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OVERVIEW

We are a leading clinical and pre-clinical stage cell therapy company in China. Our vision is to develop innovative cell therapies for the China market to transform the treatment of cancer for Chinese patients. Since our founding in 2016 by Juno and WuXi AppTec (through its wholly-owned subsidiary WXAT Shanghai), we have built an integrated platform focused on developing, manufacturing and commercializing breakthrough cell-based immunotherapies for hematological cancers and solid tumors. Relmacabtagene autoleucel (“**relma-cel**”), our lead product candidate, is an autologous anti-CD19 CAR-T therapy for relapsed or refractory (“**r/r**”) B-cell lymphoma. In June 2020 the NMPA accepted for review our NDA relating to relma-cel as a third-line treatment for DLBCL, and in September 2020 the NMPA granted priority review status to our NDA relating to relma-cel and Breakthrough Therapy Designation for relma-cel as a treatment for FL. Relma-cel is expected to be the first CAR-T therapy to be approved as a Category 1 biologics product in China, and has potential to be a superior CAR-T therapy.

We are an early entrant into the field of cell-based immunotherapy in China. Cell-based immunotherapy is a field which represents a paradigm shift and the latest advancement in the treatment of cancer. Cell-based immunotherapies, including CAR-T treatments, are an innovative treatment method that uses human immune cells to fight cancer. Supported by multiple clinical studies, cell-based immunotherapies could lead to long-lasting remissions of B-cell lymphomas and leukemias which are refractory to other treatments. According to Frost & Sullivan, the target indications for relma-cel, namely 3L DLBCL, 3L FL and 3L MCL, had an addressable market estimated to have a prevalence of approximately 28.7 thousand, 5.2 thousand and 3.4 thousand patients respectively in China in 2019, after taking into account the effectiveness of prior lines of treatment in China. Given the unmet medical needs that can be effectively addressed by CAR-T therapies, according to Frost & Sullivan, the market for CAR-T therapies in China is expected to grow from RMB0.6 billion in 2021 to RMB5.4 billion in 2024, and to RMB24.3 billion in 2030. We believe that we are well positioned to take advantage of this rapidly growing market. CAR-T therapies are considered to be significantly high-risk in nature, as they represent emerging approaches to cancer treatment that face significant challenges and hurdles.

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The following chart summarizes the development status of each of our cell-based immunotherapy product candidates to treat hematological cancers and solid tumors as at the Latest Practicable Date. All of the product candidates in the following chart are autologous cell therapies.

Product	Target	Indication	Commercial Rights	Pre-clinical	IND	Phase I	Pivotal / Phase II	Pivotal / Phase III	NDA	NMPA Classification	Partner
Hematologic Malignancies	JWCAR029 / Relmacabtagene Autoleucel (relma-cel) ^{*3}	3L DLBCL	China, Hong Kong, Macau	Submitted in June 2020 and received priority review in September 2020						Category I	JUNO Juniper Therapeutics Company
		3L FL	China, Hong Kong, Macau	Registrational trial							
		3L MCL	China, Hong Kong, Macau	Registrational trial							
		2L DLBCL	China, Hong Kong, Macau								
		3L ALL	China, Hong Kong, Macau								
		3L CLL	China, Hong Kong, Macau								
	JWCAR129 ⁴	BCMA	r/r MM	China, Hong Kong, Macau	IND enabling					Category I	JUNO Juniper Therapeutics Company
Nex-G		CD19	NHL	China, Hong Kong, Macau						Category I	JUNO Juniper Therapeutics Company
Solid Tumors	JWATM203	AFP	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN	²					Category I	EUREKA
	JWATM213 ¹	AFP	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN						Category I	EUREKA Lyell
	JWATM204	GPC3	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN						Category I	EUREKA
	JWATM214 ¹	GPC3	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN						Category I	EUREKA Lyell

Abbreviations: DLBCL = diffuse large B-cell lymphoma; FL = follicular lymphoma; MCL = mantle cell lymphoma; ALL = acute lymphoblastic leukemia; CLL = chronic lymphocytic leukemia; MM = multiple myeloma; NHL = non-Hodgkin lymphoma; HCC = hepatocellular carcinoma; NSCLC = non-small cell lung cancer; r/r = relapsed or refractory; 3L = third-line; 2L = second-line

* Denotes a Core Product Candidate.

¹ Developing using Lyell technology.

² JWATM203 is currently in Phase I/II trial in the U.S. conducted by Eureka under an IND.

³ Relma-cel is based on the same CAR construct as Juno’s product lisocabtagene maraleucel (liso-cel), which is the subject of a BLA currently under review by the U.S. FDA.

⁴ JWCAR129 is based on the same CAR construct as Juno’s product orvacabtagene autoleucel (orva-cel), which is currently the subject of a Phase I/II clinical trial in the United States.

We have developed a comprehensive and differentiated cell-based immunotherapy pipeline, with a risk-balanced approach that has shown clear benefit in the field of cell therapies for hematological cancers and provides an opportunity to expand into the nascent field of cell therapies for solid tumors. Our product pipeline features a mix of product candidates targeting both proven and novel tumor antigens. We have strategically designed and are developing a cell-based immunotherapy product pipeline of autologous cell therapy candidates, covering both hematological cancers and solid tumors, and we also have an option to acquire two allogeneic cell therapy candidates for treatment of hematological cancers and solid tumors.

Historically we have not conducted in-house product discovery, and have instead accessed discovery capabilities through our relationships with counterparties such as Juno, Eureka and Acepodia. In the medium- to longer-term, however, we intend to establish our own in-house product discovery capability, including through leveraging the ARTEMIS platform that we in-licensed from Eureka in June 2020.

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Our cell-based immunotherapy product candidates for treatment of hematological cancers include the following:

- **Relma-cel**, our lead product candidate, is a potential superior autologous CAR-T product for the treatment of various B-cell malignancies. The registrational clinical trial for relma-cel for treatment of heavily pre-treated, poor prognosis r/r DLBCL patients, demonstrated efficacy results of best ORR of 75.9% and best CRR of 51.7% as of data cut off date June 17, 2020. Relma-cel demonstrated a potentially superior safety profile relative to CAR-T therapies currently approved for treatment of DLBCL based on reported data. In the registrational trial, sCRS or sNT were observed in 5.1% or fewer of treated patients, and no treatment-related deaths were reported. The NDA for relma-cel for the third-line treatment for DLBCL was submitted and accepted for review by the NMPA in June 2020. If our NDA is approved on the timeline that we currently anticipate, relma-cel is expected to be the first CAR-T therapy approved as a Category 1 biologics product in China, and has potential to be a superior CAR-T therapy. To fully explore the clinical potential of relma-cel, we intend to develop relma-cel for a number of other hematological indications, including FL, MCL, CLL, second-line DLBCL and ALL. According to Frost & Sullivan, the target indications for relma-cel, namely 3L DLBCL, 3L FL and 3L MCL, had an addressable market estimated to have a prevalence of approximately 28.7 thousand, 5.2 thousand and 3.4 thousand patients respectively in China in 2019, after taking into account the effectiveness of prior lines of treatment in China.

We have developed relma-cel using our own optimized processes, which we originally established in collaboration with Juno, a global leader in cell therapy and our largest shareholder; and relma-cel is based on a CAR construct that we have in-licensed from Juno for China, Hong Kong and Macau.

- **JWCAR129** is an autologous CAR-T therapy we are developing for the treatment of multiple myeloma (“MM”). JCAR129 targets B-cell maturation antigen (“BCMA”), a protein which is highly expressed in a number of hematological malignancies including MM. MM is a highly aggressive disease representing approximately 10 percent of all hematological malignancies. There is a significant unmet medical need for the treatment of MM since patients eventually become refractory to existing treatments after relapse. We are conducting IND-enabling pre-clinical pharmacology and toxicology studies as well as manufacturing process development studies for this candidate, with the intention of commencing clinical studies as early as the first half of 2021.

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In addition to being a leader in hematological cancer treatments in China, we adopt a differentiated approach to address the unmet medical needs in solid tumors. Based on our collaborations with Eureka and Lyell Immunopharma, Inc. (“**Lyell**”), we are developing T-cell therapy candidates that are designed to enhance T-cell functions, persistence and infiltration into solid tumors with an improved safety profile. Our cell-based therapy product candidates for the treatment of solid tumors include the following:

- **JWATM203**, a potentially superior autologous T-cell receptor mimic T-cell therapy targeting alpha-fetoprotein (“**AFP**”) for the treatment of hepatocellular carcinoma (“**HCC**”). Treatment of HCC represents a huge unmet medical need in China. We believe JWATM203 has the potential to be a promising treatment option for patients with AFP-positive HCC. Eureka has advanced its AFP TCRm T-cell therapy product candidate into a Phase I/II clinical trial in the United States. Through our collaboration with Lyell, we are developing another autologous TCRm T-cell therapy targeting AFP for the treatment of HCC, **JWATM213**, which may further enhance T-cell function and improve efficacy.
- **JWATM204**, a novel autologous T-cell therapy product candidate targeting glypican-3 (“**GPC3**”). We believe JWATM204 has the potential to be a promising treatment option for patients with GPC3-positive HCC. Similar to JWATM203 and JWATM213, we will use the Lyell technology to develop another autologous GPC3-targeting T-cell therapy product candidate, **JWATM214**.

These product candidates are based on novel technology platforms, which form the foundation of our differentiated approach to address the significant unmet needs in solid tumors in China:

- Eureka’s **ARTEMIS platform** is the basis for JWATM203 and JWATM204. It is a novel technology platform that is intended to create potentially more effective and safer T-cell therapies than are currently available. As part of our agreement with Eureka in June 2020, we acquired the rights to develop, manufacture and commercialize JWATM203 and JWATM204 for China, Hong Kong, Macau, Taiwan and the member countries of ASEAN, the right to use the ARTEMIS platform in connection with our improvements to those products, as well as exclusive rights to commercialize in those jurisdictions all products that Eureka develops using the ARTEMIS Platform. For further details, please see “— Collaboration and License Agreements — Asset Purchase Agreement with Syracuse Cayman and License Agreement with Eureka” in this section.

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- **Lyell’s technology** is designed to increase T-cell functionality and reduce T-cell exhaustion in the tumor micro-environment to potentially improve the anti-tumor effects. We obtained access to the Lyell technology to develop novel product candidates based on JWATM203 and JWATM204. For further details, please see “— Collaboration and License Agreements — Lyell Collaboration Agreement” in this section.

In addition to our China, Hong Kong, Macau, Taiwan and the member countries of ASEAN rights to commercialize products that Eureka develops using the ARTEMIS platform, we have opportunities to in-license additional product candidates from Juno and product candidates from Acepodia. These opportunities, together with our strong business development capabilities, will support further expansion of our pipeline. Our opportunities to in-license include the following next generation cell-based therapy product candidates:

- **Juno Pipeline:** We have a right of first negotiation to develop and commercialize five Juno engineered T-cell products in China, Hong Kong and Macau. These highly novel candidates target promising pathways including CD22, WT1, CD171, MUC16 and ROR1. These candidates cover a wide range of hematological cancer and solid tumor indications.
- **Acepodia Pipeline:** We have an option to acquire from Acepodia the right to develop and commercialize in China, Hong Kong and Macau an allogeneic natural killer (“NK”) cell therapy product that targets HER2. This novel candidate is designed to treat certain types of breast cancer and other malignancies, including gastric cancer, which have a significant unmet medical need in China. JWACE002 is designed as an allogeneic product, an “off-the-shelf” ready-made cell therapy that is manufactured from cells of a “cell line” unrelated to the patient.

In the field of cellular immunotherapy, the manufacturing process significantly influences product characteristics, and accordingly we believe that in cellular immunotherapy, even more than in other contexts, “the process is the product.” We have proven translational research, analytical development and manufacturing process development capabilities. We have developed a proprietary commercial-scale manufacturing process for relma-cel which has been proven during the registrational clinical trials of relma-cel, with a 100% manufacturing success rate of the relma-cel products used in the Phase II registrational clinical trial. Moreover, we are developing a set of new technologies and platforms to enable the next generation CAR-T product and manufacturing processes with a shorter production cycle time, higher quality, better product characterization and improved product efficacy and safety profile, at a lower cost. We believe that this will establish a foundation for our next-generation anti-CD19 CAR-T product, as well as other products in our pipeline.

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Our cell therapy development platform also includes robust clinical development capabilities. Having completed Phase I clinical trials and a registrational Phase II clinical trial in ten hospitals across China relating to relma-cel, we have involved more sites in our clinical trials in China than any other CAR-T company, according to Frost & Sullivan. In addition, we believe we have enrolled more patients in our IND anti-CD19 CAR-T trials in China than any other company. Moreover, we have a proven track record in clinical execution, having progressed relma-cel from IND to NDA filing to NDA acceptance in a short time frame.

Our industry-leading commercial manufacturing infrastructure is centered on our newly constructed manufacturing facility in Suzhou, which provides approximately 9,976 square meters for commercial-scale manufacturing. The Suzhou facility is designed to house four independent modules, of which two are currently constructed, qualified and operating in compliance with international cGMP and QMS standards. It can support a wide range of cell platforms, including those using gene-modified autologous T-cells and NK cells, gene-modified or non-gene-modified tumor-infiltrating lymphocytes (“TIL”) and gene-modified allogeneic immune cells, as well as facilities to produce clinical grade viral vectors that are used to genetically modify these cells. Our current design has estimated capacity to support treatment of up to 5,000 patients per year. The degree of automation and in-process control designed into our commercial manufacturing processes lead to reliable product supply, and our manufacturing operations are optimized for high capacity and labor utilization, allowing cost-effective manufacturing.

Our plan to commence revenue generation centers on the commercialization of relma-cel. Having achieved NMPA acceptance of our NDA for relma-cel, we intend to drive full-scale commercialization of relma-cel upon approval. We plan to establish a focused in-house sales force to market relma-cel to the top hematology hospitals in China, including a specialized team in medical affairs to build on our strong existing relationships with physicians and KOLs in the field of hematology in China and to provide the necessary site support for healthcare providers and patients to manage all steps in the safe delivery of this product.

Our history can be traced back to 2016, when our principal operating subsidiary, JW Shanghai, was co-founded by two global pharmaceutical research and development companies, Juno and WuXi AppTec, through its wholly-owned subsidiary WXAT Shanghai. Since inception, our success has been guided predominantly by the efforts of the management team under the leadership of our executive Director, chairman of the Board and CEO, Dr. Li. Our management team has expertise gained from extensive experience in the international biopharmaceutical industry as well as in-depth local knowledge of the China market including access to top-tier hospitals, PIs and KOLs in the field of immuno-oncology.

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OUR STRENGTHS

Potential superior anti-CD19 CAR-T product

Relma-cel has potential to be a superior third-line treatment for certain hematological cancers in China. It targets an antigen called CD19, which is expressed in a broad range of B-cell hematological cancers including DLBCL, FL, MCL and CLL. All of these indications are types of a broader category of cancers known as “B-cell non-Hodgkins lymphoma” or “**NHL**”), which is a market estimated to include approximately 514.2 thousand patients in China in 2020 and is expected to increase to approximately 730.0 thousand patients in China by 2030, according to Frost & Sullivan.

We believe that relma-cel is a potential superior third-line treatment for DLBCL, with a potentially superior safety profile and comparable efficacy relative to other currently approved anti-CD19 CAR-T products globally. In our Phase II registrational trial involving heavily treated, poor prognosis patients with r/r DLBCL, relma-cel produced a best ORR of 75.9% and a best CRR of 51.7% as of data cutoff date June 17, 2020, with sCRS or sNT observed in 5.1% or fewer of treated patients, and no treatment-related deaths were reported. While head-to-head clinical comparisons have not been conducted, the safety data achieved in this clinical trial are superior to those achieved by other approved anti-CD19 CAR-T products globally, and the efficacy data are comparable.

In June 2020, the NMPA accepted and agreed to review our NDA relating to relma-cel as a third-line or greater treatment for DLBCL, and in September 2020 the NMPA granted priority review status to our NDA relating to relma-cel and Breakthrough Therapy Designation for relma-cel as a treatment for FL. If approved by the NMPA for marketing in China on the timeline that we currently anticipate, relma-cel would be the first CAR-T therapy approved as a Category 1 biologics product in China, and has potential to be a superior CAR-T therapy. To fully explore the clinical potential for relma-cel, we are also developing relma-cel for a number hematological indications, including FL, MCL, CLL and ALL, and as a second-line treatment for DLBCL.

Comprehensive and differentiated cell therapy pipeline covering both hematological cancers and solid tumors

We have built a pipeline of product candidates intended to treat hematological cancers, an area in which CAR-T has proven to be effective, and to treat solid tumors, which represents substantial potential given the significant unmet medical needs and relative market size. Our product portfolio has also been strategically developed to cover various next-generation approaches that improve the benefit to risk ratio of our products, including allogeneic approaches,

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combination strategies with small molecules and other CAR-T products with new gene modifications. We believe that our product candidates have the potential to become groundbreaking treatments in their respective indications.

Hematological cancers

In addition to relma-cel as a prospective treatment for FL, MCL, CLL, second-line DLBCL and ALL, we are strategically developing our product pipeline to cover broader hematological cancer indications such as multiple myeloma (“MM”). JWCAR129 is a CAR-T product targeting BCMA, which is expressed in MM and is a promising target for CAR-T therapies. As with relma-cel, we have in-licensed the CAR construct for JWCAR129 from Juno and have used our own processes in its development.

Solid tumors

Based on our collaborations with Eureka and Lyell, we are developing T-cell therapy candidates that are designed to have enhanced T-cell functions, persistence and infiltration into solid tumors with an improved safety profile. Our pipeline of product candidates for the treatment of solid tumors is centered on JWATM203 and JWATM204, which are cell therapy products intended for the treatment of HCC:

- **JWATM203**, a potentially superior TCRm T-cell therapy targeting AFP for the treatment of HCC. Treatment of HCC represents a huge unmet medical need in China. We believe JWATM203 has the potential to be a promising treatment option for patients with AFP-positive HCC. Our in-licensing partner Eureka has advanced its AFP TCRm T-cell therapy product candidate into a Phase I/II clinical trial in the United States. Through our collaboration with Lyell, we are developing **JWATM213**, another TCRm T-cell therapy targeting AFP for treatment of HCC, which may further enhance T-cell function and improve efficacy.
- **JWATM204**, a novel T-cell therapy product candidate targeting GPC3. We believe JWATM204 has the potential to be a promising treatment option for patients with GPC3-positive HCC. Similar to JWATM203 and JWATM213, we will use the Lyell technology to develop another GPC3-targeting T-cell therapy product candidate, **JWATM214**.

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Next Generation Candidates through Dual Source of Innovation

We expect to continue to enrich our pipeline by bringing novel next generation cell therapy candidates through in-house research capability, as well as opportunities to in-license and our strong business development capabilities. Our industry leadership in China regarding cell therapy manufacturing and clinical development has allowed us to be viewed as a valued partner in this market, increasing business development partnership, licensing and acquisition opportunities. Our acquisition of product rights and platform technology rights from Eureka establishes a strong precedent for expansion of our pipeline by means of acquisitions and in-licensing arrangements. Moreover, we believe we have strong business development capabilities to forge collaborations with leading global cell therapy players, focusing on solid tumors and cutting edge science.

Our product candidates addressing solid tumors are based on novel technology platforms, which form the foundation of our differentiated approach to bring future candidates to our pipeline:

- Eureka’s **ARTEMIS platform** is the basis for JWATM203 and JWATM204. It is a novel technology platform that is intended to create potentially more effective and safer T-cell therapies than are currently available. ARTEMIS T-cells have $\gamma\delta$ TCR-based effector domains coupled to antibody-based antigen-binding domains, which allow the engineered T-cells to recognize either surface proteins or peptide fragments of proteins inside the tumor cells presented by MHC. The ARTEMIS platform utilizes intrinsic T-cell responses and regulatory mechanisms, which we believe can limit excessive T-cell expansion and classic toxicities associated with CAR-T therapies, such as CRS. Unlike other TCR-T approaches that utilize $\alpha\beta$ TCR chains, ARTEMIS effector domain utilizes $\gamma\delta$ TCR chains which we believe would avoid unwanted cross-reactivity and associated toxicities due to mispairing.

As part of our agreement with Eureka in June 2020, we acquired exclusive rights to develop, manufacture and commercialize JWATM203 and JWATM204 for China, Hong Kong, Macau, Taiwan and the member countries of ASEAN and to use the ARTEMIS platform in connection with our improvements to those products, as well as exclusive rights to commercialize in those jurisdictions all other products that Eureka develops using the ARTEMIS Platform, subject to separate license agreements to be entered into between us.

- **Lyell’s technology** is designed to increase T-cell functionality and reduce T-cell exhaustion in the tumor micro-environment to potentially improve the anti-tumor effects. We obtained access to the Lyell technology to develop novel product candidates based on JWATM203 and JWATM204.

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In addition to our rights to commercialize products that Eureka develops using the ARTEMIS platform, our opportunities to in-license include the following:

- **Juno Pipeline:** Five engineered T-cell products that Juno is currently developing. These highly novel candidates target promising pathways including CD22, WT1, L1CAM, MUC16 and ROR1. These candidates cover a wide range of hematological cancer and solid tumor indications. These candidates provide us an option to further broaden our pipeline to cover more cancer indications/enrich our cell therapy pipeline mix for the development of combo therapies. Under our strategic alliance with Juno, we possess a right of first negotiation to develop and commercialize these candidates in China, Hong Kong and Macau.
- **Acepodia Pipeline:** A natural killer cell (“NK”) cell therapy product that targets HER2, an antigen that is expressed in some cancers, including 20-30% of breast cancers and 10-15% of gastric cancers. This novel candidate is developed under an allogeneic approach which would create an inventory of off-the-shelf cell therapy drugs to deliver readily available treatment faster, more reliably, at greater scale and to more patients. We have an option to acquire from Acepodia the right to develop and commercialize JWACE002 and JWACE055 in China, Hong Kong and Macau. JWACE002 and JWACE055 are allogeneic products.

Fully integrated cell therapy development platform

We seek to ensure our products are developed at the highest quality by applying our unique and fully integrated in-house cell therapy development capabilities, and by leveraging Juno’s CAR-T process development know-how. Our uniquely designed and fully integrated development capabilities range from translational research and analytical development through process development and clinical development to regulatory affairs. These capabilities provide us with a platform that helps us ensure that we continue to maintain operational excellence and that each of our treatments are produced at the highest quality. We believe our robust and fully integrated development platform enables seamless collaboration among different functional groups throughout the development lifecycle of a new product candidate and helps us increase the efficiency of development and the likelihood of success. Moreover, we believe we have unique and highly differentiated capabilities to develop a product candidate through the clinical development process to obtain regulatory approval in China.

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Analytical and process development

In the field of cellular immunotherapy, the manufacturing process significantly influences product characteristics, and accordingly we believe that in cellular immunotherapy, even more than in other contexts, “the process is the product.” Variations in the manufacturing process can lead to significant variations in the characteristics of the final product. Moreover, because different patients have different characteristics, such as the number and distribution of different types of cells with different phenotypes, the starting material for the cell therapy manufacturing process is more variable than for the biologics or small molecule manufacturing processes, and such variability in starting material is a major challenge for reliable and consistent production of cell therapies.

