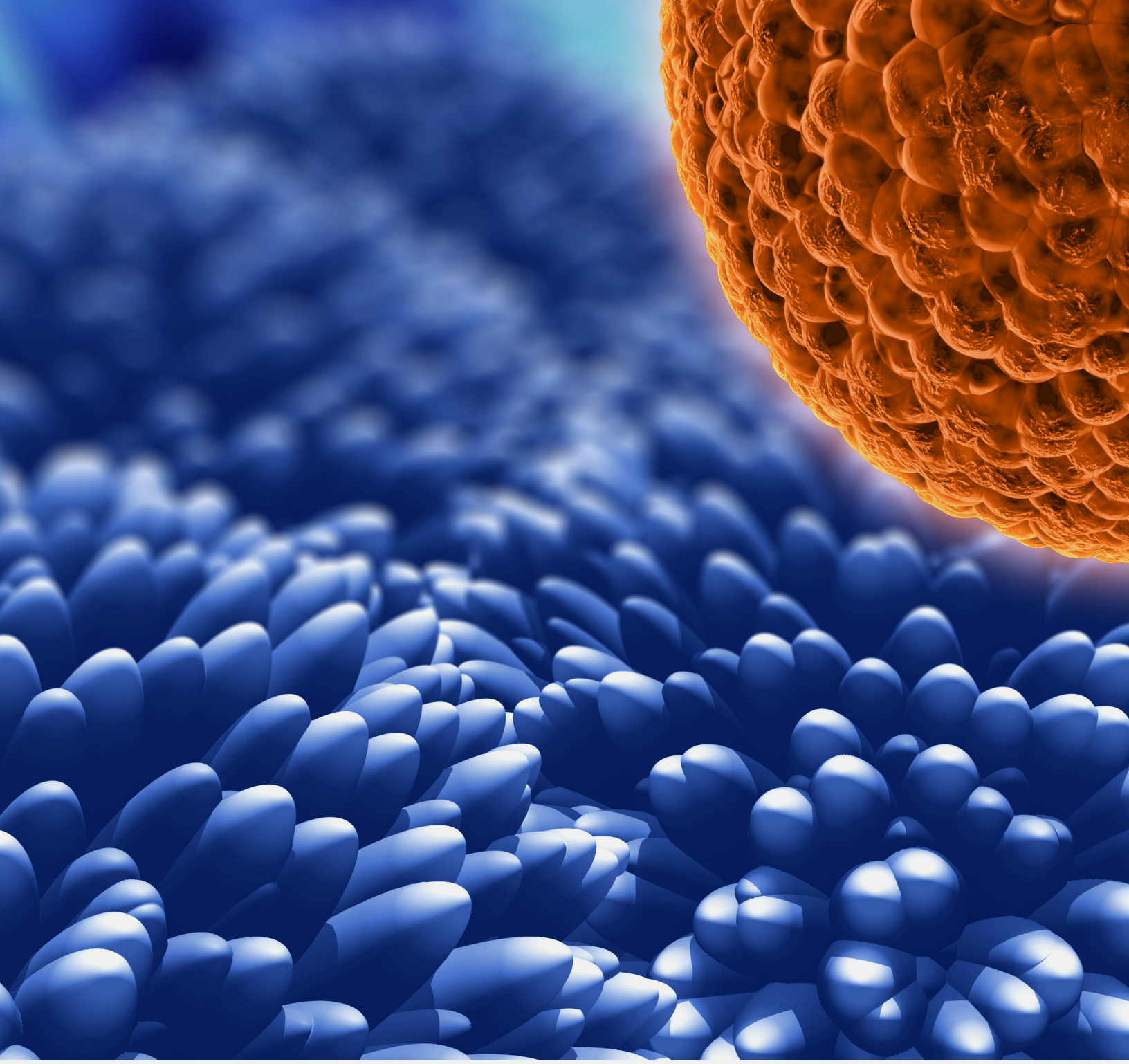

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