Through process development, we have designed a manufacturing process designed to allow us to optimize cell characteristics and cellular conditions and increase production consistency. We generated our process development capabilities based on internal development and optimization of technology in-licensed from Juno. By the time we locked down our clinical manufacturing process for relma-cel, the process was able to accommodate the significant variability in starting material to generate products that have consistent attributes and meet clinical dosing requirements.

Our fully integrated processes consist of a full suite of analytical development, process development and quality control and quality assurance functions:

- Our *process development capabilities* include process transfer-in/out; process development and optimization; process and product characterization; and development of new technologies and platforms for plasmids, viral vector and cell therapy products.
- Our *analytics development capability* consists of a PCR/qPCR lab, flow cytometry lab, biochemical and physical-chemical lab and cell-based assay platform, aiming to support in-process testing and product characterization of plasmids, vector and cell therapy as well as to bring in new characterization measurement for better understanding of the process and our product.
- Our established *quality system* meets requirements of Chinese health authorities and the ICH. We implement a holistic quality control strategy including raw material control, in-process, and release testing designed for gene and cell therapy products with high specificity, sensitivity and fast turnaround.

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Based on our analytical and process development capabilities, we were able to achieve a 100% success rate during clinical manufacturing of relma-cel for our Phase II registrational trial. We have a robust process to account for variability in starting material due to patient characteristics and to generate reliable product, with consistent product attributes a wide range of cell doses and capacity to deliver prescribed product over wide dosing range. Moreover, our cell therapy process platform is designed based on autologous T-cell process as a basic platform, with the flexibility to adapt to other processes.

Moreover, we are developing a set of new technologies and platforms to enable the next generation CAR-T product and manufacturing processes with a shorter production cycle time, higher quality, better product characterization and improved product efficacy and safety profile, at a lower cost. We believe that this will establish a foundation for our next-generation anti-CD19 CAR-T product, as well as other products in our pipeline.

Clinical development

We conduct all of our clinical operations in-house to ensure quality and execution efficiency. We were the first company to have an IND approved by the NMPA for clinical trials of an anti-CD19 CAR-T therapy in China, according to Frost & Sullivan. Having completed Phase I clinical trials and a registrational phase II trial in ten hospitals across China relating to relma-cel, we have involved more sites in our clinical trials in China than any other CAR-T company, according to Frost & Sullivan. In addition, we believe we have enrolled more patients in our IND clinical trials in China than any other anti-CD19 CAR-T company, and that this contributed substantially to the NMPA’s rapid acceptance of our initial NDA for relma-cel. Moreover, because we have worked with a larger number of clinical trial centers, we believe that relma-cel is relatively better known to a number of physicians who may play pivotal roles in determining treatment plans for patients who are eligible to use relma-cel.

Regulatory affairs

We believe that we are viewed by regulators as one of the key players in providing input from a commercial perspective on the development of China’s cell therapy regulatory environment. We provided input on the development of cell therapy regulatory guidance by the NMPA’s Center for Drug Evaluation (“CDE”), and we regularly communicate with the CDE on issues related to cell therapy. We also provided feedback to the CDE on the Drug Administration Law and the CAR-T GMP inspection guide. Our feedback and input to the CDE on these matters have typically taken the form of participation in workshops convened by the CDE, to which regulators, academics and industry representatives have been invited. Our primary goal in providing such feedback and input was to promote the consistency of emerging PRC industry regulatory standards with existing

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international standards. Moreover, as founding chair of the Shanghai CAR-T Alliance and as a member of the China Pharmaceutical Innovation and Research Development Association (PhIRDA), we are one of the key players in building the CAR-T industry in China.

Leading commercial manufacturing infrastructure and supply chain

We manufacture in China with a commercial-ready, highly automated, single train process to select, activate, transduce and expand CAR T-cells with consistent product attributes at a wide range of cell doses with capacity to deliver prescribed product over a wide dosing range.

Learning from our extensive clinical manufacturing experience, we designed a modular, multi-product cell therapy manufacturing facility. In June 2020, we received a production license approval from the Medical Product Administration of Jiangsu Province. The Suzhou facility provides approximately 9,976 square meters for commercial and clinical manufacturing and quality in compliance with cGMP and QMS standards and currently has estimated design capacity to support treatment of up to 5,000 patients per year. It is designed to include four independent modules, of which two are currently constructed, qualified and operating in compliance with international cGMP and QMS standards. Moreover, it can support a wide range of cell platforms, including those using gene-modified autologous T-cells and NK cells, gene-modified or non-gene-modified TIL and gene-modified allogeneic immune cells, and includes facilities to produce clinical grade viral vectors that are used to genetically modify these cells.

We have promoted operational excellence at our manufacturing facilities through a variety of means. We believe the degree of automation that we have designed into our commercial manufacturing processes improves production efficiency and lowers manufacturing costs. The manufacturing process is based on a unit operations concept with an automated and standardized device for each unit operation. Such automation minimizes human error and improves efficiency. We adopt closed processing manufacturing, which prevents contamination and allows concurrent processing of multiple patient samples in a large “ballroom” with a lower grade of classified cleanroom requirements. Our implementation of a computerized manufacturing execution system ensures a robust chain of identity, which further prevents error and lowers production costs.

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Seasoned management and strong shareholders’ support

Management and Directors

We have assembled a well-known team of industry executives with extensive experience in multinational pharmaceutical companies. Our success is, to a large extent, the product of our management’s leadership and expertise, which cover the full spectrum of the cell therapy development process, from pre-clinical studies through design and execution of clinical studies to regulatory processes, as well as extensive prior experience in manufacturing processes.

Dr. James Li, M.D., brings nearly 30 years of leadership experience in the pharmaceutical industry to our Company. Dr. Li was formerly the founding General Manager for Amgen in China and a partner in the life science practice of Kleiner Perkins Caulfield & Byers. From 1991 to 2006, Dr. Li held leadership roles in clinical research, regulatory affairs, new product development and franchise development at Merck & Co. Inc.

We also have assembled a team of experienced industry veterans with extensive collective experience in the biopharmaceutical industry, including Harry Lam, Ph.D., Executive Vice President and Chief Technology Officer; Mr. Xin Fu, Senior Vice President and Chief Finance Officer; Dr. Hongxia Zheng, M.D., Ph.D., Senior Vice President for Clinical Development, executive director of Clinical Research Operations; Mr. Wen-jun Sun, MBA, Vice President and Head of Business Development; and Dr. Su Yang, executive director of Clinical Research Operations. Our management team has expertise gained from extensive experience in the international biopharmaceutical industry as well as in-depth local knowledge of the China market including access to top-tier hospitals, PIs and KOLs in the field of immuno-oncology.

Additionally, in September 2020, Alex Wu joined our Company as Senior Vice President and Chief Commercial Officer, to support the building of a focused in-house sales and marketing team to market relma-cel across China. Mr. Wu is responsible for the overall commercial functions, including sales, marketing, market access and channel management.

Our Board of Directors also brings world-leading expertise in cell therapy to our Company. Members of our Board include: Mr. Hans Edgan Bishop, currently Chief Executive Officer of Grail, Inc., who among other things co-founded Juno in 2013 and acted as its Chief Executive Officer until 2018; Dr. Ann Li Lee, currently Senior Vice President and head of cell therapy development operations at Celgene; Dr. Krishnan Viswanadhan, currently Senior Vice President and global cell therapy franchise lead at Bristol Myers Squibb; and Dr. Cheng Liu, founder and Chief Executive Officer of Eureka.

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Shareholders and Partners

Strong support from our founding shareholders endows us with the best of both worlds. Juno brings excellence in the science of CAR-T therapies and the related technology platform, including its revolutionary engineered T-cell products and its experience and expertise in process development and manufacturing framework for CAR-T products. WuXi AppTec brings excellence in manufacturing processes (including vectors and supply chain) as well as strong knowhow, infrastructure, reputation, relationships and network of stakeholders in China.

OUR STRATEGIES

Drive full-scale commercialization of relma-cel and build upon our significant first mover advantage

Following the NMPA’s acceptance of our NDA relating to relma-cel, we intend to drive full-scale commercialization of relma-cel, with a specific focus on manufacturing, sales and marketing/academic education functions ahead of relma-cel’s upcoming launch:

Manufacturing. Our Suzhou manufacturing facility was approved by the Medical Product Administration of Jiangsu Province for cGMP manufacturing in June 2020. Based on our estimation, the facility is expected to service up to 5,000 patients annually, with capacity to expand further as needed. Quality is a key focus of our manufacturing approach, and we aim to translate our strong manufacturing record in the clinical setting, where we recorded a 100% success rate for the manufacture of relma-cel throughout the Phase II registrational clinical trial, into our commercial manufacturing efforts. We also plan to optimize our production protocols by leveraging our extensive clinical and CMC data derived from a single version of manufacturing process, building a proprietary data integration platform, and deploying machine learning approaches to develop critical insights for our autologous CAR-T therapy platform. In parallel, we are also developing our next-generation process to simultaneously improve our cost of goods, manufacturing cycle times, and potentially clinical outcomes.

Sales. We plan to build a focused in-house sales and marketing team to market relma-cel across China. Our initial target is to create, at the initial commercialization of relma-cel, a sales team of approximately 60-70 people to cover approximately 50 of the top hospitals in China with the best hematological and transplantation centers, which are equipped with the technology and physicians to administer our CAR-T therapies. In particular, we plan to set up sales and operations teams at the target hospitals to facilitate and administer the use of our products. These teams will ensure our CAR-T therapies are executed in accordance with the applicable standards and provide advice to the medical team at the site. A significant number of these hospitals have acted as clinical trial centers for relma-cel, as a result of which many relevant physicians in those hospitals

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will already be familiar with relma-cel. As our business grows over the next three years, we anticipate expanding our sales force to approximately 100-120 people in order to support the administration of our CAR-T therapies across the top 100 oncology hospitals in China.

Marketing/Academic education. CAR-T therapies are a new and comprehensive treatment process that is unlike any other treatment currently approved in the market. As such, we expect significant efforts will be necessary to educate physicians and patients on the potential benefits of CAR-T therapies, and to demonstrate the proper process for administering and monitoring the treatment (including timely and proportionate measures to mitigate adverse effects).

Because physicians are expected to play a key role in this process, not only in administering CAR-T therapies but also in educating patients about their potential benefits, we intend to design our marketing and academic education strategy around close and continued engagement with physicians. We believe that we have established strong relationships with a significant number of physicians and other KOLs across China through the extensive clinical trials that we have conducted, both in gaining recognition of the merits of relma-cel and in enhancing physicians’ familiarity with the product, and we plan on continuing to work with those physicians to optimize our product and processes even after we have commenced commercialization of relma-cel. In addition, we plan to be pro-actively involved in the policy making framework relating to cell therapy by actively participating in consultation sessions with the relevant authorities, particularly on improving medical procedures and standards.

We plan to enhance our existing collaboration with these physicians and other KOLs through the establishment of a specialized team for medical affairs, which will oversee the training and support that we provide to physicians. In addition, we plan to develop a specialized, standardized training program that will allow us to onboard and train physicians and treatment centers that have not been involved in our clinical trials, with the ultimate goal of gaining widespread acceptance of relma-cel across the medical community and the general public. We are also working with academic organizations in China to update the guidelines on lymphoma treatment to reflect the treatment results, and promote awareness, of relma-cel.

Solidify our leadership in hematological cancers by progressing and expanding clinical development of relma-cel for earlier lines of treatment and additional indications, as well as clinical development of JWCAR129

Having achieved NMPA acceptance of our NDA relating to relma-cel as a third-line treatment for DLBCL, we intend to further expand our hematological portfolio by conducting additional clinical trials for relma-cel for other indications and pursuing clinical trials for JWCAR129.

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Our approach to expand relma-cel’s indications involves two key pillars: advancing relma-cel into earlier lines of DLBCL treatment and developing relma-cel as a potential therapy for other hematological cancers that express the CD19 antigen.

- *Our earlier-line strategy:* As relma-cel has demonstrated strong efficacy and safety results during the clinical trials for third-line treatment of DLBCL, we believe relma-cel has the potential to be accepted for use in earlier lines of treatment where we are able to treat and benefit a broader population of patients with DLBCL. Our earlier-line strategy currently revolves around progressing relma-cel as a second-line treatment for DLBCL, in which we have commenced clinical trials in the third quarter of 2020.
- *Our indication expansion strategy:* As relma-cel has demonstrated strong efficacy and safety results in treating third-line DLBCL by targeting the CD19 antigen, we believe that relma-cel has the potential to treat and benefit a broader population of patients with other hematological cancers that also similarly express the CD19 antigen. We currently intend to conduct further clinical research with the goal of filing additional NDAs with the NMPA for approval of relma-cel for other hematological cancers, including FL, MCL, CLL and ALL. We believe that our unique CAR construct and manufacturing excellence potentially enable relma-cel to produce strong efficacy results and potential best-in-class safety results for treatment of other hematological cancers aside from DLBCL.

Furthermore, to expand our product portfolio and solidify our leadership in hematological cancers, we expect to file an IND in China for JWCAR129 as early as first half of 2021. As patients with MM are afflicted by frequent complications, for which there continues to be no viable cure, we believe that MM is a market with significant untapped potential. Our approach in tackling MM revolves around the BCMA, which is a proven and as such de-risked cellular target for the treatment of MM. In addition to our unique CAR technology, we believe our capabilities in process improvements and our manufacturing expertise potentially allow us to produce a differentiated product for the treatment of MM. In addition, we intend to explore novel approaches such as combination therapies with gamma secretase inhibitors and with other CAR-T products to further enhance the overall efficacy and safety of JWCAR129.

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Leverage our integrated cell therapy platform to expand into the emerging solid tumor market

We intend to complement our leading hematological franchise with a pipeline of innovative cell therapies for solid tumors. Our vision is to bring the latest cutting-edge cell therapies across all oncological indications for the benefit of Chinese patients, and we plan to continuously introduce new and novel technologies into our platform while leveraging our unique developmental capabilities to enhance our position in the emerging solid tumor segment.

Our solid tumor portfolio is headlined by the JWATM203 and JWATM204 platforms, two pre-clinical stage assets that are potential superior T-cell therapies for the treatment of HCC. We are currently in the process of conducting technology transfer for the two products, after which we plan to leverage our proprietary strengths in process development to further develop the JWATM203 and JWATM204 assets into potential novel treatments in HCC. We currently anticipate initiating IND-enabling studies as early as the first half of 2021, with a view to advance JWATM203 and JWATM204 into clinical trials and eventually widespread commercialization in China.

We also expect our expansion into the solid tumor market to benefit from our collaboration agreement with Lyell signed in August 2020. Lyell provides an approach to improving T-cell function to enhance initial response rates in solid tumors and to prevent relapses due to loss of T-cell functionality. We believe there is an opportunity to use these technologies as a platform for multiple new cell therapies that can be applied across a broad range of rare and prevalent solid cancers, including HCC as well as others.

In addition, our solid tumor portfolio is further augmented by our option to acquire from Acepodia a novel allogeneic NK product that targets the antigen HER2, which is expressed in some breast and gastric cancers. While the current CAR-T therapy landscape has focused on primarily on treatments within the hematological cancer space, we believe that solid tumors represent a significant, untapped market opportunity for cell therapies in China.

The market for cell therapies targeting solid tumors represents a key part of our future growth strategy. As such, in addition to our existing and potential pipeline, we intend to continuously seek out new and novel approaches to solid tumors, both internally through our discovery platforms and externally through potential in-licensing and acquisitions opportunities.

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Continuously enhance our manufacturing and supply chain through innovation and scale

Our manufacturing facilities in Suzhou are equipped with the technology to support a full range of cell platforms including those using autologous T-cells and NK cells, TILs, allogeneic immune cell approaches, as well as a facility for clinical grade viral vector production. Given the specific technical and personalization requirements in manufacturing CAR-T therapies, we intend to manufacture all of our treatments in-house, where we have control over the quality consistency, technology and execution of the entire manufacturing process.

Our current manufacturing processes have so far demonstrated a 100% success rate for the manufacture of relma-cel throughout the Phase II registrational clinical trial. However, we intend to invest in further optimizing our manufacturing processes through technological enhancements and achieving economies of scale, with the ultimate goal of making the production of our cell therapies better, faster and more cost-effective.

One of our key initiatives in optimizing our manufacturing has been our “Nex-G” strategy, which is aimed at reducing manufacturing costs, in order to make cell therapies accessible to a broader segment of the population. Through our “Nex-G” strategy, we aim to significantly lower the cost of our cell therapies, while maintaining and enhancing the efficacy, safety and overall quality of our products. This strategy includes:

- Leveraging our extensive clinical and CMC data derived from a single version of manufacturing process, we are building a proprietary data integration platform, and deploying machine learning approaches to develop critical insights for our autologous CAR-T therapy platform. We are developing our next-generation process to simultaneously improve cost of goods, manufacturing cycle time, and potentially clinical outcomes.
- Significantly reducing cost of raw materials by eliminating wastes and scraps; as well as pursuing substitutions by lower cost materials and elimination where feasible.
- Securing a world-class, high-quality and cost-effective supply network; and establishing long-term supply agreements in order to simultaneously achieve lower costs and increase reliability.
- Leveraging economies of scale by expanding our scale through opening up additional modules for commercial use within our existing facilities.

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Grow our business through in-licensing opportunities, partnerships and selective acquisitions, as well as in-house research and development

Since the establishment of our Company, we have utilized a mix of in-licensing opportunities from our partners, selective acquisitions sourced through our business development capabilities and in-house R&D to fuel our growth into a leading cell therapy player in China. We intend to continue our three-pronged approach to expand into new frontiers in cell therapy, as we believe our strategy combines the ability to leverage from our trusted, reputable partners with an established track record in the cell therapy industry, identify and develop a select group of cell therapies which we believe has the potential disrupt existing standards of care and discover novel approaches to cell therapy using our proprietary know-how.

Our in-licensing approach. We have leveraged our exclusive licenses of certain China rights from Juno to introduce relma-cel and JWCAR129 into our pipeline, and we intend to explore other opportunities with Juno through our right of first negotiation on Juno’s engineered T-cell products.

Our selective acquisitions approach. Additionally, we intend to continue to accelerate our business growth through in-licensing of suitable product rights and selective acquisition of suitable companies. Our recent acquisition of Syracuse Hong Kong and our recent collaboration agreement with Lyell exemplify this approach. We believe we have established a reputation in China as a preferred partner in cell therapy due to our proprietary platform and clinical track record, and we plan to leverage our global platform and network to focus on potential opportunities in the cell therapy space that we deem to possess high growth or breakthrough technology potential that is currently outside our platform. These potential opportunities include but are not limited to growth opportunities in alternative allogeneic approaches and new cellular targets which we believe represent novel and groundbreaking approaches to the treatment of cancer.

Our in-house R&D approach. In-house research and development is a core part of our platform. Since the establishment of our Company, research and development with respect to our processes as well as our products has played an instrumental role in our growth. We intend to continue to invest in our R&D capabilities to further fortify our end-to-end cell therapy platform. Given that we believe we possess differentiated strengths in product development, we plan to continue focusing a significant part of our R&D efforts on the clinical development and execution of our in-licensed products, and on enhancing our manufacturing capabilities to deliver affordable, high-quality treatments to patients. However, we also have significantly enhanced our discovery platform through acquisition in June 2020 of certain rights to use Eureka’s ARTEMIS and E-ALPHA platforms, and we intend to leverage on our enhanced discovery platform to potentially identify and develop the next groundbreaking solution in cell therapy.

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Finally, in addition to our three-pronged approach, we plan to continue to leverage our network of strategic partners including Juno and WuXi AppTec, leaders in the cell therapy field and the CRO field, respectively, as we continue to advance into new, undiscovered cellular targets and treatments.

BACKGROUND ON CANCER AND THE IMMUNE SYSTEM

Cancer is characterized by the uncontrolled proliferation of abnormal cells and is the second leading cause of death worldwide. Cancer cells contain mutated proteins and may overexpress other proteins normally found in the body at low levels. For decades, nearly all forms of cancer have been treated with surgical resection, radiation therapy, systemic chemotherapy or other anti-tumor agents. While these treatment modalities and their combinations, have led to incremental improvements in the survival of cancer patients, many patients still have cancer that does not respond or does not respond well to these traditional approaches. Furthermore, each of these treatment modalities is associated with significant adverse events that can also result in significant patient morbidity and mortality. Over the past decade, cancer immunotherapy, a new pillar of cancer therapy has emerged that focuses on the patient’s own immune system to treat cancer. Cancer immunotherapy includes checkpoint inhibitors, therapeutic cancer vaccines and cytokines, and cellular immunotherapies, which use a patient’s own immune cells themselves to fight cancer.

The immune system recognizes danger signals and responds to threats at a cellular level. It is often described as having two arms. The first arm is known as the innate immune system, which recognizes non-specific signals of infection or abnormalities as a first line of defense. The innate immune system is the initial response to an infection, and in some cases cancer cells, and the response is the same every time regardless of prior exposure to the infectious agent. One key part of the innate immune system is the NK cell. The second arm is known as the adaptive immune system, which is composed of highly specific, targeted cells that can provide long-term recognition and protection not only from infectious agents but also from abnormal processes such as cancer. The adaptive immune response is further subdivided into humoral, or antibody-based, and cellular, which includes T-cell-based immune responses. Both NK cells and T-cells have the ability to kill tumor cells and can be used to target and treat cancers in patients.

The most significant components of the cellular aspect of the adaptive immune response are T-cells, so called because they generally mature in the thymus. T-cells are involved in both sensing and killing infected or abnormal cells, as well as coordinating the activation of other cells in an immune response. These cells can be classified into two major subsets, CD4+ T-cells and CD8+ T-cells, based on cell surface expression of CD4 or CD8 glycoprotein. Both subsets of T-cells have specific functions in mounting an immune response capable of clearing an infection or eliminating cancerous cells. CD4+ T-cells, or helper T-cells, are generally involved in coordinating the immune

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response by enhancing the activation, expansion, migration, and effector functions of other types of immune cells. CD8+ T-cells, or cytotoxic T-cells, can directly attack and kill cells they recognize as infected or otherwise abnormal, and are aided by CD4+ T-cells. Both types of T-cells are activated when their T-cell receptor recognizes and binds to a specific protein structure expressed on the surface of another cell. This protein structure is composed of the major histocompatibility complex (“**MHC**”) and a small protein fragment, or peptide, derived from proteins either inside the cell or on the cell surface. Circulating CD4+ and CD8+ T-cells survey the body differentiating between MHC/peptide structures containing “foreign” peptides and those containing “self” peptides. A foreign peptide may signal the presence of an immune threat, such as an infection or cancer, causing the T-cell to activate, recruit other immune cells, and eliminate the targeted cell.

Unlike the adaptive immune response involving T-cells, the innate immune system, involving NK cells, is ready-made to kill foreign cells without prior exposure to an infectious agent or a cancer cell. These cells are present in blood, bone marrow and tissues, and survey the body looking for general signals of abnormal or infected cells, such as a lack of some normal cell surface proteins. Fundamentally, NK cells have evolved to kill a cell unless it expresses proteins that inhibit the NK cells’ killing machinery. Most viral infections and cancer cells tend to down regulate these inhibitory cell surface proteins because these same surface proteins are needed to allow the adaptive immune response to recognize and kill the abnormal cell. Therefore, NK cells are a complementary defense mechanism to the adaptive immune response.

Although the immune system generally is able to identify foreign or abnormal proteins expressed on tumor cells, this process often turns out to be defective in cancer patients. The defective process sometimes occurs when the cancer cells closely resemble healthy cells and go unnoticed, or if tumors lose the expression of the protein being targeted by the immune system. Additionally, cancer cells employ a number of mechanisms to escape immune detection or to suppress the function of these immune cells. Some tumors also encourage the production of regulatory T-cells that block cytotoxic T-cells that would normally attack the cancer.

To override some of these processes, the novel technology of CAR-T was developed over the past ten years. CAR-T are T-cells that have been genetically engineered to express a receptor made up of parts of several proteins (a so-called chimeric antigen receptor or “**CAR**”), which re-direct the T-cell to attack a target protein on tumor cells through a stronger activation signal provided by the CAR. These CAR-T have been demonstrated to be effective in specific r/r patients with hematological malignancies with high rates of durable complete responses, suggesting these patients may be cured. As a result, several CAR-T products, such as axicabtagene ciloleucel, tisagenlecleucel, lisocabtagene maraleucel and idecabtagene vicleucel, have been approved or are

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expected to be approved by regulatory authorities in the US and EU to treat many types of lymphoma, leukemia or myeloma. Therefore, CAR-T therapies in these settings have been a revolutionary advance for patients.

However, despite the hope in cancer treatment provided by CAR-T, there remains unmet medical need. For example, not all eligible patients have access to these therapies either due to limited manufacturing capabilities or to a lack of appropriate clinical evaluation in specific regions, such as Asia. In particular, these early commercial manufacturing processes were not fully optimized to produce functional and robust T-cell products, in part, because the relationships between manufacturing changes and key clinical outcomes were not known even though the processes had to maintain short production time and low production failure rates.

Furthermore, we believe existing CAR-T therapies can be further improved. For example, FDA- and EU-approved CAR-T therapies are associated with potentially fatal adverse effects during the first month after treatment, requiring the treatment to take place only at specialized centers and limiting their access to a broader range of patients. For example, registrational studies of axicabtagene ciloleucel and tisagenlecleucel in patients with DLBCL had between 15-25% ICU utilization due mostly to CAR-T toxicities, and early real-world experience with axicabtagene ciloleucel reported a 30-35% rate of ICU use in a similar population. Hospital or ICU utilization as a result of these toxicities can be a significant added cost to a healthcare system. Newer CAR-T products, such as relma-cel, have demonstrated lower levels of these common toxicities, reducing the risk to patients and reducing the cost of care, and, in some cases, even permitting broader sites of delivery (such as outpatient settings or hospitals without previous experience with CAR-T therapies), which improves access to these novel agents. We believe that such improvements in the safety profile of CAR-T therapies may be driven by advancements in the methods of manufacturing processes and controls.

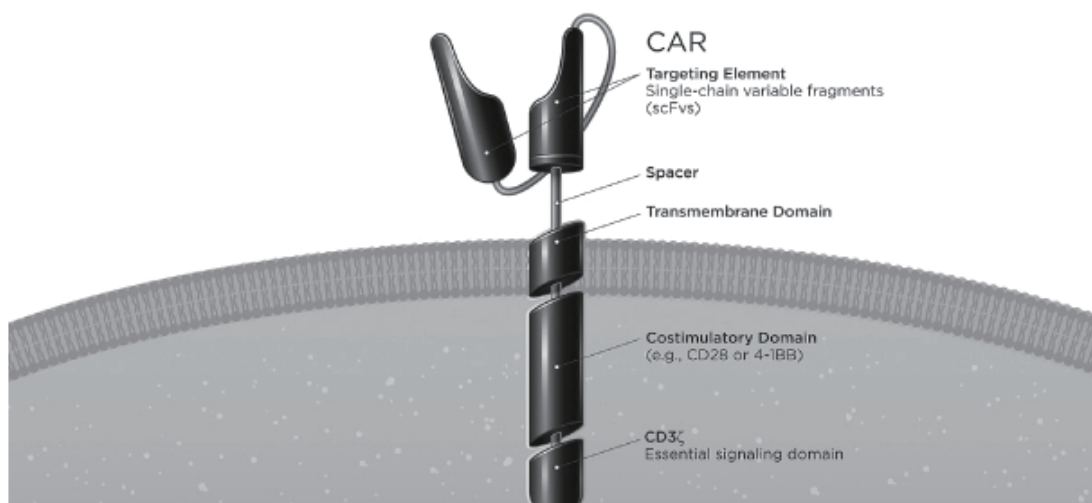
While there are many unique clinical benefits associated with CAR-T therapies, there is room for improvement. In studies of T-cell therapies against solid tumor targets, attempts to treat a wider range of cancers with CAR-Ts directed against novel solid tumor targets have failed to show significant treatment effects beyond anecdotal cases. These shortcomings are likely to be the result of immune evasion mechanisms associated with tumors that have not been fully characterized and CARs targeting proteins that are not expressed at high enough levels. Attempts to re-engineer CAR-T to either avoid or overcome these mechanisms are now being identified and tested in animal models and early phase clinical trials and we anticipate that some of these will be the key to the next generation of CAR-T therapies, and immune cell therapies, in general. The health of CAR-T in the manufacturing process may also be important in providing a product that can overcome these barriers with sufficient persistence in the body to clear a patient’s cancer. Thus, both manufacturing technology and biological innovation are fundamental to the next generation of immune cell therapy products for cancer.

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OUR T-CELL AND IMMUNE CELL TECHNOLOGIES

Overview

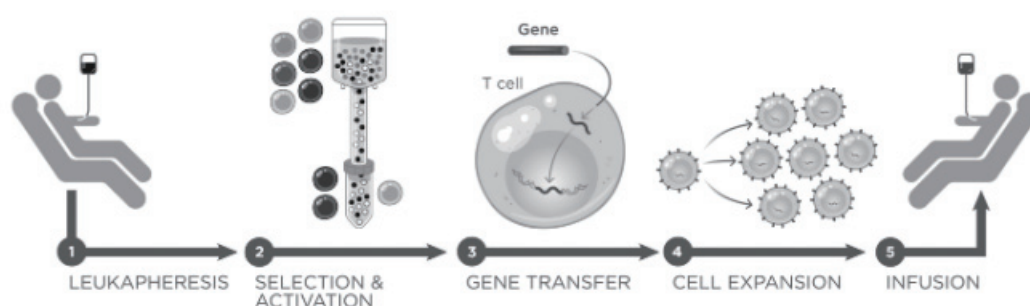
CAR-T therapy involves genetically modifying T-cells *ex vivo* to better recognize tumor-associated surface proteins (i.e., glycoproteins or glycolipids that are expressed abundantly on the surface of tumor cells but in relatively small quantities on the surface of normal cells) or normal cell surface proteins that are also expressed on tumors but if eliminated pose no significant health risk to the patient (such as B cells). After transduction, purification and large-scale expansion, CAR-T can specifically identify tumor-associated antigens so that the ability to target, antitumor activity and durability of effector T-cells are significantly enhanced as compared to unmodified T-cells. The extracellular portion of a CAR protein usually consists of mouse-derived single-chain variable fragments (scFv) that recognize target antigens (e.g., CD19). The intracellular portion of a CAR protein contains a T-cell signal transduction (CD3- ζ) domain and a costimulatory domain (e.g., CD28 or 4-1BB). Each intracellular domain plays an important role in T-cell expansion, CAR-T survival *in vivo*, and T-cell activation required for antitumor activity *in vivo*. Once the CAR protein binds to the target antigen on the cell surface, the intracellular domain can promote CAR-T expansion and trigger subsequent effector functions that eliminate tumor cells. These T-cells have an “auto-regulatory” capability that stimulates their multiplication in the presence of the target protein and a reduction in the number of such cells as the target protein declines. The following diagram illustrates the structure of a CAR protein.



Source: Company Information

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Our current portfolio of product candidates comprises novel cell therapies against hematological malignancies and solid tumors. Our CAR-T technologies provide personalized therapy for patients by altering T-cells *ex vivo*, or outside the body, so that the T-cells can recognize specific proteins on the surface of cancer cells or other diseased cells in order to kill those cells. As depicted below, (1) we harvest a patient’s white blood cells in a process called leukapheresis, and (2) while *ex vivo* we select and activate certain T-cells of interest. (3) Gene sequences for the CAR construct are transferred into the T-cell DNA using a viral vector, such as a lentivirus. (4) The number of cells is expanded until it reaches the desired dose. (5) These genetically engineered cells are then infused back into the patient. The following indicates the flow of the personalized therapy for patients using our CAR-T technologies.



In our clinical trials with our lead product candidate, relmacabtagene autoleucel or “relma-cel,” after a patient goes through leukapheresis, the patient is administered chemotherapeutic agents before infusion of the engineered T-cells in order to provide an environment for the engineered T-cells to thrive. We refer to this process as conditioning chemotherapy or lymphodepletion. It is an active area of research to determine the optimal lymphodepletion regimen to use in conjunction with engineered T-cell therapy, in terms of dose, duration, and type or combinations of chemotherapeutic agents, such as cyclophosphamide or fludarabine. Currently, we effectively utilize what we believe to be the lowest intensity lymphodepletion in the field that is effective, while seeking to minimize potential toxicity from this chemotherapy. This regimen is a modification of doses used for pediatric patients and administered over three days.

We believe that optimizing immune cell attributes and preserving cell function and homing of cell products used in treatment may have a significant impact on cell persistence, efficacy, and/or tolerability, particularly when addressing the use of these cell therapies with solid tumors. We are investing significant resources in understanding the optimal cells and cell conditions for treatment. Animal study data have shown that specific cell attributes or genetic modifications can improve the frequency, robustness, and duration of an anti-tumor response. Animal data have also shown that certain genes, when introduced, allow T-cells to persist without exhaustion of their function, which may lead to a longer duration of the therapeutic effect in patients.

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Immunogenicity reactions occur with any biological therapeutic (e.g. antibody therapy, protein therapy, cell therapy) and generally speaking do not impact dosing, efficacy or safety. For relma-cel, the CAR construct binder is derived from mouse sequences, which may generate cellular immunity and antibody responses once infused. Our therapy uses lymphodepleting chemotherapy ahead of the single infusion to significantly reduce the risk of CAR-T rejection. Patients may have pre-existing or develop antibody responses to relma-cel, but there is no clear evidence that this impacts the product’s efficacy or safety. Regarding dosing frequency, this is a single dose product for all patients (see “— Our Product Pipeline — Our Core Product Candidate — relmacabtagene autoleucel (“**relma-cel**”) — Market Opportunity and Competition — Current Treatment Options and Limitations — Treatment-related”).

Keys to Further Advances in CAR-T Therapies

Despite the advancements in the field, there remain a number of keys to further advances in the development of CAR-T therapy.

- ***Selecting an appropriate tumor antigen target and having access to quality targeting elements (“binders”):*** the antigen targets that are recognized by CAR-T are membrane-bound cell surface proteins/complexes. Limited distribution in normal tissue, over- or homogeneous expression in tumors, and lack of shedding or internalization are critical factors related to the target antigen that need to be considered for target selection for developing CAR-T therapies. While expression of target antigens on normal tissues increases the risk of on-target/off-tumor toxicity, reduced or loss of expression due to shedding or internalization on tumor cells can decrease the treatment efficacy. The most important key is having access to binders that can be used with any number of unique CAR or TCR approaches. Few cell therapy companies have the internal capability or access through partnerships to both (1) the means to efficiently screen binders of a specific target and (2) a broad and robust library of binders from which to select lead and back up development candidates for their CAR constructs against tumors. Without this capability or access, companies would not be able to easily expand their portfolio into new indications or against novel targets.
- ***Designing and selecting CAR constructs to optimally activate T-cells, preserve T-cell function, and infiltrate tumors to promote tumor cell killing:*** the properties of the CAR construct are crucial to the overall success of CAR-T therapy. The affinity and flexibility of the antigen binding domain(s) are important in enhanced tumor-specific recognition as noted above, however the co-stimulation during CAR-T activation regulates metabolism, survival and functions of T-cells. A common side effect with CAR-T therapy is excessive T-cell activation when encountering its target antigen that can result in toxicities known as cytokine release syndrome (or “**CRS**”), a

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life-threatening condition caused by high levels of inflammatory cytokines, or a range of neurological toxicities that can range from confusion to potentially fatal seizures and coma. These adverse events may result either from the manufacturing process or from the CAR construct used.

Moreover, while CAR-T therapies have been effective in treating hematological malignancies, this approach has been rarely effective against solid tumors. Much of the challenge in treating solid tumors appears to result from a lack of CAR-T “homing” to the site of the tumor, as well as the ability of these tumors to render the CAR-T dysfunctional due to chronic but incomplete activation signaling. This process, often referred to as T-cell “exhaustion,” is believed to be part of the reason a patient’s immune system cannot clear their tumor. Both of these mechanisms are likely important in developing effective CAR-T therapies for solid tumors. Recently, it has been discovered that use of specific novel CAR co-stimulatory signals can significantly increase T-cell infiltration into tumors in animal model systems. Further, other studies have shown that specific internal cell signals can override the mechanisms of T-cell exhaustion and potentially also increase tumor infiltration. Therefore, to develop potentially effective and safe T-cell therapies against solid tumors, it is important to have an optimal genetic modification of a T-cell product through the right CAR construct and internal cell signaling.

- ***Having experience and capabilities to produce commercial and clinical products for timely clinical development and regulatory approval:*** Manufacturing of CAR-T therapies is difficult due to the variability of cells collected from individual patients. Limited economies of scale can be realized given the bespoke nature of autologous CAR-T manufacturing. A robust manufacturing process is important to account for variability in patient characteristics and ensure consistent product quality.
- ***Having commercial-ready manufacturing infrastructure:*** We manufacture in China with a commercial-ready, highly automated, single train process to select, activate, transduce and expand CAR-T with consistent product attributes and to manufacture any specified cell dose with capacity to deliver a prescribed product over a wide dosing range. Key challenges with CAR-T manufacturing today include maintaining consistent quality across different batches. We have designed our manufacturing processes to optimize these factors for our products and to ensure high consistency of product attributes, and have achieved a 100% manufacturing success rate throughout the DLBCL registrational clinical trial of relma-cel. Our manufacturing process is based on a unit operations concept with an automated and standardized device for each unit operation, which minimizes human error and improves efficiency. We adopt closed processing manufacturing, which prevents contamination and allows concurrent processing of multiple patient samples in a large “ballroom” with lower grade cleanroom

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requirements. We have also implemented a computerized manufacturing execution system which ensures a robust traceability/chain of identity, and further prevents error and lowers production costs.

- ***Having experienced site support and robust product supply chain infrastructure to maintain chain of identity and ensure proper and safe product administration to conduct high quality multi-center clinical trials and commercialize approved products:*** Individualized cell therapy products require the robust processes to schedule, collect, and securely ship patient derived materials collected during apheresis as a raw material for the manufacturing process. Equally robust processes are needed to securely ship and track cryopreserved product back to the patient since the product can only be used for that individual. Collectively, these process steps and the tracking of patient material and cell product is known as the chain of identity. A manufacturer must have these processes in place, and must also have systems that can track multiple patients at different points in the process, to not only permit proper monitoring but also allow for coordination with treatment centers to arrange for patient preparation and care. These processes and systems are a large up-front investment in the T-cell therapy field, especially when manufacturing is required for more than one site of delivery. We have not only established these processes but also conducted large multicenter trials in China to validate these systems.
- ***Having clinical, translational, regulatory support experienced in T-cell therapy of cancer to both properly train site personnel, effectively manage T-cell therapy product development in oncology and minimize potential toxicities of CAR-T therapies, including those that may arise in patients with solid tumors:*** CAR-T therapy is unlike most cancer therapeutic agents in that it is (1) an individualized therapy — i.e., an individual lot product is made for only one specific patient, (2) a living therapy — i.e., the cells expand after infusion into the patient from the administered dose to hundreds or thousands of times the original dose, and (3) a novel therapy — i.e., to date, not many hospitals or clinics have managed these products. The need to have experienced staff to manage sites, help manage administration and potential adverse events, to conduct translational research with quality sample collection and analytical assays is critical to the success of a CAR-T development program as well as having the ability to translate that experience into medical support for sites using commercial products in the future.

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In addition, in China specifically, but also in other parts of the world, the regulatory landscape is still being developed, including key regulatory requirements as well as engaging with regulators having only an early foundational understanding of the potential risks, benefits, use and manufacture of these novel products, including knowledge of the potential differences between CAR-T products. For example, given the uniqueness of CAR-T and human cell therapies and that the regulatory pathway for such therapies is still evolving in China, standardization for CAR-T therapies is difficult to achieve and therefore approval would be assessed on a case-by-case basis. In China today, this expertise cannot be reliably contracted and most often needs to be built as internal capabilities as there is limited cell therapy expertise within the country. We have built our internal clinical, translational and regulatory capability and fostered an early and active engagement with Chinese regulatory authorities to educate, guide and establish relevant and necessary standards in this field for China. As a result, we have conducted clinical studies under IND involving more sites in China than any other CAR-T company as of the Latest Practicable Date, according to Frost & Sullivan, and had our NDA submission of the data from the study accepted for review in days following submission. China has a dual-track regulatory approval pathway for conducting T-cell therapy clinical trials. The first pathway is approval as a healthcare clinical study, which is managed by the NHC. The second pathway is to register as a biological drug, which requires an IND, registrational clinical trial and NDA approval by CDE/NMPA prior to commercialization. For more details, see “Regulatory Overview — Regulations on Human Cell Therapy” in this document. We initially started pilot studies through the IRB process, because the IRB studies allow early access to patients with critical clinical needs which provide data that can support the IND study design and filing, before switching our studies to the classic registrational pathway upon receiving the IND approval from the NMPA. We have insisted from the beginning that all trials be conducted under the GCP as codified in international guidelines.

Finally, cell therapy by its nature requires the capability to integrate and analyze data from multiple separate sources — including manufacturing, clinical and translational data sets, even though data from these different functions are rarely analyzed for associations or correlations between them. In cell therapy, this capability is essential to both understand the T-cell product, and improve on platform and future technologies.

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Components of our Technology

We believe that our technology distinguishes us from many other cell therapy companies based on our ability to enable current generation CAR-T in hematological malignancies, advance novel platforms to overcome hurdles in treating solid tumors with immune cell therapies and leverage our knowledge, and our experience and know-how in manufacturing, to continually improve our cell therapy products. There are several key components to our technology, each of which may have a significant impact on its utility in cancer immunotherapy:

- ***Targeting Elements and Their Selection.*** Targeting elements, also referred to as a binding domain, are used to recognize a target protein of interest. Our targeting elements can be used either as a single chain variable fragment (“scFv”) in a classic CAR design or as a split or two chain variable fragments for attaching to each TCR subunit transmembrane element. These targeting elements are derived from the portion of an antibody that specifically recognizes a target protein, and when they are expressed on the surface of a T-cell and subsequently bind to a target protein on a cancer cell, are able to activate the T-cell. For example, our lead CAR-T program uses a scFv from a mouse-derived antibody to target the B-cell surface protein CD19, but others have human-derived sequences. Our pipeline currently contains T-cell therapies using targeting elements to CD19, BCMA, AFP and GPC3. While most of our targeting elements recognize cell surface proteins, some are TCRs, which can recognize small peptide fragments of proteins inside the tumor cell presented on the cell surface by a specific tissue protein (known as MHC) through a natural cell process.
- ***Classic Constructs.*** Upon recognition and binding of the targeting element to the cancer cell, there is a conformational change that leads to an activation signal to the CAR-T through CD3-zeta, an intracellular signaling protein. We intend to use both classic and next generation CAR/TCR mimic constructs. Our initial CAR constructs are classic CAR constructs based on Juno design. Our classic CAR constructs contain the targeting element CD3-zeta and a co-stimulatory domain all together in the same chimeric protein. These classic CAR constructs include the 4-1BB costimulatory signaling domain used to mimic a “second signal” that amplifies the activation of the CAR-T. There are other co-stimulatory domains that have been used in classic CAR-T, such as CD28; however, while head-to-head clinical comparisons have not been conducted, in some disease settings some pre-clinical and early clinical evidence has suggested that 4-1BB has some advantages over CD28 as a costimulatory domain, including increased persistence and a metabolic profile supporting gradual expansion, as opposed to rapid expansion often associated with severe CRS and NT. Our early clinical data with our lead anti-CD19 CAR-T candidate supports this view. We have incorporated the 4-1BB costimulatory domain into our first two cell therapy products, relma-cel and

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JWCAR129. These two classic constructs for CD19 and BCMA, respectively, have been evaluated in the clinic, and for relma-cel, these data were submitted to NMPA as part of our NDA application. For further information on relma-cel and JWCAR129, please see “— Our Product Pipeline — Our Core Product Candidate — relmacabtagene autoleucel (“relma-cel”)” and “— Our Product Pipeline — JWCAR129” in this section.

- ***Novel Constructs.*** We have licensed Eureka Technologies’ novel construct platform consisting of the ARTEMIS antibody TCR and solid tumor technology. This platform has two core functional components: (1) antibody-based antigen-binding domain and (2) TCR-based effector domain. The design of the ARTEMIS receptor allows it to engage intrinsic cellular response and regulatory mechanisms normally employed by endogenous TCRs. Use of the endogenous activation through the TCR/CD3 complex is thought to limit excessive T-cell expansion associated with CRS. Because the design does not directly couple intracellular signaling domains to co-stimulatory domains, such structure has the potential to avoid T-cell hyperactivation and classic CAR-T associated toxicities, such as CRS.

ARTEMIS receptors are designed to provide a potentially more effective T-cell therapy. Specifically, the ARTEMIS platform has been shown to enhance the functionality of T-cells to fight cancer cells in solid tumor models, in part through a novel co-stimulatory domain that has been associated with greater tumor infiltration of T-cells. T-cell products manufactured using the ARTEMIS platform have been used in early phase clinical trials and demonstrated preliminary safety profile.

- ***Self-activating lentiviral vectors.*** Gene-modification of T-cells has primarily been done with the use of a retroviral vector. All of our retroviral vectors are self-activating lentiviral vectors which provide a potentially safer cell product with regards to genotoxicity and infection from replication competent retrovirus (“**RCR**”). Lentiviral vectors have been used in a number of clinical trials of gene-modified T-cells and pluripotent stem cells without any case of cell product transformation or RCR. Given the limited amount of retroviral genetic material to integrate into cells with the use of these vectors, patients who may otherwise harbor other RNA viruses, such as the hepatitis C virus, may also be candidates for future cell therapies.

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- *Technologies to improve the function of our T-cell products*

Lyell provides an approach to improving T-cell function to enhance initial response rates in solid tumor cancers and to prevent relapses due to loss of T-cell functionality. Lyell’s technology, in combination with the AFP and GPC3 ARTEMIS T-cell products, is intended to create a potentially differentiated treatment for HCC by enhancing T-cell infiltration into tumor regions, increasing T-cell functionality, and reducing T-cell exhaustion in the tumor micro-environment to improve anti-tumor therapeutic effects. For further information on Lyell’s technology, please see “— Our Product Pipeline — Our Solid Tumor Platform — Lyell Technology” in this section.

Next-Generation CAR Technology



We are investing significant resources in business development to leverage our expertise and capabilities to secure additional technologies, as we believe these will be the key determinants to ensure the long-term ability to create novel CAR-T products with improved patient benefit. One such technology extends our pipeline beyond autologous T-cell therapy candidates. We have the option to acquire from Acepodia the rights in China, Hong Kong and Macau to develop, manufacture and commercialize an allogeneic NK product (“**JWACE002**”) that targets an antigen called HER2, which is expressed in some cancers, including 20 to 30% of breast cancers and 10 to 15% of gastric cancers. Unlike other allogeneic approaches, JWACE002 does not require time-consuming and expensive genetic editing of the allogeneic immune cells extracted from the patient to manufacture the final product. In addition, it utilizes a unique proprietary method which uses a binding element to re-direct NK cells against a tumor target that does not require a viral vector transduction and may be used with binding elements against tumor targets beyond HER2. JWACE002 has demonstrated enhanced tumor cell killing activities both *in vitro* and *in vivo*, while maintaining a favorable safety profile in GLP toxicology studies. In pre-clinical studies JWACE002 has shown enhanced tumor kill efficacy against HER2 IHC 1+, 2+ and 3+ cancer cells, which may have broader coverage on different HER2 expression level compared to Herceptin. JWACE002 is an innovative product that just entered early phase clinical trials in the US which are expected to provide near-term data to support our development of this platform.

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OUR PRODUCT PIPELINE

Overview

The following chart summarizes the development status of each of our cell-based immunotherapy product candidates to treat hematological cancers and solid tumors as at the Latest Practicable Date. All of the product candidates in the following chart are autologous cell therapies.

	Product	Target	Indication	Commercial Rights	Pre-clinical	IND	Phase I	Pivotal / Phase II	Pivotal / Phase III	NDA	NMPA Classification	Partner
Hematologic Malignancies	JWCAR029 / Relmacabtagene Autoleucel (relma-cel) +3	CD19	3L DLBCL	China, Hong Kong, Macau	Submitted in June 2020 and received priority review in September 2020						Category I	JUNO Bristol Myers Squibb Company
			3L FL	China, Hong Kong, Macau	Registrational trial							
			3L MCL	China, Hong Kong, Macau	Registrational trial							
			2L DLBCL	China, Hong Kong, Macau								
			3L ALL	China, Hong Kong, Macau								
			3L CLL	China, Hong Kong, Macau								
	JWCAR129 ⁴	BCMA	r/r MM	China, Hong Kong, Macau	IND enabling					Category I	JUNO Bristol Myers Squibb Company	
	Nex-G	CD19	NHL	China, Hong Kong, Macau						Category I	JUNO Bristol Myers Squibb Company	
Solid Tumors	JWATM203	AFP	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN		2					Category I	EUREKA
	JWATM213 ¹	AFP	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN							Category I	EUREKA 
	JWATM204	GPC3	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN							Category I	EUREKA
	JWATM214 ¹	GPC3	HCC	China, Hong Kong, Macau, Taiwan, and member countries of ASEAN							Category I	EUREKA 

Abbreviations: DLBCL = diffuse large B-cell lymphoma; FL = follicular lymphoma; MCL = mantle cell lymphoma; ALL = acute lymphoblastic leukemia; CLL = chronic lymphocytic leukemia; MM = multiple myeloma; NHL = non-Hodgkin lymphoma; HCC = hepatocellular carcinoma; NSCLC = non-small cell lung cancer; r/r = relapsed or refractory; 3L = third-line; 2L = second-line

* Denotes a Core Product Candidate.

¹ Developing using Lyell technology.

² JWATM203 is currently in Phase I/II trial in the U.S. conducted by Eureka under an IND.

³ Relma-cel is based on the same CAR construct as Juno’s product lisocabtagene maraleucel (liso-cel), which is the subject of a BLA currently under review by the U.S. FDA.

⁴ JWCAR129 is based on the same CAR construct as Juno’s product orvacabtagene autoleucel (orva-cel), which is currently the subject of a Phase I/II clinical trial in the United States.

According to Frost & Sullivan, in 2019, in China, the cancer incidence reached approximately 3.1 thousand cancer patients per million people. Additionally, in 2019, the total cancer incidence reached approximately 4,400 thousand, among which approximately 200 thousand are hematological cancers accounting for 4.5% of overall cancer incidence in China. Clinical trials for CAR-T product candidates are still predominantly for hematological cancers. According to Frost & Sullivan, as of July 31, 2020, only one CAR-T product had initiated clinical trials in China for solid tumors, while the remaining 15 clinical trials are for hematological cancers.

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Our Core Product Candidate — relmacabtagene autoleucel (“relma-cel”)

Overview

Relma-cel is a potential superior autologous CAR-T therapy that targets the CD19 antigen, which is expressed in a broad range of B-cell hematological cancers including DLBCL, FL, MCL, CLL and ALL. While head-to-head clinical comparisons have not been conducted, available clinical data as of the Latest Practicable Date suggest that relma-cel has the potential to achieve best-in-class safety results, with comparable efficacy results relative to peers in China. We have developed relma-cel using our own optimized processes, which we originally established in collaboration with Juno; and relma-cel is based on a CAR construct that we have in-licensed from Juno for China, Hong Kong and Macau. For further information on the terms of our in-licensing arrangements relating to relma-cel, please see “— Collaboration and License Agreements — License Agreements with Juno — Relma-cel” in this section.

Through relma-cel, we are an early entrant into the cell therapy industry in China. In June 2018, with our IND for relma-cel, we became the first company to have an IND approved by the NMPA for clinical trials of an anti-CD19 CAR-T therapy in China. In June 2020, our NDA for relma-cel as a third-line treatment for DLBCL was submitted to and accepted for review by the NMPA, and in September 2020 the NMPA granted priority review status to our NDA relating to relma-cel and Breakthrough Therapy Designation for relma-cel as a treatment for FL. If approved by the NMPA for marketing in China on the timeline that we currently anticipate, relma-cel would be the first CAR-T therapy approved as a Category 1 biologics product in China, and has potential to be a superior CAR-T therapy.

Additionally, to fully explore the clinical potential of relma-cel, we are also developing relma-cel for a number of hematological indications, including third-line treatment for FL, and pediatric ALL, a third-line treatment for MCL and as a second-line treatment for DLBCL.

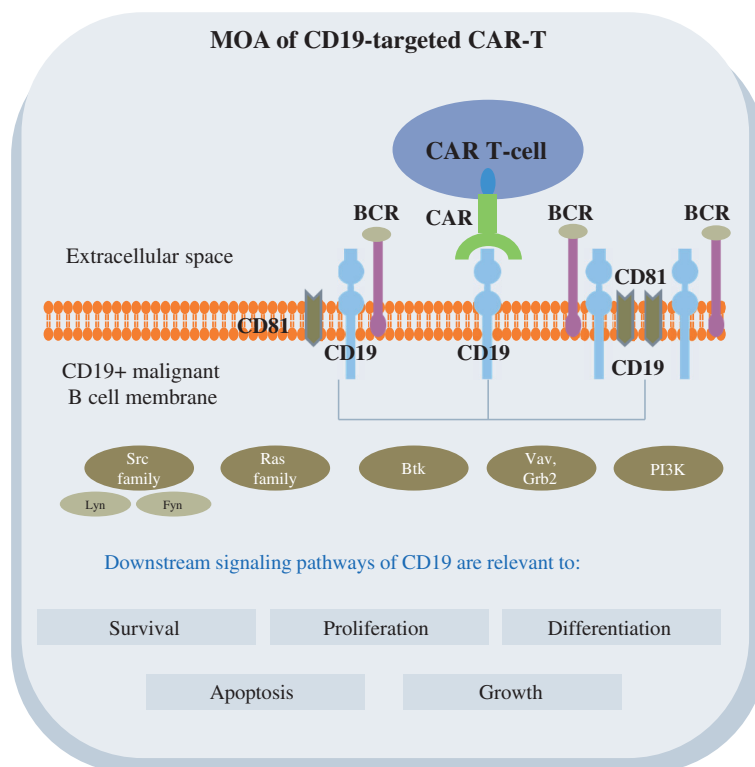
From acceptance of our NDA for relma-cel by the NMPA in June 2020 through and including the Latest Practicable Date, we have not received any concerns or objections from the NMPA on our clinical development plans, nor have any material unexpected or adverse changes occurred since the date of issue of the relevant regulatory approval for relma-cel.

Mechanism of Action

As a target for immunotherapies, CD19 has been validated through regulatory approval of three anti-CD19 products globally. It is a cell surface protein expressed on normal and malignant B lymphocytes that is involved in regulating B cell activation. CD19 is highly expressed on B cell lymphoma and leukemia, and its expression varies between different types of these malignancies.

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Importantly, CD19 is not expressed by hematopoietic stem cells or normal non-hematopoietic cells. Thus, with the exception of B-cell aplasia, which is generally managed without significant risks to a patient, early phase clinical studies suggest that toxicity associated with on-target/off-tumor interactions is not expected to be a concern with agents targeting CD19. Relma-cel T-cells express a CAR that binds to the extracellular domain of CD19, causing the intracellular domain of the CAR to promote T-cell expansion and triggering subsequent effector functions that eliminate tumor cells.



Source: Literature Review, Frost & Sullivan Analysis

Market Opportunity and Competition

Target Indication

Relma-cel is intended primarily for the treatment of B-cell NHL, a type of cancer that starts in white blood cells called lymphocytes, which are part of the immune system. NHL includes a number of different subtypes of lymphomas that all share some of the same characteristics, including the fact that these cancers originate in the lymph nodes. According to Frost & Sullivan, B-cell NHL represents more than 85% of all NHL.

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Cancer of B-cell lymphocytes can also originate in blood or bone marrow, and in these cases it is referred to as B-cell leukemia. CLL/SLL is the chronic type, involving cancer cells called “small lymphocytes,” and acute lymphoblastic leukemia (“**ALL**”) is the acute type, involving an uncontrolled proliferation of lymphoblasts, or immature white blood cells.

Market Opportunity

According to Frost & Sullivan, the prevalence of NHL in China reached 485.5 thousand in 2019 representing a CAGR of 5.4% between 2015 and 2019. The prevalence of NHL in China is expected to grow to reach approximately 610.9 thousand patients in 2024, representing a CAGR of 4.7% between 2019 and 2024, and to further increase to approximately 730.0 thousand patients in 2030, representing a CAGR of 3.0% between 2024 and 2030.

Among the types of NHL in China, DLBCL is the most common, accounting for approximately 41.0%, while FL, MCL and CLL account for 6.1%, 3.4% and 4.6% of all patients, respectively.

- **DLBCL:** In China, DLBCL prevalence reached 199.1 thousand in 2019, and is expected to grow to approximately 250.5 thousand in 2024, and to approximately 299.3 thousand in 2030.
- **FL:** In China, FL prevalence reached 29.6 thousand in 2019, and is expected to grow to approximately 37.3 thousand by 2024, and to approximately 44.5 thousand in 2030.
- **MCL:** In China, MCL prevalence reached 16.5 thousand in 2019, and is expected to grow to approximately 20.8 thousand by 2024, and to approximately 24.8 thousand in 2030.
- **CLL/SLL:** In China, CLL/SLL prevalence reached 22.3 thousand in 2019, and is expected to grow to approximately 28.1 thousand by 2024, and to approximately 33.6 thousand in 2030.

According to Frost & Sullivan, the target indications for relma-cel, namely 3L DLBCL, 3L FL and 3L MCL, had an addressable market estimated to have a prevalence of approximately 28.7 thousand, 5.2 thousand and 3.4 thousand patients respectively in China in 2019, after taking into account the effectiveness of prior lines of treatment in China.

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Current Treatment Options and Limitations

There are many challenges and unmet needs regarding the current treatment of NHL in China, including disease-related, treatment-related and other challenges:

- *Disease-related.* In China, the prevalence of NHL reached 485.5 thousand patients in 2019, with an overall 5-year survival rate of NHL of 37.0%, slightly lower than that of cancer in general in China. Some aggressive types of NHL, such as DLBCL, can involve organs other than the lymph nodes, progressing rapidly and becoming fatal due to invasion across all areas of the body if treatment is not administered at an early stage. Only early-stage detection and treatment can lead to a higher chance of survival. On the other hand, indolent subtypes of NHL, such as FL, despite slow progression, can be long-standing over years and are less likely to be cured with current treatment methods. The current treatment paradigm and survival rate have demonstrated the difficult nature of NHL, indicating significant unmet clinical needs.
- *Treatment-related.* Currently, major treatment options for NHL in China vary by patient condition and NHL subtypes, but generally comprise a monoclonal antibody (rituximab) in combination with chemotherapies. Such options generally have limited efficacy due to drug resistance and therefore lead to high relapse rates. While emerging targeted drugs, such as BTK inhibitors, provide wider treatment options for MCL and CLL patients and potentially patients of other NHL subtypes in the future, it typically leads to drug resistance eventually, which is a common limitation shared by targeted therapies. About half of all NHL patients will eventually experience disease progression due to drug resistance. Another limitation of current treatments is the severe systemic adverse effects that result from off-target toxicity, such as vomiting, nausea and hair loss. All of these factors may exert a heavy economic and physiological burden on patients, creating an urgent need for new treatment options that have a better safety and efficacy profile. In particular, around 15% of DLBCL patients (the most common subtype of NHL) are characterized as primary refractory after first-line R-CHOP treated therapy. For these patients, treatment options with new modalities are more necessary.

In addition, unlike CAR-T, which generally only requires single dosing, traditional chemotherapy or monoclonal antibody drugs typically require several months of treatment through a number of treatment cycles (typically 6-8 cycles) and extended hospital stays to facilitate monitoring by physicians. The toxicity increases both in incidence and severity with each additional cycle, which leads to certain patients having to stop the treatment due to tolerability issues.

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CAR-T products, such as relma-cel, are living cell products capable of expansion and persistence in the body. As with any T-cell, these cells can survive and respond for years. By contrast, antibody therapies are proteins, and have a definable half-life due to degradation or elimination from the body over a few days to weeks. For this reason, CAR-T therapy is a single dose product for all patients.

- *Other.* The risk of NHL increases with age. In China, due to a rapidly aging population, the number of individuals above 65 years old has grown to 176.0 million in 2019, and is expected to continue its growth momentum into the future. The aging population, including elderly NHL patients, will increase correspondingly, making the treatment of NHL even more challenging. In particular, elderly patients are relatively more fragile, and also are not eligible for some standard treatment options.

Approved anti-CD19 CAR-Ts

The following table sets forth certain information concerning Kymriah, Yescarta and Tecartus, the anti-CD19 CAR-T products that have received regulatory approval for marketing to the public in a major market to date, according to Frost & Sullivan. As of the Latest Practicable Date, no CAR-T product has received regulatory approval in China.

Company	Generic Name	Brand Name	Product	Target	Approved Indications	Status	Region and Year of Approval
Kite / Gilead	Brexucabtagene Autoleucel	Tecartus [®]	CAR-T	CD19	R/R MCL	Approved*	US (2020)
Kite / Gilead	Axicabtagene Ciloleucel	Yescarta [®]	CAR-T	CD19	R/R LBCL (3 rd Line)	Approved	US (2017) EU (2018)
Novartis	Tisagenlecleucel	Kymriah [®]	CAR-T	CD19	R/R B-cell ALL (2 nd Line) R/R LBCL (3 rd Line)	Approved	US (2017) EU (2018)

Note: *Tecartus was approved under accelerated approval in the US; R/R = Relapsed or refractory; MCL = Mantle Cell Lymphoma; R/R LBCL = R/R Large B-cell Lymphoma, including DLBCL NOS, high grade LBCL, and DLBCL arising from FL; ALL = Acute Lymphoblastic Leukemia =ALL.

Note: Market information as of July 31, 2020.

Source: FDA, Frost & Sullivan

Competitive Advantage

We believe that relma-cel has a significant competitive advantage in the CAR-T market in China, due to its potential best-in-class safety profile with competitive efficacy, physicians’ familiarity with our product due to the large number of clinical sites we have engaged in China with respect to relma-cel’s clinical trials, and our manufacturing quality.

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Safety Profile

The following tables set forth certain efficacy and safety data relating to relma-cel, Yescarta and Kymriah in r/r DLBCL and Tecartus in MCL. The trials performed for the competing CAR-T products are separate studies done at different times, targeting different indications or patients with different disease conditions, and enrolling patients with different composition of ethnic groups, and therefore are not comparable to each other in a head-to-head manner. Although head-to-head studies have not been conducted, we believe these data indicate the competitive efficacy and potential best-in-class safety profile of relma-cel, according to Frost & Sullivan:

Product Information							Efficacy			Safety (Adverse Events)				
Drug Name	Trial Name	Trial Date ¹	Trial Code	Trial Location	Medium Follow-up ²	Indications	Evaluable Patients	ORR	CR	Evaluable Patients	NT (Any)	NT (=Grade 3)	CRS (Any)	CRS (=Grade 3)
Relma-cel	/	Mar 2019	CTR20182325	China	N/A*	r/r DLBCL	58	75.9%	51.7%	59	20.3%	3.4%	47.5%	5.1%

Note: Clinical data for relma-cel is not from a head-to-head comparison study with other CAR-T product; NT = Neurologic Toxicities, CRS = Cytokine Release Syndrome. 1. Refers to “首次公示信息日期” from CDE website.

* N/A = not available, median follow-up was not calculated because patient follow-up was ongoing at the time of this interim data cut off.

Product Information							Efficacy			Safety (Adverse Events)				
Drug Name	Trial Name	Trial Date ¹	Trial Code	Trial Location ²	Medium Follow-up ³	Indications	Evaluable Patients	ORR	CR	Evaluable Patients	NT (Any)	NT (=Grade 3)	CRS (Any)	CRS (=Grade 3)
Yescarta	ZUMA - 1	Jan 2015	NCT02348216	6 countries	7.9 mo	r/r LBCL	101	72%	51%	108	87%	31%	94%	13%
Kymriah	JULIET	May 2015	NCT02445248	10 countries	9.4 mo	r/r LBCL	68	50%	32%	106	58%	18%	74%	23%
Tecartus	ZUMA - 2	Nov 2015	NCT02601313	4 countries	8.6 mo	r/r MCL	60	87%	62%	82	81%	37%	91%	18%

Note: Clinical data for each product is obtained independently from the label, but not from head-to-head comparison study; r/r LBCL = r/r Large B-cell Lymphoma, including DLBCL NOS, high grade LBCL, and DLBCL arising from FL; NT = Neurologic Toxicities, CRS = Cytokine Release Syndrome. 1. Refers to First Posted Date from clinicaltrial.gov. 2. For ZUMA-1 trial, the study locations include US, Canada, France, Germany, Israel and Netherlands; for JULIET trial, the study locations include US, Australia, Austria, Canada, France, Germany, Italy, Japan, Netherlands, Norway; for ZUMA-2 trial, study location include US, France, Germany, Netherlands; 3. The medium follow-up period is with respect to duration of response.

Source: FDA, clinicaltrials.gov, Literature Review, Frost & Sullivan

Manufacturing Success Rate

We attribute the potential best-in-class safety profile of relma-cel to three factors. First, the relma-cel CAR construct contains a 4-1BB costimulatory domain and other unique proprietary properties that give rise to fewer mechanism-based AEs. We believe that the 4-1BB costimulatory domain produces a metabolic profile supporting gradual expansion, as opposed to rapid expansion often associated with severe CRS and NT. (See “— Our T-Cell and Immune Cell Technologies — Components of Our Technology — Classic Constructs.”) Second, our unique proprietary process allows us to administer relma-cel to all the patients at a fixed dose, compared to other approved products that have to be administered to patients in variable doses, which could be a source for increased AEs/severe AEs. Third, Juno and we have developed our own AE management algorithm to manage all AEs, which has helped to reduce severe AEs in our clinical studies.

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We have had a 100% success rate for the manufacture of relma-cel during our DLBCL registrational clinical trial, which we believe compares favorably to other approved anti-CD19 CAR-Ts.

In CAR-T manufacturing, there are typically two major causes for failure: bacterial contamination and failure to meet product specifications, such as a viable cell number. We believe we were able to achieve a high success rate primarily by addressing these two major potential causes of failure through the below:

- Our manufacturing process consists of a sequence of individual operations (building blocks) that are highly automated and use standard off-the-shelf equipment. This significantly reduces potential operational errors, which is the most common cause for contamination. In addition, a substantial part of our operations are performed with completely closed containers, and any connections to and from the containers are performed using aseptic techniques that ensure process streams are completely isolated from the environment.
- Our manufacturing process for relma-cel is designed to ensure that 1) the maximum anticipated dose of CAR-T will be achieved, 2) the products meet all the product specifications, and 3) manufacturing operates within all critical process parameters. For example, our process limits the number of CD3+ T-cells for activation and transduction to the lowest number (discard excess cells), thereby limiting the variability of the number of viable CD3+ T-cells in the apheresis product collected from the patient. This process ensures that the expansion process for activated and transduced T-cells starts with a consistent number of cells and is consistent with expansion durations, regardless of the dosage used during clinical trials. As a result, we are able to produce products with consistent cell characteristics and quality.

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The following table set forth information concerning the manufacturing success rates of Yescarta, Kymriah and Tecartus, respectively in their registrational clinical trials, according to Frost & Sullivan.

Manufacturing Success Rate of Commercialized CAR T Products

CAR T Product	Company	Manufacturing Success Rate*
Yescarta	Gilead/Kite	99% ¹
Kymriah	Novartis	91% ² - 93% ³
Tecartus	Gilead/Kite	96% ⁴

Note: *Calculated from registrational clinical trial data in the label and not from head to head comparison study. 1. for patients with r/r LBCL; 2. for patients with r/r ALL; 3. for patients with r/r LBCL; 4. for patients with r/r MCL; LBCL includes DLBCL NOS, high grade LBCL, and DLBCL arising from FL.

Source: FDA, Frost & Sullivan Analysis

Clinical Data Related to Relma-cel

We have administered relma-cel to more than 80 Chinese patients as of June 17, 2020 across two trials, a Phase I trial (n=32) that enrolled patients with r/r B-cell NHL and a Phase II trial (n=48) that enrolled patients with r/r B-cell DLBCL. Data from these two trials served as the basis for our NDA submission relating to relma-cel as a third line treatment for DLBCL in June 2020 with 59 patients (11 patients from Phase I and 48 patients from Phase II) and were included in the key safety and efficacy analyses for NMPA review. Details of these trials are provided below.

Relma-cel shares the same CAR construct with Juno’s product lisocabtagene maraleucel (“**liso-cel**”), the experience from which served as a basis for the clinical studies that we have conducted with respect to relma-cel. Liso-cel has been administered to more than 300 r/r B-cell NHL patients in the U.S. and the EU, and data from 268 r/r B-cell DLBCL patients were submitted to regulatory authorities in the U.S. and the EU as part of Juno’s BLA, with most receiving a single dose of 100 million CAR+ T after lymphodepletion with 30mg/m²/day of fludarabine and 300mg/m²/day cyclophosphamide over three days. Top-line results for liso-cel in r/r B-cell DLBCL were presented at ASH 2019 and included an ORR of 73% and a CRR of 53% with relatively low rates of CRS (42%, any grade; 2% severe grades) and neurotoxicity (30%, any grade; 10% severe grades). The median OS was 19.9 months. Juno has conducted and reported promising results from clinical trials in the U.S. using liso-cel in third line CLL, third line MCL and second line DLBCL.

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Phase I Clinical Studies of Relma-cel

Our Phase I trial data were published in two abstracts at ASH 2019. The primary objective of this trial was definition of a preliminary safety profile of relma-cel. Secondary objectives included determination of a recommend Phase II dose and preliminary anti-tumor activity. A total of 32 NHL patients were enrolled and treated, and 29 were evaluable for response. Enrolled patients had a median age of 52 years (ranging from 29 to 68 years) and were heavily pre-treated with a median of four prior lines of treatment, and some (34%) had rapidly progressing disease that required bridging chemotherapy after T-cell collection. NHL subtypes included 20 DLBCL patients, 6 FL patients, 2 MCL patients and one mucosa-related lymphoid tissue (“**MALT**”) patient. Enrolled patients received a single dose of either 25 million, 50 million, 100 million or 150 million CAR+ T after lymphodepletion with 25mg/m²/day of fludarabine and 250mg/m²/day cyclophosphamide over three days.

Efficacy Data. Among the 29 evaluable patients, the best ORR was 89.7% (85% for DLBCL patients). The ORR of all evaluable patients at 1, 3 and 6 months were 86.2%, 69%, 58.6% respectively, and for the 20 DLBCL patients the ORR was 80%, 55% and 45% respectively. The CR of all evaluable patients at 1, 3 and 6 months were 65.5%, 62.1% and 55.2% respectively, and for the 20 DLBCL patients the CR was 60%, 55% and 45%, respectively.

Safety Data. No dose-limiting toxicities (“**DLTs**”) or treatment-related deaths were reported. CRS was reported in 17 patients, 16 with grade 1 or 2 severity and one with grade 3 severity. No grade 4 or 5 CRS was observed. Main symptoms were fever, fatigue and muscle soreness. The rate of CRS was similar across dose level groups. NT was observed in 5 patients, all grade 1 or grade 2 severity. Most common AEs included leukopenia, lymphopenia and neutropenia.

PK, PD and Biomarker Data. PK parameters for relma-cel (including median C_{max}, T_{max} and AUC₀₋₂₈) demonstrated significant CAR-T expansion post-infusion, but did not differ significantly across the four dose levels tested. These data also showed that relma-cel persisted at least 3 months, with 82% and 48% of patients having detectable CD8+ and CD4+ CAR+ T, respectively. Relma-cel expansion post-infusion was higher in patients with disease response and in those experiencing CRS or neurotoxicity. Anti-therapeutic antibodies were identified in 28% of patients, but there was no clear association between the presence or development of these antibodies and PK parameters, response rates or toxicity rates. Of note, CD4/CD8 ratio of cryopreserved relma-cel products (range of 0.23 to 5.50, or a CD4% range of 19% to 84%) was not associated with response.

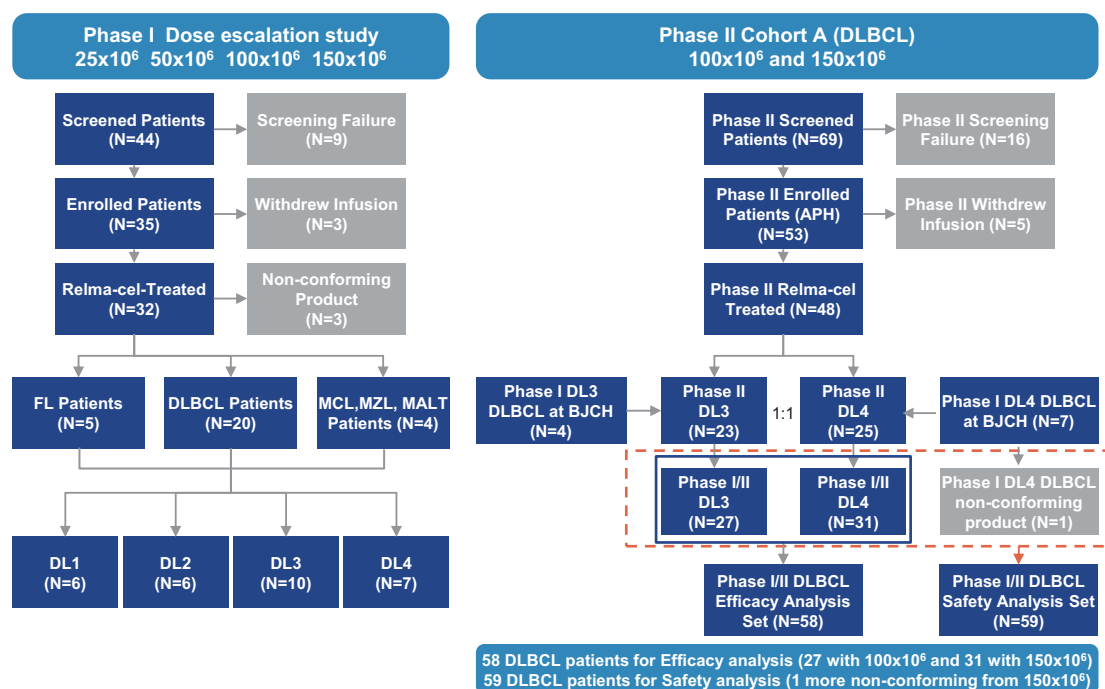
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Conclusion. This Phase I trial defined the preliminary efficacy and safety profile of relma-cel, demonstrating low rates and severity of CAR-T associated toxicities and relatively high rates of disease response in heavily pre-treated, r/r NHL patients. These data supported further testing in registrational trials in the NHL subtypes treated, in particular DLBCL and FL with a recommended Phase II dose between 100 million and 150 million CAR-T in these indications.

Phase II Registrational Clinical Study of Relma-cel

The results of our Phase I r/r B-cell NHL trial led to the initiation of a registrational single arm Phase II trial, which enrolled 48 patients with r/r B-cell DLBCL using the same general study design as the Phase I trial except patients were randomly assigned to one of two recommended Phase II doses (100 million or 150 million CAR+ T). The primary endpoint for the Phase II agreed by the CDE was 3-month ORR. For the final datasets submitted to the CDE, 11 DLBCL patients who were treated at the dose levels of 100 million cells or 150 million cells in the Phase I trial were added to the 48 patients treated in the Phase II trial, resulting in final analysis sets of 58 patients for the efficacy analysis set and 59 patients for the safety analysis set. One patient was excluded from the efficacy analysis because the cell product infused as part of the Phase I trial did not meet the potency release specifications (see below).

The following diagram illustrates the design of our Phase I trial and pivotal Phase II trial:



Abbreviations: DL= Dose level; FL = Follicular Lymphoma; DLBCL = Diffuse Large B-Cell Lymphoma; MCL = Mantle Cell Lymphoma; MZL= Marginal Zone Lymphoma; MALT = Mucosa Associated Lymphoid Tissue; BJCH = Beijing Cancer Hospital

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The primary endpoint was ORR at 3 months post-CAR-T infusion as evaluated by primary investigators (“**PIs**”) at each site. In addition, patient response data, including restaging scans, were assessed by an independent review committee (“**IRC**”) as a sensitivity analysis to corroborate the findings of the PIs. A high degree of concordance was observed in the re-staging assessments between the PIs and the IRC. Additional key endpoints included CRR, DOR, PFS and OS.

The 59 patients in the DLBCL analysis group were treated with either 100 million or 150 million CAR-T cells. These r/r patients had a median age of 56.0 years (ranging from 18 to 75 years) and were heavily pre-treated with a median of two prior lines of treatment. 81.4% of the patients were refractory to last therapy, and 42.4% of the patients had rapidly progressing disease that required bridging chemotherapy after T-cell collection.

Efficacy Data — At time of data cut off June 17, 2020, the pre-specified efficacy analysis set from the Phase I and Phase II trials (n=58) met the pre-defined endpoint with a 3 months ORR of 60.3% as evaluated by PIs. The excluded patient had cell product infused as part of the Phase I trial did not meet potency release specifications, but achieved CR at Day 29 that is ongoing for >1 year. At time of data cut off June 17, 2020, the best overall response (as evaluated by the PIs) was 75.9% and 51.7% for ORR and CR, respectively. At time of data cut off, June 17, 2020, median DOR was 8 months, and median DOCR, median PFS and median OS have not been reached. Although efficacy data were pooled across the two dose levels for statistical analyses, ad hoc analysis of response at each dose level did not demonstrate an improved ORR or CR at the higher dose level (150 million cells).

Safety Data — When relma-cel was administered to r/r DLBCL patients, AEs were generally manageable, and most were of low grade (grades <3) severity. Severe (grades ≥3) AEs occurring in more than 5% of patients are shown in the table below. Overall rates of AEs commonly associated with CD19 CAR-T therapy, such as CRS and NT, were observed in less than half of all treated patients (47.5% and 20.3%, respectively, as of data cut off date June 17, 2020), and severe grades of CRS and NT (defined as grade 3 or higher) were observed in approximately 5% or less of all treated patients (5.1% and 3.4%), respectively. Anti-cytokine therapy and/or steroids were used in 28.8% and 15.3% of the 59 patients in the safety analysis set, respectively. All cases of CRS and neurotoxicity were resolved in those treated at the 100 million cell dose level. For those treated with the 150 million cell dose level, as of June 17, 2020, all CRS and NT events had resolved except two CRS events, one with unresolved sequelae of CRS and one ongoing Grade 4 CRS event at the time of death on Day 8 post-infusion from sepsis and one ongoing Grade 3 NT event. As of June 17, 2020, eleven patients (18.6%) had died during the trial, nine from disease progression, one from sepsis and one from unknown reasons (the patient was evaluated as PD on Day 90 and died > Day 205 after infusion; patient’s family was not willing to provide the cause of death and exact date of death). None of these deaths was considered related to relma-cel.

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The following table sets forth the severe adverse events reported in more than 5% of patients.

Severe Adverse Events Reported in >5% of Patients*	All Grade (n=59) N (%)	Grade ≥3 (n=59) N (%)
Hematological AEs		
Leukopenia	17 (29%)	7 (12%)
Neutropenia	13 (22%)	7 (12%)
Anemia	10 (17%)	3 (5%)
Lymphopenia	7 (12%)	3 (5%)
Thrombocytopenia	9 (15%)	3 (5%)
CAR-T-associated AEs**		
CRS	28 (47%)	3 (5%)
Non-hematological AEs		
Lung infection	4 (7%)	3 (5%)
Febrile neutropenia	3 (5%)	3 (5%)
Hypotension	11 (19%)	3 (5%)

* Source: clinical study report; For all AE preferred terms reported in >5% of patients, excluding laboratory investigations

** Severe grades of NT were observed in 3 treated patients (3.4% of all treated patients)

Dose Considerations — Given the overall high best ORR rates, and that the higher dose appeared to have more frequent or severe toxicity without clear improvement in response rates, we are recommending in our NDA filing that relma-cel be used at the lowest effective dose of 100 million CAR+ T for r/r B-cell DLBCL patients.

We employ a very basic principle in drug development, one that is often required by regulators, to use the lowest effective dose. The data from our Phase II registrational trial clearly establishes that 100M and 150M cell doses are effective, with no improvement in efficacy outcomes with the higher dose. In addition, while our Phase II registrational trial is not powered to differentiate between these two doses, patients receiving the 150M cell dose did experience slightly higher rates of common CAR-T toxicities. Thus, both based on drug development principles and the findings in our Phase II registrational trial, we are seeking to label the 100M cell dose.

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Plan for Further Clinical Development of Relma-cel

We are conducting or planning to commence trials of relma-cel in several other B-cell malignancy indications, including third-line FL, third-line MCL, third-line CLL, third-line pediatric and adult ALL and second-line DLBCL.

- *3rd line FL* — FL is the second most common type of NHL, which has historically been treated with chemotherapy or chemoimmunotherapy for multiple rounds before the lymphoma either becomes resistant to standard therapy or transforms into DLBCL. We are conducting a single arm Phase II registrational trial in China that will evaluate relma-cel in certain FL patients. We anticipate that trial follow up will be completed in mid-2021.
- *3rd line MCL* — MCL is a unique type of NHL that has historically been resistant to standard therapy, or therapies have provided only short periods of response. We have started a single arm Phase II registrational trial in China. Patient enrollment is expected to begin by the fourth quarter of 2020. The study will evaluate relma-cel in MCL patients for whom the use of BTK inhibitors has failed.
- *3rd line CLL* — CLL is a chronic type of leukemia that has historically been effectively treated for long periods of time with conventional therapies, but ultimately transforms into aggressive forms of leukemia or lymphoma. Several subtypes of CLL, principally those containing certain cytogenetic or cell biology markers, have a much worse prognosis even without transformation. We intend to conduct a single arm Phase I/II trial in China that we expect will begin by the second quarter of 2021. The study will evaluate relma-cel in high risk CLL patients for whom the use of BTK inhibitors has failed.
- *3rd line ALL* — ALL is an acute type of leukemia that occurs in both children and adults. While children tend to have high durable remission rates with frontline therapy, the length (3 years) and intensity of the multi-drug chemotherapy can take a toll on their long term development and cognitive abilities. For both children and adults, relapse after initial induction chemotherapy carries a very poor prognosis with median survival rates in adults being less than one year. We intend to conduct a single arm Phase I/II registrational trial in China that we expect will begin by the second quarter of 2021 subject to discussion with the CDE. The study will evaluate relma-cel in pediatric and young adult patients with r/r ALL after at least two lines of therapy.

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- *2nd line DLBCL* — We have commenced a Phase I single arm trial in China in the third quarter of 2020. The study will evaluate relma-cel in DLBCL patients who are refractory to primary treatment. We anticipate that data from this trial will be used to establish a multi-center trial in 2nd line DLBCL patients, such as those with primary progressive disease, and expanded to sufficient patient numbers to support registration of relma-cel in this indication.

Registrational status for our clinical trials relating to relma-cel as a third-line treatment for DLBCL, FL and MCL was granted by the NMPA in the customary manner: we approached the NMPA with a proposal for a clinical study including study design, number of patients and expected outcome. We requested and received confirmation in writing from the NMPA that following completion of the trials, and assuming satisfactory results, the results could be used for registrational purposes (i.e., that the NMPA would approve relma-cel for marketing to the public for the relevant additional indications).

Additionally, we plan on conducting post-marketing studies to obtain more data on (i) relma-cel’s long-term efficacy and safety, and (ii) relma-cel’s real world efficacy and safety. The details of these studies are still in discussion with the CDE, however, we plan on commencing them after regulatory approval of each indication of relma-cel and target for them to be completed three to five years post-approval.

As of the Latest Practicable Date, we have not received monetary sponsorship from Juno for our research and development activities. We have received technical assistance from Juno from time to time in the past and may do so in the future pursuant to the terms of the License and Strategic Alliance Agreement with Juno. For further details, please see the sections headed “Business — Collaboration and License Agreements — License Agreements with Juno — Strategic Alliance with Juno” and “Future Plans [REDACTED]” in this document.

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The following table sets forth the clinical status of relma-cel and other CD19 candidates in China, according to Frost & Sullivan:

Company	Partner	Product	Target	Indications	Principal Investigator and Affiliation	Status	Date	Clinical Trial Number
JW Therapeutics	Bristol Myers Squibb (Juno)	CAR-T	CD19	R/R B-cell NHL	Jun Zhu (Beijing Cancer Hospital)	NDA	2020-6-30	/
Fosun Kite	Kite	CAR-T	CD19	R/R B-cell NHL	Weili Zhao (Ruijin Hospital Affiliated with Shanghai Jiaotong University Medical College)	NDA	2020-2-26	/
Novartis	None	CAR-T	CD19	R/R B-cell NHL	Jun Zhu (Beijing Cancer Hospital)	Phase III	2020-6-15	CTR20200561
Carsgen Therapeutics	None	CAR-T	CD19	R/R B-cell NHL	Jie Jin (The First Affiliated Hospital, Zhejiang University School of Medicine)	Phase II	2019-6-13	CTR20191134
Immunochina Medical	Simcere	CAR-T	CD19	R/R B-cell NHL	Yubin Song (Beijing Cancer Hospital)	Phase I/II	2020-6-30	CTR20200754
Hrain Biotech	None	CAR-T	CD19	R/R B-cell NHL	Peng Liu (Zhongshan Hospital, Fudan University)	Phase I	2018-8-19	CTR20181354
				R/R ALL	Xianmin Song (Shanghai General Hospital)	Phase I	2019-1-4	CTR20181970
Galaxy Biomedical	None	CAR-T	CD19	R/R B-cell NHL	Ting Liu (West China Hospital, Sichuan University)	Phase I	2019-3-14	CTR20190470
Shanghai Cell Therapy	None	CAR-T	CD19	R/R B-cell NHL	Lugui Qiu (Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences)	Phase I	2019-8-23	CTR20191703
Precision Biotech	None	CAR-T	CD19	R/R B-cell ALL	Jianfeng Zhou (Tongji Hospital, Huazhong University of Science and Technology)	Phase I	2019-11-25	CTR20191243
Huadiao CAR T	None	CAR-T	CD19	R/R ALL R/R B-cell NHL	Jianmin Yang (Changhai Hospital)	Phase I	2019-12-2	CTR20192479, CTR20192478
Juventas Biotech	CASI Pharma	CAR-T	CD19	R/R B-cell NHL	Dehui Zou (Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences)	Phase I	2020-1-13	CTR20192705
				R/R ALL	Jianxiang Wang (Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences)	Phase I	2020-1-16	CTR20192701

- Note:*
- (1) Pipeline information as of July 31, 2020; for NDA candidates, date refers to the NDA acceptance date while for clinical-stage candidates, date refers to CDE initial public date (首次公示信息日期). The partner refers to any licensing partners, either in-license or out-license, regarding the corresponding CAR-T product.
 - (2) The information of principal investigator and affiliation is summarized from CDE registration information and may change in the clinical trial operation.
 - (3) It is common market practice that a leading PI would be allocated to clinical trials for competing products. Dr. Zhu Jun, as a professional and seasoned PI, has followed and will follow pre-defined protocols and guide the clinical trial process for different products accordingly.

Source: CDE, Frost & Sullivan Analysis

Cautionary Statement required by Rule 18A.05 of the Listing Rules of the Hong Kong Stock Exchange: WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET RELMA-CEL SUCCESSFULLY.

JWCAR129

Overview

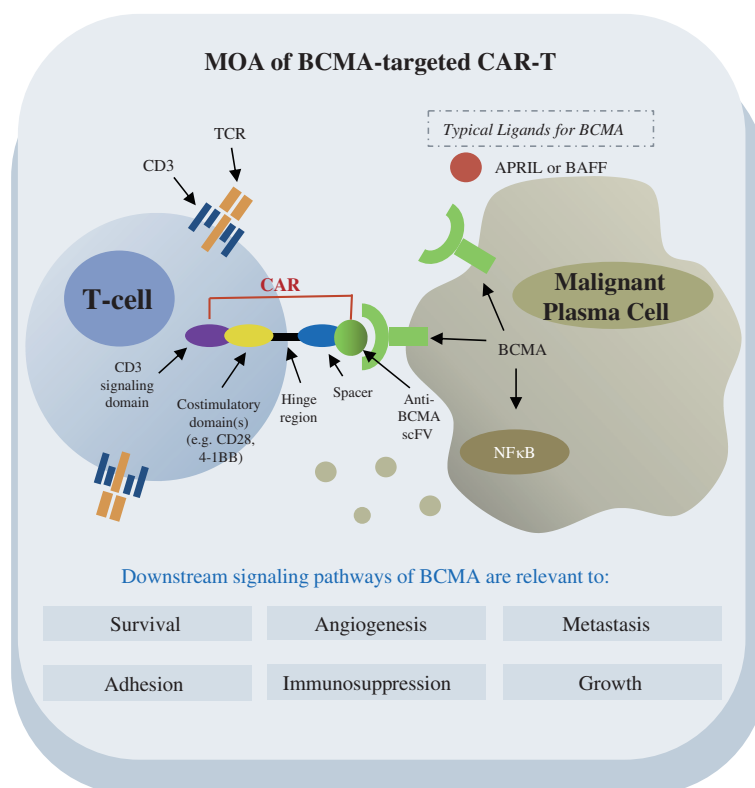
JWCAR129 is an autologous CAR-T product that targets BCMA, which is expressed in MM and is a promising target for CAR-T therapies. Other anti-BCMA CAR-T therapies have demonstrated high response rates and manageable toxicity profiles in patients with r/r MM who have failed up to ten prior lines of therapy. As with relma-cel, we have developed JWCAR129 using our own optimized processes, which we originally established in collaboration with Juno; and JWCAR129 is based on a CAR construct that we have in-licensed from Juno for China, Hong

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Kong and Macau. We intend to file an IND in China for use of JWCAR129 in clinical trials as early as the first half of 2021. For further information on the terms of our in-licensing arrangements relating to JWCAR129, please see “— Collaboration and License Agreements — License Agreements with Juno — BCMA License Agreement” in this section. JWCAR129 is currently in the pre-clinical phase of development.

Mechanism of Action

B-cell maturation antigen (BCMA), a member of the TNF receptor superfamily, is a cell surface protein expressed on normal and malignant plasma cells that is involved in regulating the maturation of B cells and differentiation into plasma cells, the cell type from which myeloma derives. BCMA is induced during differentiation of plasma cells in parallel with the loss of expression of a related receptor for B-cell activation factor (BAFF-R). Binding of BCMA to its ligands, BAFF and/or APRIL, leads to survival of plasma cells, resulting in enhanced antibody production, also known as humoral immunity. BCMA is highly expressed in MM cell lines and in cells from patients with MM, and expression appears to increase with progression of the disease. Importantly, BCMA is not expressed by hematopoietic stem cells, naïve B cells, or normal non-hematopoietic cells. Thus, with the exception of B-cell aplasia, which is generally managed without significant risks to a patient, early phase clinical studies suggest that toxicity associated with on-target/off-tumor interactions is not expected to be a concern with agents targeting BCMA.



Source: Literature Review, Frost & Sullivan Analysis

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Market Opportunity and Competition

Indication

MM is a cancer of plasma cells. Normal plasma cells are found in the bone marrow and are an important part of the immune system. When B cells respond to an infection, they mature and change into plasma cells. Plasma cells make immunoglobulins, which are antibodies that help the body to attack and kill germs. MM is a condition in which plasma cells become cancerous and grow out of control. Although there are many therapies that have been approved to treat MM either alone or in combinations of two, three or four drugs, none of these regimens has consistently demonstrated the ability to cure this disease. BCMA specific CAR-T have demonstrated high levels of disease response in a significant portion of MM patients. However, they have not yet demonstrated their potential to produce long-term disease remissions.

Market Opportunity

According to Frost & Sullivan, the prevalence of MM in China reached 101.9 thousand in 2019, having increased at a CAGR of 14.1% between 2015 and 2019, and is expected to increase at a CAGR of 10.4% from 2019 through 2024 to reach 167.2 thousand, and further at a CAGR of 8.1% from 2024 through 2030 to reach approximately 266.3 thousand.

Current Treatment Options and Limitations

There are many challenges and unmet needs regarding the current treatment of MM in China, including disease-related, treatment-related and other challenges:

- *Disease-related.* MM prognoses are quite heterogeneous, influenced by genetics, treatment plans and other factors, which make MM hard to manage. Moreover, as MM progresses, it is often accompanied by various, often serious, complications, described as CRAB (hypercalcemia, renal failure, anemia and bone disease). These symptoms may also require corresponding medical interventions.
- *Treatment-related.* Currently, primary treatment options for MM generally comprise small molecule targeted therapy in combination with chemotherapy, and such options generally have limited efficacy due to drug resistance leading to high relapse rates. While emerging monoclonal antibody drugs, such as CD38 inhibitors, provide a new option for MM patients, they also eventually lead to drug resistance, which is a common limitation shared by targeted therapies. Another limitation of current treatments is the severe systemic adverse effects that result from off-target toxicity, potentially leading to

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side effects such as vomiting, nausea and hair loss. All of these factors may exert a heavy economic and physiological burden on patients, creating an urgent need for new treatment methods that have a better safety and efficacy profile.

- *Other.* The risk of MM increases with age. In China, due to a rapidly aging population, the number of individuals above 65 years old has grown to 176.0 million in 2019, and is expected to continue its growth momentum into the future. The aging population, including elderly MM patients, will increase correspondingly, making the treatment of MM even more challenging. In particular, elderly patients are relatively more fragile, and also are not eligible for certain standard treatment options.

Competitive Landscape

As at the Latest Practicable Date, there are no approved MM CAR-T products globally. There are four ongoing clinical trials for r/r MM in China, all of which target BCMA. The following table sets forth the clinical status of the four BCMA CAR-T product candidates in clinical trials in China, according to Frost & Sullivan:

Company	Partner	Product	Target	Indications	Principal Investigator and Affiliation	Clinical Trial Status	Date	Clinical Trial Number
Legend Biotech	JNJ	CAR-T	BCMA	R/R MM	Saijuan Chen (Ruijin Hospital Affiliated with Shanghai Jiaotong University Medical College)	Phase II	2018-8-13	CTR20181007
Carsgen Therapeutics	None	CAR-T	BCMA	R/R MM	Wenming Chen (Beijing Chao-yang Hospital, Capital Medical University); Chengcheng Fu (The First Affiliated Hospital of Soochow University)	Phase I	2019-6-6	CTR20190955
Hrain Biotech	None	CAR-T	BCMA	R/R MM	Weijun Fu (Shanghai Changzheng Hospital)	Phase I	2019-6-13	CTR20191141
IASO Biotherapeutics/ Innovent Biologics	None	CAR-T	BCMA	R/R MM	Chunrui Li (Tongji Hospital, Huazhong University of Science and Technology)	Phase I	2020-1-14	CTR20192510

- Note:*
- (1) Pipeline information as of July 31, 2020; for clinical-stage candidates, date refers to CDE initial public date (首次公示信息日期). The partner refers to any licensing partners, either in-license or out-license, regarding the corresponding CAR-T product.
 - (2) The information of principal investigator and affiliation is summarized from CDE registration information and may change in the clinical trial operation.
 - (3) In addition to the foregoing, there are some BCMA-targeted CAR-T products currently in the pre-clinical phase of development, including the Company’s JWCAR129.

Source: CDE, Frost & Sullivan Analysis

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Relevant Clinical and Pre-clinical Data

Juno’s Clinical Data relating to JCARH125 (“orva-cel”)

Our product candidate JWCAR129 is based on a CAR construct that we have in-licensed from Juno. Juno’s product JCARH125 (or “orva-cel”) is based on the same CAR construct, although we are using and will continue to use our processes for the development of JWCAR129. Orva-cel is an investigational, BCMA-directed CAR-T product with a human binder.

Orva-cel has been administered to at least 90 r/r MM patients in the US, most of whom had received multiple prior lines of therapy (ranging from 3-18), often including autologous stem cell transplant. Orva-cel has been evaluated in a Phase I/II trial, primarily as a single dose of between 300 million and 600 million CAR+ T after lymphodepletion with 30mg/m²/day of fludarabine and 300mg/m²/day cyclophosphamide over three days. Top-line results for 51 r/r MM patients treated with higher doses of orva-cel were presented at ASCO 2020 and included an ORR (sCR, CR, VGPR and PR) of 91% and a CR/sCR rate of 39% with relatively low rates of severe CRS (2%) and severe neurotoxicity (4%). Severe anemia, thrombocytopenia and infections were observed in less than half of these patients (21%, 44% and 14%, respectively). We expect to use the relma-cel manufacturing platform to manufacture JWCAR129, which we believe may allow us to deliver JWCAR129 at the highest doses tested with orva-cel, including the orva-cel RP2D dose of 600 million CAR+ T. This “Version 1 process” for the manufacture of JWCAR129 will be developed based on the relma-cel manufacturing platform but will be used with a BCMA CAR vector instead of a CD19 CAR vector.

The most significant feature of our optimized processes for JWCAR129 (and for relma-cel), as compared to Juno’s processes, is the simultaneous selection of CD4 and CD8 T-cells from the apheresis starting material versus the selection of CD4 and CD8 T-cells separately in the Juno processes. Our processes significantly reduce costs while maintaining similar CAR-T safety, efficacy, and quality as demonstrated in the comparable clinical trial results observed between relma-cel and Juno’s liso-cel.

Our Pre-clinical Data relating to JWCAR129

We have successfully conducted pre-clinical trials and plan to file an IND for JWCAR129 with the CDE as early as the first half of 2021. Our pre-clinical IND-enabling studies comprised 3 sections: (1) in vitro pharmacology, including target binding characterization, functional assay (cytolytic activity, activation, proliferation, cytokine release assays), tissue cross-reactivity analysis, integration site analysis, as well as assessment of ScFv-Fc binding profile using

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membrane protein arrays; (2) in vivo pharmacology study combined PK/biodistribution study in tumor-bearing immunocompromised mice for 13 weeks; and (3) in vivo pivotal toxicology study (GLP) in tumor-bearing immunocompromised mice for 8 weeks.

In addition, to support late phase trials and to monitor long term toxicity of JWCAR129, a long-term (26 weeks) toxicity study will be conducted, which is not required for an IND submission and will not impact IND approval, as this long-term study is intended to support late phase clinical trials and an NDA filing. The 26-week toxicity study is part of the NDA application because the NMPA believes that 26-week toxicity in mice or rats may help predict the safety profile of the product in humans.

Summary of Pre-clinical data (in vivo) from our Version 1 process

In-vivo POC study. An experimental animal model was established by xenotransplantation of human tumor cells expressing BCMA into immunodeficient mice. After a single administration of JWCAR129, the test animals showed obvious tumor suppression, and they could survive until they were dissected as planned (which occurred in the 13th week after the first dose of administration). Meanwhile, the animals from the vehicle control group were euthanized because the tumor volume grew too large in the 6th week. After a single intravenous injection of JWCAR129, the CAR genome copy numbers were mainly detected in spleens, lungs and tumor tissues. The CAR copy number in spleens and lungs of most animals reached a peak on day 2 and the tumor size reached a peak on day 8. Then the tumor gradually subsided. The copy number of CAR in tumors also gradually decreased.

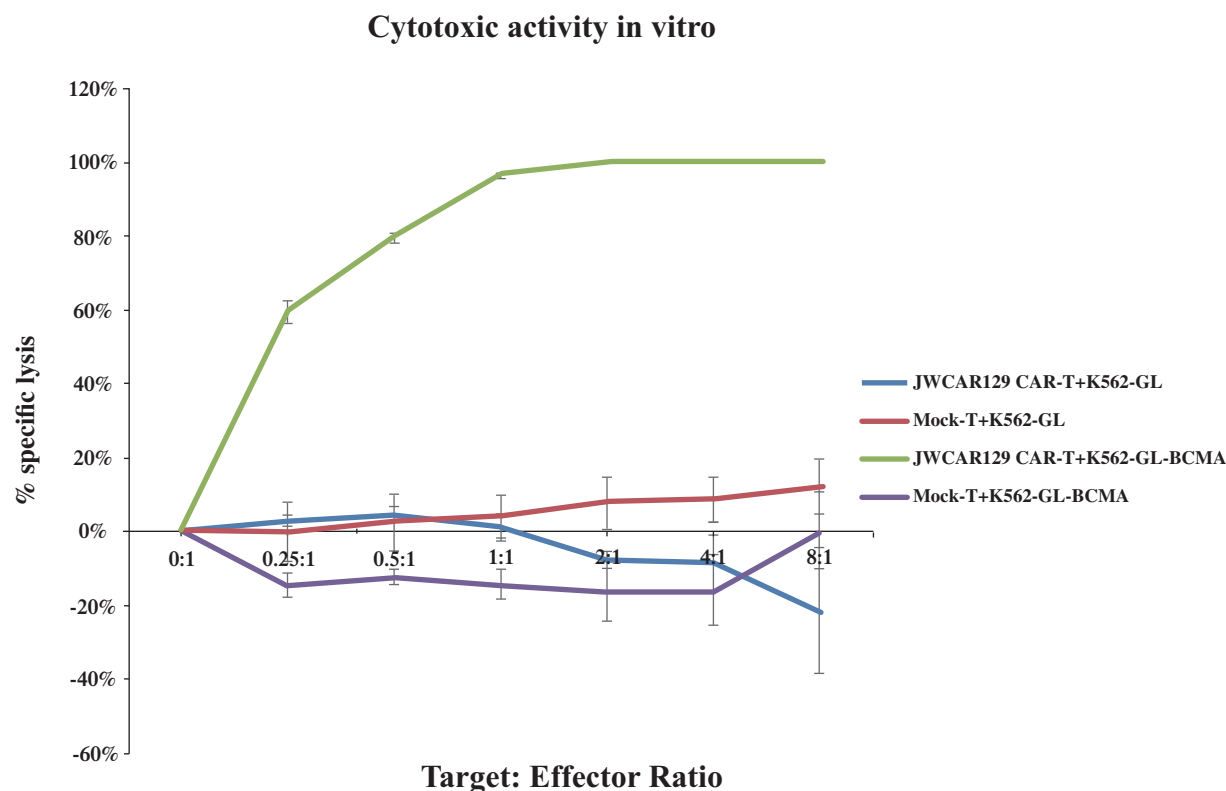
In-vivo toxicology study. An experimental animal model was established by xenotransplantation of human tumor cells expressing BCMA into immunodeficient mice. After a single administration of JWCAR129 and a 6-month observation, other than the death of one female test animal of graft versus host disease from the 2E6 cells/dose group on day 33, the rest of the animals in the testing group demonstrated good tolerance, and no histopathological changes related to the test product were observed.

In vitro cytotoxicity

JWCAR129 can only be activated and proliferated in vitro by cell lines expressing BCMA positively, secreting cytokines IL-2, IFN- γ and TNF- α , and is only cytotoxic to target cells expressing BCMA (not affected by the presence of soluble BCMA). When co-cultured with cell lines expressing negative BCMA, the above-mentioned effects did not occur, which indicated that these reactions are antigen-specific for BCMA.

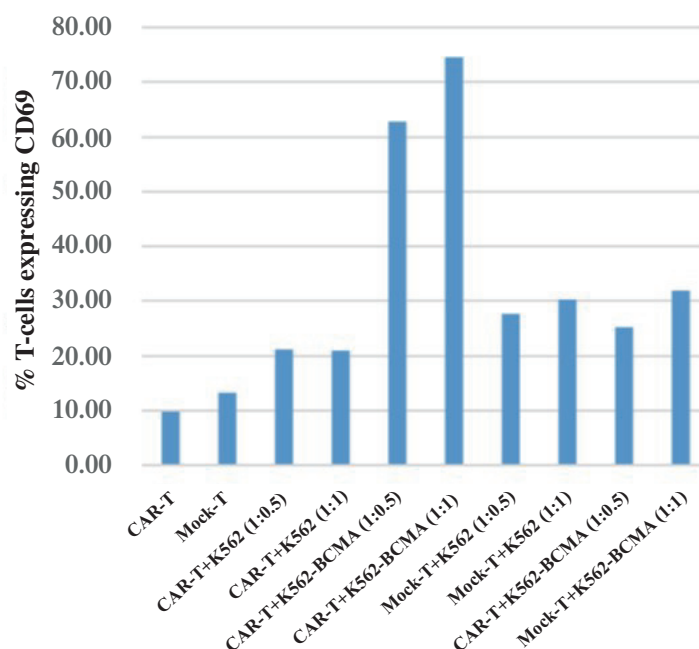
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The below chart demonstrates that JWCAR129 showed an antigen specific cytotoxic activity in vitro. The effector cells, in this case, JWCAR129 CAR-T or Mock T-cells (which have not been transduced and do not express a CAR) were co-cultured with the target cells, in this case, antigen positive cells (BCMA expressing cells, K562 GL-BCMA) and antigen negative cells (cells without BCMA expressing K562 GL) at different effector to target ratio (x-axis). The JWCAR129 CAR-T showed an antigen specific and dose dependent cytotoxic activity in vitro (green line).



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The below chart demonstrates that JWCAR129 exhibited low CD69 expression, which is a marker indicating T-cell activation, when cultured alone. JWCAR129 exhibited a significantly higher CD69 expression upon co-culture with antigen positive cells (CAR-T+K562-BCMA) as compared to co-culture with antigen negative cells (CAR-T+K562) or Mock T-cells (not transduced and not expressing a CAR) upon co-culture with antigen positive cells (Mock-T+K562-BCMA), indicating antigen specific and dose dependent T-cell activation in vitro.



Plan for Further Clinical Development of JWCAR129

As noted above, a clinical POC trial conducted by Juno to evaluate orva-cel, a CAR-T product using the same CAR construct as JWCAR129, treated over 90 patients in the U.S. and established both a high durable response rate and a preliminary safety profile. We believe this clinical experience is relevant to JWCAR129 both in suggesting higher doses may be more efficacious and in showing that these dose levels can potentially be delivered safely.

We intend to submit an IND application for JWCAR129 as early as the first half of 2021. We intend to conduct a dose escalation trial with JWCAR129 to confirm the clinical observations from the orva-cel clinical POC trial and establish a recommended Phase II dose for JWCAR129. The registrational Phase II trial will be designed to evaluate JWCAR129 in a single arm, multi-center trial as a single infusion after lymphodepleting chemotherapy with fludarabine and cyclophosphamide in patients with r/r MM who have failed at least three prior therapies. We anticipate that JWCAR129 advantages will include the ability to manufacture healthy CAR-T products at high dose.

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We intend to further develop JWCAR129 as part of its lifecycle management in several ways. First, if the Phase II trial is successful in achieving its objectives, we believe CAR-T has the potential to replace autologous stem cell transplant, the recommended but under-utilized second-line MM modality in China. We anticipate this will likely require a randomized trial testing JWCAR129 versus physician’s second-line therapy of choice. Second, we will explore the use of other agents in combination with JWCAR129 for patients with r/r MM. We intend to begin some of these trials over the next two to three years assuming success of our monotherapy development program.

As of the Latest Practicable Date, we have not received monetary sponsorship from Juno for our research and development activities. We have received technical assistance from Juno from time to time in the past and may do so in the future pursuant to the terms of the License and Strategic Alliance Agreement with Juno, which may include advice on product commercialization of JWCAR129 and technical guidance on product development. For further details, please see the sections headed “Business — Collaboration and License Agreements — License Agreements with Juno — Strategic Alliance with Juno” and “Future Plans and [REDACTED]” in this document.

Cautionary Statement required by Rule 18A.05 of the Listing Rules of the Hong Kong Stock Exchange: WE MAY NOT BE ABLE TO ULTIMATELY DEVELOP AND MARKET JWCAR129 SUCCESSFULLY.

Our Solid Tumor Platform

Overall Market for HCC Treatments in China

Market Opportunity

Due to factors such as alcohol abuse and HBV and HCV infections, new cases of HCC in China reached 369.4 thousand in 2019, representing a CAGR of 2.6% from 2015 to 2019, and are expected to increase at a CAGR of 2.4% from 2019 to 2024, and further to 473.4 thousand in 2030, representing a CAGR of 2.2% from 2024 to 2030. The prevalence of HCC in China increased to 551.3 thousand in 2019, and is expected to grow to approximately 810.7 thousand in 2024 representing a CAGR of 8.0% from 2019, and to approximately 1.2 million in 2030 representing a CAGR of 6.8% from 2024. For further information, see “Industry Overview.”

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Current Treatment Options and Limitations

The following table describes the current treatment paradigm for HCC in China, according to Frost & Sullivan:

Disease Stage	Recommended Therapies					Summary
Early Stage	Liver Resection	Tumor Ablation	Radiation Therapy	Radio - immuno - therapy	Liver Transplant - ation	Early stage HCC treatment options are mainly locoregional ones such as liver resection, ablation, radiation therapy, radioimmunotherapy, which can be used in combination with TACE, immunomodulators, chemotherapy or targeted therapies to achieve a better treatment outcome.
	TACE	Immuno - modulators	Chemotherapy	Targeted Therapy (e.g. sorafenib)		
Late Stage	Small molecule targeted therapy (1 st Line: Sorafenib, Lenvatinib, Donafenib; 2 nd Line: Regorafenib, Apatinib)					Late stage HCC treatment options are mainly systemic treatments, including small molecular targeted therapy, checkpoint inhibitor alone or with anti-angiogenic monoclonal antibodies (such as bevacizumab) as well as chemotherapy.
	Checkpoint inhibitors + (Monoclonal antibody) (1 st Line: Atelizumab + bevacizumab; 2 nd Line: PD-1 inhibitor)					
	Chemotherapy (Oxaliplatin -based, etc.)					

Source: CSCO 2020, Frost & Sullivan Analysis

The following table shows the survival rates and ORR of current treatment options for HCC in China:

	Sorafenib	Lenvatinib	Atelizumab + Bevacizumab
Medium PFS (months)	3.6	9.2	6.8
Medium OS (months)	10.5	14.7	NA
ORR	15.8%	44.6%	28%

Note: Efficacy data for sorafenib and lenvatinib is from the head to head study of the two drugs on Chinese subpopulation in REFLECT study (A phase 3, multinational, randomized, non-inferiority trial compared the efficacy and safety of lenvatinib (LEN) and sorafenib (SOR) in patients with unresectable hepatocellular carcinoma (uHCC)) and the data for atelizumab and bevacizumab are obtained from Imbrave150 Trial.

Source: Literature Review, Frost & Sullivan Analysis

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Competitive Landscape

Currently there is only one CAR-T therapy for treatment of HCC that is under clinical development in China, which is Carsgen Therapeutics’ “CAR-GPC3 T-Cell” product. This product candidate, which is targeted at GPC3, is in Phase I clinical development. There are currently no CAR-T clinical trials being conducted in China that target AFP for the treatment of HCC. The scarcity of CAR-T therapies for treatment of HCC that are currently under clinical development in China indirectly demonstrates the high technical barriers currently preventing expansion of CAR-T therapies toward treatment of solid and hematological tumors.

JWATM203 Program (JWATM203 and JWATM213)

Overview

The JWATM203 program comprises two cell therapy product candidates, both using the ARTEMIS 3.0 technology: One with ARTEMIS 3.0 alone (JWATM203) and another with ARTEMIS 3.0 combined with the Lyell technology (JWATM213).

JWATM203 is a pre-clinical stage and potential superior autologous candidate to treat AFP-positive HCC. JWATM203 is built on the ARTEMIS platform and E-ALPHA platform. The ARTEMIS platform is a novel technology platform intended to create potentially more effective and safer T-cell therapies than are currently available. The E-ALPHA platform is an antibody discovery platform which comprises a highly diverse human-derived antibody phage library and a robust workflow with specificity screens designed to develop highly specific antibodies against target antigens. The E-ALPHA platform is designed to enable development of highly specific antibodies for both conventional targets, such as cell surface markers, and TCR targets, such as intracellular peptides displayed by the MHC. In June 2020, we in-licensed from Eureka the rights to develop, manufacture and commercialize JWATM203 for China, Hong Kong, Macau, Taiwan and the member countries of ASEAN, and we intend to incorporate our own processes in its clinical development. For further information on our rights to JWATM203, please see “— Collaboration and License Agreements — Asset Purchase Agreement with Syracuse Cayman and License Agreement with Eureka” in this section.

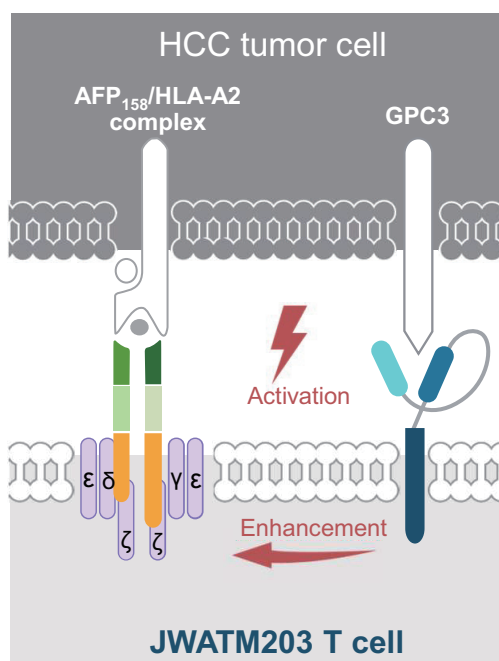
Through our partnership agreement with Lyell, we plan to combine Lyell’s technology in T-cell anti-exhaustion functionality with JWATM203 and the ARTEMIS technology platform to create JWATM213 as a next generation innovative autologous cell therapy for HCC treatment. Eureka has advanced its AFP TCRm T-cell therapy product candidate into a Phase I/II clinical trial in the United States.

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Mechanism of Action

Within HCC, approximately 70% of patients are estimated to have high serum levels of AFP, a protein which is normally present in high levels in fetal blood but drops to low levels shortly after birth. JWATM203 T-cells express a TCR-mimic (TCRm) antibody that binds to an AFP-peptide/HLA-A2 complex on cancer cells, fused to the γ (gamma) and δ (delta) TCR chains as the effector domain. In addition, these T-cells also co-express an anti-GPC3 binding domain fused to a T-cell co-stimulatory domain. We believe the expression of this GPC-targeting protein provides additional co-stimulatory signal which may be beneficial for the treatment of AFP+ HCC by optimizing T-cell activation and expansion.

The following diagram illustrates the mechanism of action of JWATM203 in greater detail:



Future Pre-clinical and Clinical Development Plan

We are currently conducting a technical transfer of product manufacturing and release testing assays, which includes minor process improvements to be commercial-ready and adapt our facility design. IND-enabling studies for the JWATM203 program could initiate as early as the first half of 2021. These pre-clinical studies will evaluate JWATM203 genetically-modified with ARTEMIS 3.0 transgenes with a comprehensive battery of studies required for IND submission or IND amendment for the specific product.

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Our preliminary plans for the clinical development of JWATM203 will focus on 3L+ advanced HCC in patients who express HLA-A2 and have high levels of AFP serum. In addition, we intend to enroll adult patients who have mild liver impairment, and to include patients with HCC resulting from chronic viral infections, alcohol toxicity and unknown etiologies. We currently anticipate filing IND applications in China with respect to JWATM203 and JWATM213 in the first half of 2023. As of the Latest Practicable Date, we have not received monetary sponsorship from Eureka for our research and development activities. We have received technical assistance from Eureka from time to time in the past and may do so in the future pursuant to the terms of the license agreement with Eureka. For further details, please see the sections headed “Business — Collaboration and License Agreements — Asset Purchase Agreement with Syracuse Cayman and License Agreements with Eureka” and “Future Plans and [REDACTED]” in this document.

JWATM204 Program (JWATM204 and JWATM214)

Overview

The JWATM204 program comprises two cell therapy product candidates, both using the ARTEMIS 3.0 technology: one with ARTEMIS 3.0 alone (JWATM204) and another with ARTEMIS 3.0 combined with the Lyell technology (JWATM214).

JWATM204 is a pre-clinical stage, novel autologous TCR candidate built on the ARTEMIS and E-ALPHA platforms to treat GPC3-positive HCC. We believe that JWATM204 has the potential to be a promising treatment option for patients with GPC3-positive HCC due to its unique dual GPC-3 binding domains that provide additional co-stimulatory signals, which in turn can result in significant tumor growth inhibition. As with JWATM203 and JWATM213, we plan to combine Lyell’s technology in T-cell anti-exhaustion functionality with JWATM204 and the ARTEMIS platform to create JWATM214, an autologous product candidate. We in-licensed the rights in China, Hong Kong, Macau, Taiwan and the member countries of ASEAN in relation to JWATM204 from Eureka in June 2020 and intend to incorporate our own processes in its pre-clinical and clinical development. For further details, please see “— Collaboration and License Agreements — Asset Purchase Agreement with Syracuse Cayman and License Agreement with Eureka” in this section.

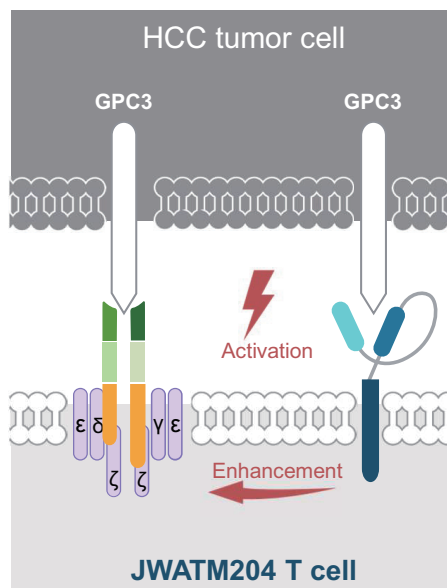
Mechanism of Action

Glypican 3, or GPC3, is a cell surface protein of the heparin sulfate proteoglycan family that is expressed in an estimated 80% of HCC in China. GPC3 has limited expression in adult tissues, including ovary, mammary gland, mesothelium, lung and kidney. JWATM204 T-cells express a GPC3-targeting antibody that binds to the extracellular domain of GPC3, fused to the $\gamma\delta$ TCR

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chains as the effector domain. In addition, these T-cells co-express a second anti-GPC3 binding domain fused to a T-cell co-stimulatory domain. We believe the expression of this GPC-targeting protein provides additional co-stimulatory signal which may be beneficial for the treatment of GPC3-positive HCC by optimizing T-cell activation and expansion.

The following diagram illustrates the mechanism of action of JWATM204 in greater detail:



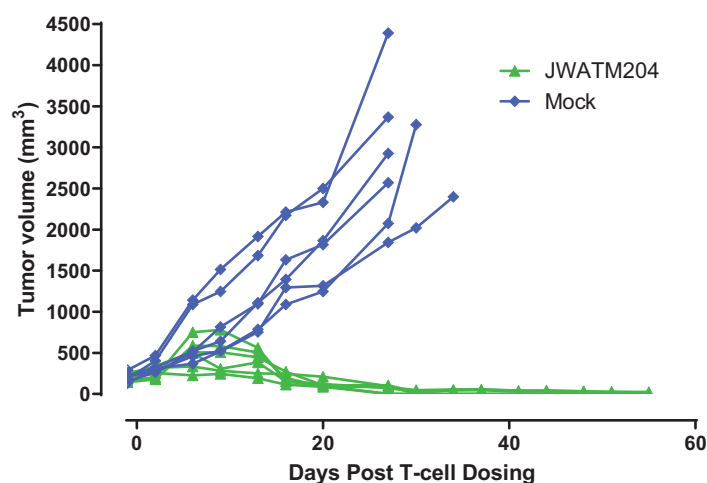
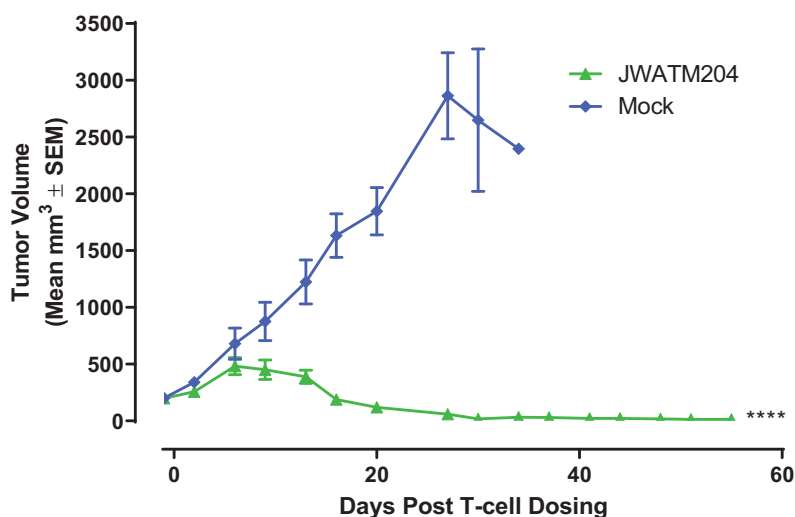
For further information on our rights to JWATM204, please see “— Collaboration and License Agreements — Asset Purchase Agreement with Syracuse Cayman and License Agreement with Eureka” in this section.

Pre-clinical Studies

Pre-clinical studies with JWATM204 have demonstrated anti-tumor activities in vitro and in mice. JWATM204 T-cells were tested in an established human GPC-3 positive Hep3B liver cancer xenograft model and compared with mock T-cells. JWATM204 T-cell treatment resulted in significant tumor growth inhibition.

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The following diagrams show results from an early JWATM204 pre-clinical in vivo pharmacology study testing anti-tumor activity.



Source: Company Information

We intend to use these pre-clinical pharmacology studies along with pre-clinical short and long term toxicology studies as well as others conducted with JWATM204 to support our IND for JWATM204 in China.

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Future Pre-clinical and Clinical Development Plan

As with the JWATM203 Program, we also intend to conduct IND-enabling studies for the JWATM204 Program, which could initiate as early as the second half of 2021. Separate studies will be conducted for JWATM214 to enable IND filings for this program.

The JWATM204 Program is not yet in clinical testing. We are beginning process development work for this program and anticipate that commercial-ready manufacturing process lock will occur as early as the fourth quarter of 2021. One substantial difference from JWATM203 is that JWATM204 does not require HLA-A02 expression as JWATM204 targets GPC3. As a result, we expect that many more HCC patients will be eligible for this therapy.

Our preliminary plans for the clinical development of JWATM204 will focus on 3L+ advanced HCC in patients who have mild liver impairment, and include patients with HCC resulting from chronic viral infections, alcohol toxicity and unknown etiologies.

We plan to further expand the development of JWATM204 or JWATM214 in earlier lines of treatment of HCC, in randomized trials as compared to either monotherapy or combinations of TKI and CPI agents. We currently anticipate filing IND applications in China with respect to JWATM204 and JWATM214 in the first half of 2023 and the second half of 2023, respectively. As of the Latest Practicable Date, we have not received monetary sponsorship from Eureka for our research and development activities. We have received technical assistance from Eureka from time to time in the past and may do so in the future pursuant to the terms of the license agreement with Eureka. For further details, please see the sections headed “Business — Collaboration and License Agreements — Asset Purchase Agreement with Syracuse Cayman and License Agreements with Eureka” and “Future Plans and [REDACTED]” in this document.

Lyell Technology

On August 7, 2020, we entered into the Lyell Collaboration Agreement. For further information, please see “— Collaboration and License Agreements — Lyell Collaboration Agreement” in this section. Lyell is a cell therapy company dedicated to understanding and developing technologies to overcome the fundamental barriers to curative cancer cell therapies. Lyell is focused on advancing the science of T-cell differentiation, functionality, and target specificity in order to develop curative treatments for solid tumors. We believe there is an opportunity to use these technologies as a platform for multiple new cell therapies that can be applied across a broad range of rare and prevalent solid cancers, such as HCC. We believe that Lyell’s technology, combined with AFP and GPC3 ARTEMIS T-cell products in the form of JWATM213 and JWATM214, will create a potentially differentiated treatment for HCC. It potentially can enhance T-cell infiltration into tumors, increase T-cell functionality, and reduce T-cell exhaustion in the tumor micro-environment to improve the anti-tumor therapeutic effects.

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Next-generation (“Nex-G”) anti-CD19 Product Candidate

We are developing a set of new technologies and platforms to enable the next generation CAR-T product and manufacturing processes with shorter production cycle time, higher quality, better product characterization and improved product efficacy and safety, at a lower cost. We believe that this will establish a foundation for our next-generation autologous anti-CD19 product, as well as other products in our pipeline.

POTENTIAL PIPELINE PRODUCTS

We expect to continue to enrich our pipeline by bringing in novel next generation cell therapy candidates through opportunities to in-license. The following chart sets forth information about our opportunities to in-license as of the Latest Practicable Date. Except for JWACE002 and JWACE055, which are allogeneic cell therapies, all of the following products in the chart below are autologous cell therapies.

	Product	Target	Indication	Commercial Rights	Pre-clinical	IND	Clinical	NDA	Partner
Hematologic Malignancies	JWACE055*	Undisclosed **	Hematologic tumors	China, Hong Kong, Macau					Acepodia
	Juno Pipeline Product 1^	CD22	ALL, NHL	China, Hong Kong, Macau					Juno Bristol Myers Squibb Company
Solid Tumors	JWACE002*	HER2	Solid tumors	China, Hong Kong, Macau					Acepodia
	Juno Pipeline Product 2^	WT1	AML, NSCLC, Mesothelioma	China, Hong Kong, Macau					Juno Bristol Myers Squibb Company
	Juno Pipeline Product 3^	L1CAM	Solid tumors	China, Hong Kong, Macau					Juno Bristol Myers Squibb Company
	Juno Pipeline Product 4^	MUC16	Solid tumors	China, Hong Kong, Macau					Juno Bristol Myers Squibb Company
	Juno Pipeline Product 5^	ROR1	Solid tumors	China, Hong Kong, Macau					Juno Bristol Myers Squibb Company

Abbreviations: ALL = acute lymphoblastic leukemia; NHL = non-Hodgkin lymphoma; AML = acute myeloid leukemia; NSCLC = non-small cell lung cancer; HER2 = human epidermal growth factor receptor 2

^ We have the right of first negotiation on the opportunity to develop and commercialize these Juno pipeline products in China, Hong Kong and Macau. For further details, please see “— Collaboration and License Agreements — License Agreements with Juno” in this section. Besides Juno Pipeline Product 2, all Juno pipeline products are undergoing Phase I clinical trials in the U.S. The Juno Pipeline Product 2 is undergoing Phase I/II clinical trial in the U.S.

* JWACE055 and JWACE002 will become part of our pipeline when we exercise the related option with Acepodia. For further details, please see “— Collaboration and License Agreements — Acepodia Option and License Agreement” in this section. JWACE002 was approved by the U.S. FDA in January 2020.

** JWACE055 target is not disclosed due to commercial sensitivity.

Juno Engineered T-cell Pipeline Products

We have a right of first negotiation on the opportunity to develop and commercialize Juno engineered T-cell products in China, Hong Kong and Macau. For further details, please see “— Collaboration and License Agreements — License Agreements with Juno” in this section. The following discussion sets forth information concerning the Juno pipeline products that are subject to our right of first negotiation as of the Latest Practicable Date.

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Juno Pipeline Product 1

Target Indications. The target indications for this autologous product candidate are ALL and NHL. ALL is an uncontrolled proliferation of lymphoblasts, which are immature white blood cells. The lymphoblasts, which are produced in the bone marrow, cause damage and death by inhibiting the production of normal cells. In 2019, the incidence of ALL in China reached 12.6 thousand, and the mortality reached 10.7 thousand. There are two main types of ALL, B cell ALL and T-cell ALL. Approximately 75% of cases of ALL are B-cell ALL, which Juno aims to address with this product candidate. For information on NHL, please see “— Our Core Product Candidate — relmacabtagene autoleucel (“relma-cel”) — Target Indication” in this section.

Target Antigen. The target antigen for this product candidate is CD22, which is a protein expressed by some B-cell malignancies, including ALL and some types of NHL.

Juno Pipeline Product 2

Target Indication. The target indication for this autologous product candidate is acute myeloid leukemia (“AML”). In 2019, the incidence of AML reached 29.4 thousand in China, according to Frost & Sullivan. AML is often incurable with standard systemic therapy. Despite the many advances in the field of hematopoietic cell transplant (“HCT”), relapse after transplantation continues to be a major problem, particularly in patients entering HCT with high risk/poor prognosis diseases.

Target Antigen. The target antigen for this product candidate is WT1, which is an intracellular protein that is overexpressed in a number of cancers, including AML and non-small cell lung, breast, pancreatic, ovarian, and colorectal cancers.

Juno Pipeline Product 3

Target Indication. The target indication for this autologous product candidate is pediatric neuroblastoma. Neuroblastoma is a type of cancer that starts in the early nerve cells, known as neuroblasts, of infants and young children under the age of 10. In China, the incidence of pediatric neuroblastoma reached 3.6 thousand in 2019, according to Frost & Sullivan. It is the most common extracranial solid tumor identified in children.

Target Antigen. The target antigen for this drug is L1CAM, also known as CD171, which is a cell-surface adhesion molecule that is overexpressed in neuroblastoma. There is increasing evidence of aberrant expression of L1CAM in a variety of solid organ tumors, including glioblastoma, lung, pancreatic, and ovarian cancers.

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Juno Pipeline Product 4

Target Indication. The target indication for this autologous product candidate is ovarian cancer. Ovarian cancer mainly affects women over the age of 63, with incidence of 53.9 thousand in China in 2019. While all women are at risk of developing ovarian cancer, those with the BRCA2 gene mutation are at increased risk for developing this type of cancer. Treatment depends on the type of cancer and the stage of the disease.

Target Antigen. The target antigen for this product candidate is MUC16, which is a protein overexpressed in the majority of ovarian cancers. Blood levels of CA125, a protein from the cleavage of MUC16, can be correlated with ovarian cancer progression.

Juno Pipeline Product 5

Target Indications. The target indications for this autologous product candidate are non-small cell lung cancer (“NSCLC”) and triple negative breast cancer. NSCLC is the most common type of lung cancer, accounting for 85% of lung cancer patients in China, according to Frost & Sullivan. Breast cancer is the sixth most common type of cancer in China in 2019, with an incidence of 326.2 thousand, according to Frost & Sullivan. In triple-negative breast cancer, the breast cancer cells test negative for the hormones estrogen (ER-) and progesterone (PR-) and the protein HER2 (HER2-). As a result, this type of cancer does not respond to hormonal therapy or therapies that target HER2. Approximately 15% of breast cancers fall into this category in China.

Target Antigen. The target antigen for this product candidate is ROR1, which is a protein overexpressed on a wide variety of cancers including a subset of non-small cell lung cancer, triple-negative breast cancer, pancreatic cancer, and prostate cancer. It is highly expressed on B cell chronic lymphocytic leukemia and mantle cell lymphoma.

Acepodia Pipeline Product — JWACE002

Overview

We have a right to acquire an exclusive license to manufacture, develop and use certain Acepodia products targeting HER2 and an undisclosed target in China, Hong Kong and Macau. For further details, please see “— Collaboration and License Agreements — Acepodia Option and License Agreement” in this section.

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JWACE002 is a novel NK cell product developed by Acepodia that targets the HER2 antigen for the treatment of endometrial cancer, ovarian cancer, breast cancer and gastric cancer. In pre-clinical studies, JWACE002 has shown enhanced tumor kill efficacy against HER2 IHC 1+, 2+ and 3+ cancer cells, which may have broader coverage on different HER2 expression level carcinoma in treatment compared to Herceptin.

JWACE002 is also designed as an allogeneic product, an “off-the-shelf” readily made cell therapy that is manufactured from cells of “cell-line” unrelated to the patient. We believe the allogeneic qualities of JWACE002 represent a groundbreaking technology in the field of cell therapy that allows it to be produced in large quantities potentially at a lower cost for a greater number of patients.

Mechanism of Action

JWACE002 targets human HER2-expressing solid tumors using anti-HER2 conjugated NK cells. JWACE002 has demonstrated enhanced tumor cell killing activities both *in vitro* and *in vivo*, while maintaining a favorable safety profile in GLP toxicology studies.

Antibody-Conjugated Effector allogeneic NK cell treatment technology is a new technology developed by Acepodia, a Taiwan- and US-based startup developing cancer immunotherapy based on its ACC™ (Antibody Cell-Conjugation) technology platform originated from UC Berkeley. Using ACC™ technology, immune cells (NK, etc.) are conjugated with antibodies to form Antibody-Conjugated Effector cells (ACE™) to direct and evoke immune responses to eradicate cancer cells.

JWACE002 has the following features:

- Leveraging the innate immunity of NK cells, with less expected CRS or NT than T effector cells;
- Using antibodies to target well-known and established targets (i.e. HER2), and to maximize the cytolytic activities of mAb-conjugated NK cells;
- Using established NK cell lines to produce allogeneic NK cells at a large scale production system and with a well characterized conjugation process to manufacture antibody-conjugated NK cells as an off-the-shelf, allogeneic, and ready-to-use cell product at low cost for cancer treatment.

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Future Pre-Clinical and Clinical Development Plan

We believe that JWACE002, while in an early stage of development, is a high potential product that aligns with our business development pipeline strategy to move into the solid tumor space with a potential transformational technology platform — a targeted, allogeneic, non-viral, off-the-shelf, ready-to-use, low cost, NK cell product against solid tumor targets. Acepodia’s IND for JWACE002 was approved by the U.S. FDA in January 2020.

Allogeneic versus Autologous Cell Therapy Products

JWACE002 is an allogeneic cell therapy product. Allogeneic and autologous cell therapies are different in terms of manufacturing process, safety and efficacy. The primary distinction between allogeneic and autologous cell therapies is the source of the cells. Autologous therapies are manufactured by harvesting the patient’s immune cells, processing and culturing ex vivo, then infusing back to the same patient. On the other hand, allogeneic therapies are manufactured from donor-derived T-cells to express a CAR, culturing ex vivo in batches, cryopreserved if needed and are easily scalable to treat many patients. They can be made in large quantities and used to treat many patients. Autologous therapies have higher compatibility with the patients’ immune systems, whereas allogeneic therapies are more scalable for manufacturing and versatile for treatment.

In terms of safety and efficacy, autologous therapies are highly compatible with the patient’s immune system, and are proven to be strongly effective against hematological cancers and their adverse effects are manageable. Allogeneic therapies, on the other hand, bear high risk of rejection by the patient’s immune system. One of the major concerns is the potential development of graft-versus-host-disease (GvHD). In addition, treatment efficacy and durability still need to be further validated for allogeneic therapies. Currently, most immunotherapies in development are autologous.

JWACE002 is complementary to our other pipeline and potential pipeline products, because it addresses a different form of cancer. In the short- to medium term, we plan to continue to focus on our other pipeline and potential pipeline products, all of which are autologous.

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COLLABORATION AND LICENSE AGREEMENTS

License Agreements with Juno

Strategic Alliance with Juno

In December 2017, we entered into a license and strategic alliance agreement with Juno (“**License and Strategic Alliance Agreement**”) pursuant to which, until May 9, 2026, which is the seventh anniversary of the date on which our Series A-2 financing closed (“**ROFN Term**”), subject to a tail period, we have the right of first negotiation to license or otherwise obtain the rights to Juno’s engineered T-cell pipeline product candidates in the field of treatment or amelioration of cancer or auto-immune disorders (the “**ROFN Field**”) for further development and commercialization in China, Hong Kong and Macau (the “**Territory**”). Under this right of first negotiation, Juno may not license or otherwise grant to any third party, and may not engage in any negotiations or other discussions with any third party regarding any agreement to license or otherwise grant to any third party, any rights to exploit Juno’s engineered T-cell pipeline product candidate in the ROFN Field in the Territory without first delivering notice to us any time following the commencement of IND enabling studies for such product candidate. Following receipt of any such notice from Juno, at our option, we and Juno will negotiate in good faith and on commercially reasonable terms for a specified period regarding an agreement to license or otherwise obtain rights to such product.

During different time periods specified in the License and Strategic Alliance Agreement, Juno also has a right of first negotiation to license or otherwise obtain the rights to our pipeline candidates for further development and commercialization outside the Territory.

Under the License and Strategic Alliance Agreement, unless otherwise agreed in writing, during the ROFN Term and the three years thereafter, we may not, by ourselves or jointly with a third party, in-license or acquire from a third party the rights to develop and commercialize any engineered T-cell product (or related diagnostic product) that is specifically directed at the target (alone or in combination with a set of other targets) of any engineered T-cell product (or related diagnostic product) in Juno’s pipeline at that time, without notifying Juno that such product is has reached commencement of pre-clinical studies before Juno’s pipeline product is designated for commencement of pre-clinical studies. In turn, until May 9, 2025, which is the sixth anniversary of the date on which our Series A-2 financing closed, Juno may not, by itself or jointly with a third party or, in-license or acquire from a third party the rights to develop and commercialize any product in the Relma-cel Field (defined below) in the Territory if such product is specifically directed at any target (alone or in combination with a set of other targets) of any product we develop independently of Juno of which Juno receives notice in connection with its right of first negotiation to license or otherwise obtain the rights to such product, and which is then in

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development or commercialization in the Territory, subject to specified exceptions in the License and Strategic Alliance Agreement. Additionally, for the term of the License and Strategic Alliance Agreement, Juno shall not grant a license under any of the licensed patents or know-how to, or otherwise enable any third party to manufacture or commercialize any engineered T-cell product directed to CD19 in the Territory.

Rights In-licensed from Juno

We have in-licensed the CAR constructs for relma-cel and JWCAR129 from Juno. In that connection, we have ongoing arrangements with Juno in relation to those product candidates, for which we may be required to make certain milestone or royalty payments at levels that are customary for arrangements of that type and consistent with market standards.

Relma-cel

As part of the License and Strategic Alliance Agreement described above, Juno granted us an exclusive, sublicensable, transferable and fee-bearing license under Juno’s interest in or Juno’s license rights to certain patent rights and know-how, and a non-exclusive, sublicensable, transferable and fee-bearing license under certain patent rights and know-how covering Juno’s platform technology, solely to research, develop, commercialize, and manufacture or have manufactured relma-cel, or related diagnostic products, in the Territory for the treatment or amelioration of cancer or auto-immune disorders, with respect to relma-cel, and diagnosis in connection with relma-cel or auto-immune disorders, and related diagnostic products (“**Relma-cel Field**”). In addition, we and Juno will negotiate in good faith for a license to certain improvements owned or licensed by Juno that arise during the term of the agreement that would require certain additional regulatory filings or actions for incorporation into the licensed products.

In exchange for these rights, we are required to make various upfront, milestone and royalty payments. For the first upfront payment, we issued preferred shares that are *pari passu* with the Series A1 Preferred Shares to Juno with an aggregate value of approximately US\$8.9 million as at the issuance date. For the second upfront payment, we issued additional preferred shares that are *pari passu* with the Series A2 Preferred Shares to Juno such that Juno’s total holdings allowed it to have direct ownership interest of 35% of all equity interests in JW Shanghai on a fully-diluted basis. Furthermore, we are required to make a US\$5.0 million milestone payment to Juno upon the completion of the treatment of 100 patients with relma-cel in any clinical trial or upon regulatory approval of relma-cel for marketing and sale in the Territory, whichever comes first. In addition, we will pay Juno tiered royalty payments for relma-cel, and royalty payments for any related diagnostic products, in each case at rates which, expressed as a percentage of annual net sales in the Territory, are consistent with market standards, subject to certain adjustments in specified circumstances. The royalty term commences upon the first commercial sale of relma-cel or a related diagnostic product in the Territory, with the end date varying depending on the type of

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royalty owed to Juno. In addition, we are required to pay to Juno the sum of all milestone payments and royalties payable with respect to relma-cel and related diagnostic products in the Territory pursuant to in-license agreements existing at the time of such development or commercialization. While the future amounts of such payments are subject to various conditions and reductions, the amounts of these payments as a percentage of net sales of relma-cel in the Territory are consistent with market standards for similar sub-licensing arrangements.

Under the terms of the License and Strategic Alliance Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize relma-cel in the Relma-cel Field in the Territory. We also have the first right to enforce the licensed patents, except for any patents covering Juno’s platform technology, against third parties that infringe such rights if we believe such infringement would reduce the annual net sales of relma-cel or related diagnostic products in the Relma-cel Field in the Territory.

In the development and commercialization of relma-cel and related diagnostic products, we solely own inventions conceived solely by or on behalf of us, and Juno solely owns inventions conceived solely by or on behalf of Juno. Subject to the terms of the License and Strategic Alliance Agreement, we and Juno also jointly own all intellectual property jointly conceived through the development and commercialization of relma-cel and related diagnostic products (the “**Relma-cel Joint Invention**”). We and Juno granted each other a non-exclusive, fully-paid, royalty-free, irrevocable, perpetual and sublicensable license under our interest and Juno’s interest, respectively, in patent rights covering the Relma-cel Joint Inventions to make, use, sell, offer for sale and import inventions claimed in such patent rights in accordance with the License and Strategic Alliance Agreement.

The License and Strategic Alliance Agreement will remain in effect until the later of the (i) expiration of our obligation to pay royalties to Juno; or (ii) expiration or termination of all then-existing agreements entered into between us and Juno in accordance with the License and Strategic Alliance Agreement for licenses or rights to Juno pipeline products. It may also be terminated earlier by mutual agreement, by either party for the other party’s uncured material breach that has frustrated the fundamental purpose of this agreement, upon our or JW Shanghai’s dissolution, by either party upon the bankruptcy of the other party, or by Juno if either party receives notice from the relevant regulatory authority alleging significant concerns regarding a patient safety issue that Juno reasonably believes would seriously impact the long-term viability of relma-cel.

BCMA License Agreement

In April 2019, we entered into a separate license agreement with Juno (the “**BCMA License Agreement**”), whereby Juno granted us an exclusive, sublicensable, transferable and fee-bearing license under Juno’s interest in or Juno’s license rights to certain patents and know-how, and a non-exclusive, sublicensable, transferable and fee-bearing license under certain patent rights and

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know-how covering Juno’s platform technology, solely to research, develop, commercialize, and manufacture or have manufactured JWCAR129, or related diagnostic products, in the Territory for the treatment or amelioration of cancer or auto-immune disorders, with respect to JWCAR129, and diagnosis in connection with JWCAR129 of cancer or auto-immune disorders, with respect to related diagnostic products (“**JWCAR129 Field**”).

In exchange for these rights, we are required to make various upfront, milestone and royalty payments. For the first upfront payment, we issued to Juno preferred shares with an aggregate value of US\$10.0 million of Series X Preferred Shares. If no product failure will have occurred prior to April 2022, we will issue to Juno additional preferred shares with an aggregate value of US\$10.0 million of Series X Preferred Shares at nil consideration (equivalent to [4,665,530] Shares after [REDACTED]). We are also required to make regulatory and commercial milestone payments of up to US\$35.0 million, including upon first receipt of regulatory approval of JWCAR129 in the Territory. In addition, we will pay Juno tiered royalty payments for JWCAR129, and royalty payments for any related diagnostic products, in each case at rates which, expressed as a percentage of annual net sales in the Territory, are consistent with market standards, subject to certain adjustments in specified circumstances. The royalty term applies on a product-by-product and country-by-country basis commencing upon the first commercial sale of JWCAR129 or a related diagnostic product in the Territory, with the end date varying depending on the type of royalty owed to Juno. In addition, we are required to pay to Juno the sum of all milestone payments and royalties payable with respect to JWCAR129 and related diagnostic products in the Territory pursuant to in-license agreements existing at the time of such development or commercialization. While the future amounts of such payments are subject to various conditions and reductions, the amounts of these payments as a percentage of net sales of JWCAR129 in the Territory are consistent with market standards for similar sub-licensing arrangements.

Pursuant to the terms of the BCMA License Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize the licensed products, including JWCAR129, in the JWCAR129 Field in the Territory. We also have the first right to enforce the licensed patents, except for any patents covering Juno’s platform technology, against third parties that infringe such rights if we believe such infringement would reduce the net sales of JWCAR129 or related diagnostic products in the JWCAR129 Field in the Territory.

The BCMA License Agreement will remain in effect until the expiration of our obligation to pay royalties to Juno. It may also be terminated earlier by mutual agreement, by either party for the other party’s uncured material breach that has frustrated the fundamental purpose of this agreement, upon our or JW Shanghai’s dissolution, by either party upon the bankruptcy of the other party, by Juno if either party receives notice from the relevant regulatory authority alleging significant concerns regarding a patient safety issue that Juno reasonably believes would impact the long-term viability of JWCAR129 if attributable to the CAR construct licensed from Juno, by

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Juno if the additional preferred shares are not issued by the timeline set forth in the BCMA License Agreement, or by us for Juno's termination, suspension, or clinical hold of development in the United States of the licensed CAR construct related to JWCAR129 for longer than 180 days.

Independence from Juno, Celgene and Bristol Myers Squibb

Although Juno is our largest shareholder, the Group believes that, it is capable of carrying on its business independently of Juno, Celgene and Bristol Myers Squibb after the [REDACTED].

Management independence

Our management and operational decisions are made by our Board and senior management. Our Board comprises one executive Director, six non-executive Directors and four independent non-executive Directors. There are no overlapping directors between our Group and Juno, Celgene and Bristol Myers Squibb. Dr. Ann Li Lee and Dr. Krishnan Viswanadhan are senior personnel of Juno and Celgene respectively who have also been nominated by Juno to become the non-executive Directors prior to [REDACTED]. We consider that our Board and senior management will function independently from Juno, Celgene and Bristol Myers Squibb for the following reasons:

- (a) all of the other Directors, including Dr. Li who is our sole executive Director, chairman of the Board and CEO, are independent of Juno, Celgene and Bristol Myers Squibb and decisions of the Board require the approval of a majority vote from the Board;
- (b) we have appointed four independent non-executive Directors, comprising more than one-third of the total members of our Board, who have sufficient knowledge, experience and competence to provide a balance of the potentially interested Directors and independent Directors with a view to promote the interests of our Company and the Shareholders as a whole;
- (c) each Director is aware of his/her fiduciary duties as a Director which require, among other things, that he or she acts for the benefit and in the best interest of our Company and does not allow any conflict between his/her duties as a Director and his/her personal interests;
- (d) in the event that there is a potential conflict of interest arising out of any transaction to be entered into between our Group and our Directors or their respective close associates, the interested Director(s) shall abstain from voting at the relevant board meetings of our Company in respect of such transactions, and shall not be counted in forming quorum. Our Group has also adopted certain corporate governance measures for conflict situation; and

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- (e) our Company has established internal control mechanisms to identify connected transactions to ensure that our Shareholders or Directors with conflicting interests in a proposed transaction will abstain from voting on the relevant resolutions.

Operational independence

We have established our own organizational structure, with each department assigned to specific areas of responsibilities which have been in operation and are expected to continue to operate independently from Juno, Celgene and Bristol Myers Squibb. Juno currently is our sole supplier of viral vectors for our clinical trials. We believe, however, that in the event that Juno ceases to supply us with viral vectors, we would be able to acquire viral vectors from alternative suppliers. For further details, please see the section headed “Connected Transactions — License and Strategic Alliance Agreement” in this document. We are also in possession of all relevant licences necessary to carry on and operate our business and we have sufficient workforce to operate independently from Juno and its close associates. Our Directors are of the view that there is no operational dependence by us on Juno.

Financial independence

Our Group has established an independent financial department with a team of independent financial staff, as well as a sound and independent financial system and makes financial decisions according to our Group’s own business needs. Our Group has adequate capital to operate our business independently, and has sufficient internal resources to support our daily operations.

During the Track Record Period, our Group had certain transaction amounts due to Juno relating to purchase of materials, purchase of license and accruals and other payables. For further details, please see Note 33 to “Appendix I — Accountants’ Report” to this document.

Our Group has sufficient capital to operate its business independently, and has adequate internal resources and a strong credit profile to support its daily operations. There will be no financial assistance, security and/or guarantee provided by Juno, Celgene or Bristol Myers Squibb in favor of our Group or vice versa upon the [REDACTED].

We have put in place controls in relation to transactions with connected persons and their associates to ensure that any advances to or from such persons are in compliance with the [REDACTED] Rules. Having considered that our future operations are not expected to be financed by Juno or its close associates, we believe our Group is financially independent from Juno, Celgene and Bristol Myers Squibb.

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Asset Purchase Agreement with Syracuse Cayman and License Agreement with Eureka

Overview

This overview is intended primarily as a summary of information provided below and elsewhere in this Document concerning the assets and rights that we acquired in connection with the Syracuse Acquisition in June 2020, and our reasons for engaging in the Syracuse Acquisition.

Assets and Rights Acquired and Liabilities Assumed. As part of the Syracuse Acquisition, we acquired:

- 100% of the capital stock of Syracuse Hong Kong (including the employees of Syracuse Hong Kong);
- the interest of Syracuse Cayman in its Eureka License Agreement with Eureka; and
- certain ancillary assets (including primarily the rights of Syracuse Hong Kong under certain intellectual property ownership agreements with its employees),

and we assumed the liabilities of Syracuse Cayman, other than specified excluded liabilities.

The Eureka License Agreement gives us the right, among other things, to develop, manufacture and commercialize, in China, Hong Kong, Macau, Taiwan and the member countries of ASEAN (the “**JW Territory**”), Eureka products directed to AFP and GPC3, as described in greater detail below. These products are referred to elsewhere in this Document as “JWATM203” (directed to AFP) and “JWATM204” (directed to GPC3). For further information, see “— Our Solid Tumor Platform” above.

The Eureka License Agreement also gives us the exclusive right to commercialize Eureka’s ARTEMIS platform in the JW Territory, as described in greater detail below.

Stage of Clinical Development of Assets Acquired. As noted elsewhere in this Document, Eureka’s AFP-directed product is currently in a Phase I/II clinical trial in the United States conducted by Eureka under an IND. JWATM204 is in the pre-clinical stage in the United States at present, and both JWATM203 and JWATM204 are in pre-clinical stage in China at present.

Acquisition Consideration. The total consideration for the Syracuse Acquisition consisted of Shares having a value of US\$105 million. We viewed the Syracuse Acquisition as consisting of two elements: the Eureka License Agreement, to which we attributed US\$95.3 million of the total consideration, and the capital stock of Syracuse Hong Kong (together with other ancillary assets as

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described below), to which we attributed US\$9.7 million of the total consideration. We determined the total consideration for the Syracuse Acquisition based on arm’s-length negotiations after consideration of potential synergies to be realized by acquisition of the relevant assets and related technologies.

Anticipated Synergies and Future Development Plans. We expect the Syracuse Acquisition, including our acquisition of rights to JWATM203 and JWATM204, to permit synergies by complementing our hematological franchise with a pipeline of solid tumor focused cell therapy candidates. We plan to develop JWATM203 and JWATM204 for the treatment of HCC and eventually commercialize JWATM203 and JWATM204 as novel treatments for the HCC patients in China. For information on our development plan for these two products, please see the section headed “— Our Solid Tumor Platform — JWATM203 Program (JWATM203 and JWATM213) — Future Pre-clinical and Clinical Development Plan” and “— JWATM204 Program (JWATM204 and JWATM214) — Future Pre-clinical and Clinical Development Plan.”

Asset Purchase Agreement with Syracuse Cayman

In order to develop a comprehensive cell-therapy platform and accelerate our business growth, on June 30, 2020, our Company and our wholly-owned subsidiary, JWS Therapeutics, entered into the Asset Purchase Agreement with Syracuse Cayman pursuant to which Syracuse Cayman agreed to transfer and assign to JWS Therapeutics, and JWS Therapeutics agreed to purchase and assume from Syracuse Cayman a majority of Syracuse Cayman’s assets and liabilities, consisting of the Eureka License Agreement, all of the equity interest of Syracuse Hong Kong, and certain agreements relating to, among others, employee confidential information, invention assignment, employment assignment and research collaboration agreements of Syracuse Cayman and its subsidiaries, primarily Syracuse Hong Kong and its directly or indirectly wholly-owned subsidiaries, Syracuse Jiangsu, Eureka Beijing, Aeon Beijing and Aeon Wuhan. Syracuse Hong Kong was incorporated in Hong Kong in 2018 as a holding company of its four subsidiaries in China. For further details regarding the acquisition, please see the section headed “History, Development and Corporate Structure — Our Company — Syracuse Acquisition” in this document.

Syracuse Hong Kong’s results of operations have been consolidated into ours since we completed the Syracuse Acquisition on June 30, 2020. For further details on the financial information of Syracuse Hong Kong, please see the sections headed “Financial Information — Financial Information of Syracuse Hong Kong” in this document and “Appendix III — Accountant’s Report of Syracuse Biopharma (Hong Kong) Limited” to this document.

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Eureka License Agreement

In June 2020, as a part of the Asset Purchase Agreement, we acquired Syracuse Cayman’s entire right, title and interest in and to the Eureka License Agreement by and among Eureka and Eureka Therapeutics (Cayman), Inc. (collectively, “**Eureka Group**”), and Syracuse Cayman, effective as of June 30, 2020.

Pursuant to the terms of the Eureka License Agreement, we acquired (i) an exclusive, fully paid, sublicensable license under certain Eureka Group intellectual property solely (a) to develop, manufacture and commercialize Eureka Group’s product candidates directed to AFP and GPC3 existing as of June 30, 2020 or at any time during the five-year period thereafter (the “**Current Products**”) in the JW Territory, and (b) subject to separate license agreements to be entered into between Eureka and us, to commercialize Eureka Group’s TCR-based effector domain, known as ARTEMIS platform (including in connection with or as incorporated in a given product other than the Current Products), in the JW Territory, as well as (ii) a co-exclusive (with Eureka Group and its licensees) fully paid, sublicensable worldwide license under certain Eureka Group intellectual property to use the existing Eureka Group E-ALPHA antibody discovery platform and its current ARTEMIS platform to support seeking regulatory approval for and commercial activities for products (other than the Current Products) in the JW Territory. Under the terms of the Eureka License Agreement, we grant Eureka Group a reciprocal exclusive license to the Current Products and co-exclusive license to Eureka’s existing products and Eureka’s future products (other than the Current Products) under intellectual property generated by or on behalf of us that constitutes an improvement to the Current Products or Eureka Group’s ARTEMIS platform (excluding E-ALPHA antibody platform), in each case for use and commercialization by or on behalf of Eureka Group outside of the JW Territory. Under the Asset Purchase Agreement, we acquired the rights and licenses granted under the Eureka License Agreement for the total consideration of our ordinary shares in the amount of US\$95.3 million.

In addition, we and Eureka Group each granted the other a right of first offer with respect to new products that either we or Eureka Group develop from the use of Eureka Group’s licensed platform technologies, or that otherwise incorporate the licensed platform technologies, in all cases, for development and commercialization in such other party’s territory. As and when we acquire rights to products based on the ARTEMIS platform from Eureka (other than the Current Products), we expect to enter into a separate license agreement with Eureka with respect to such products, which may include customary upfront, milestone and/or or royalty payment obligations.

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Pursuant to the terms of the Eureka License Agreement, each party maintains sole ownership of any intellectual property rights developed individually and will jointly own all intellectual property rights developed jointly during the term of the agreement. Neither we nor Eureka Group have an obligation to account to the other party for profits, or to obtain the other party’s approval to license, assign or otherwise exploit the jointly developed intellectual property rights by reason of joint ownership thereof.

Prior to the fifth anniversary of the effective date of the Eureka License Agreement, neither party has the right to terminate the Eureka License Agreement. Following the initial five years of the Eureka License Agreement, either party may terminate for the uncured material breach of any material obligations under this agreement by the other party or upon the bankruptcy of the other party, provided that the licenses granted to either party under the Eureka License Agreement are perpetual in nature and will remain in force following any such termination with respect to any products that exist as of the effective date of termination.

Lyell Collaboration Agreement

In August 2020, we entered into a development and commercialization agreement with Lyell (the “**Lyell Collaboration Agreement**”), pursuant to which Lyell granted us an exclusive, sublicensable license under certain Lyell technology and Lyell’s interest in our joint inventions with Lyell, and an exclusive, fully-paid, sublicensable license under certain Lyell improvements to certain Lyell technology (T-cell anti-exhaustion functionality) to make, have made, use, import, sell and offer to sell two certain products targeting AFP and GPC3 in an ARTEMIS construct (JWATM213 and JWATM214) (together the “**Lyell Products**”), including without limitation to develop, commercialize and manufacture the Lyell Products in the field of treatment of hepatocellular carcinoma (the “**Lyell Field**”) in the JW Territory. In addition, Lyell granted us a non-exclusive sublicensable license under certain Lyell data and data from Lyell’s collaboration with Eureka and an exclusive, sublicensable license under Lyell’s interest in the data obtained by Lyell and us pursuant to the Lyell Collaboration Agreement (the “**Program Data**”) to support regulatory matters in connection with the Lyell Products in the Lyell Field in the JW Territory.

In turn, we granted Lyell a non-exclusive, sublicensable license under our background intellectual property and our interest in the Program Data to research and develop Lyell Products outside the JW Territory, in addition to an exclusive option, exercisable at Lyell’s sole discretion prior to Lyell’s filing for regulatory approval for any such product outside the JW Territory, to obtain an exclusive sublicensable license under our intellectual property to make, use, import, sell, and offer to sell Lyell Products outside the JW Territory and an exclusive, sublicensable license to our interest in the Program Data to support regulatory matters of the Lyell Products outside the JW Territory.

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In exchange for our rights, we are required to make various milestone and royalty payments. We are required to make a substantial milestone payment upon the first regulatory approval for a Lyell Product in the JW Territory. In addition, we are required to pay Lyell a royalty in the low single digits as a percentage on annual aggregate net sales of all Lyell Products by us or our sublicensee in the JW Territory. Moreover, we are required to make two additional milestone payments upon achievement of specified levels of aggregate annual net sales for all Lyell Products in the JW Territory. The amounts of these milestone payments are a mid-single digits percentage of the related annual net sales targets. Lyell also has reciprocal obligations to make certain milestone and royalty payments to us under the Collaboration Agreement if Lyell elects to exercise its option to take an exclusive license.

Our royalty obligations commence on a country-by-country basis upon the first commercial sale of any Lyell Product in the relevant country and expire on a country-by-country basis upon the later of the expiration of the last to expire patent licensed to us from Lyell containing a valid claim or ten years.

In addition, we and our affiliates, by ourselves or with a third party, are prohibited from researching, developing, manufacturing or commercializing any products in the JW Territory that (i) use counter exhaustion technologies that manipulate transcription factors involved in determining cell functional states, and (ii) target GPC-3 or AFP, including granting any licenses or other rights to a third party to do so until, as measured on a target-by-target basis, the sixth anniversary of the first regulatory approval for a Lyell Product directed to such target in the JW Territory.

In connection with our and Lyell's work pursuant to the Lyell Collaboration Agreement, we solely own improvements on certain technology controlled by us, and Lyell solely owns improvements on certain technology controlled by Lyell. Subject to the terms of the Lyell Collaboration Agreement, we and Lyell jointly own all other intellectual property made, conceived discovered, or otherwise generated by both parties in connection with the Lyell Collaboration Agreement.

The Lyell Collaboration Agreement will remain in effect until there is no remaining royalty payment or other payment obligation with respect to the Lyell Products. It may also be terminated earlier by our 180-day written notice, by either party for the other party's uncured material breach of a material term of this agreement, by either party upon the bankruptcy or insolvency of the other party, or if we voluntarily commence or assist with commencing proceedings alleging that patents covering certain Lyell technology are invalid.

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Acepodia Option and License Agreement

In January 2020, we entered into an option and license agreement with Acepodia (the “**Option and License Agreement**”), whereby Acepodia granted us an exclusive option (the “**Acepodia Option**”) to acquire from Acepodia an exclusive, sublicensable and fee-bearing right and license under certain patents and know-how, including a Chinese patent application currently owned by the Regents of University of California, to manufacture, develop, use, sell, offer for sale, import and otherwise commercialize products targeting HER2 (JWACE002) and another undisclosed target (JWACE055) (together the “**Acepodia Products**”) in the field of treatment, prevention or control of human diseases through targeting and modulation of HER2 and such other target (“**Acepodia Field**”) in the Territory. The target of JWACE055 is not disclosed due to commercial sensitivity. We have the first right to exercise the Acepodia Option upon written notice from Acepodia that certain clinical trial milestones for each Acepodia Product have been completed. As of the Latest Practicable Date, we have not exercised the Acepodia Option.

In exchange for the Acepodia Option, we are required to make various upfront, milestone and royalty payments. Upon execution of the Option and License Agreement, we made an upfront payment of US\$500,000 to Acepodia. We also agreed to pay an additional US\$500,000 to Acepodia upon submission of an IND to the FDA for each Acepodia Product. Upon exercise of the Acepodia Option, we agree to make certain upfront, regulatory and commercial milestone payments to Acepodia. Acepodia is also eligible to receive royalties in the high single to low double digits as a percentage of annual net sales in the Territory with respect to each Acepodia Product, subject to certain adjustments in specified circumstances. Royalties are payable on a product-by-product basis commencing on the first commercial sale of the Acepodia Product in the Territory and continuing until the latter of (i) the date of expiration, or a final judgment on invalidity from which no appeal has been or can be taken, of the last valid claim of a licensed patent in the Territory or (ii) the ten year anniversary of the date of the first commercial sale of such product in the Territory.

The Option and License Agreement will remain in effect until the earlier of (i) our election to not exercise the Acepodia Option for the Acepodia Products; or (ii) if we exercise the Acepodia Option, the expiration of the last to expire of the financial obligations for such Acepodia Product. It may also be terminated earlier by our prior written notice, by either party for the other party’s uncured material breach of this agreement, or upon the dissolution or the bankruptcy of either party.

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Dr. Patrick Y. Yang is the chairman of the board and co-founder of Acepodia. Dr. Patrick Y. Yang is currently our consultant. He was engaged as our Company’s consultant in January 2017 to provide talent recruitment services and high-level strategic guidance. He was also responsible in recruiting key personnel and assisting with interviewing assessment and on-job coaching. His engagement with our Company was suspended between September 2017 and January 2019 as he took up full-time role in Juno as executive vice president. After his Juno employment terminated in 2019 as a result of the Celgene acquisition of Juno, he resumed his consultancy role with the Company.

OUR PLATFORM

We have established an integrated, product-oriented platform that facilitates discovery, process development and scale-up, analytical development, technology transfer, commercial manufacturing, and quality control. This platform gives us the ability to advance product candidates from research to commercialization efficiently and effectively. In addition, we have constructed a manufacturing facility with superior automation. For further details, please see “—Chemistry, Manufacturing and Controls” in this section.

We have built our integrated cell therapy platform with the aim of identifying product candidates against novel-evidence based and novel targets with first-in-class and/or best-in-class potential, increasing the cost efficiency of development and likelihood of success. Our platform covers a wide spectrum of research and development functionalities for our product candidates in the field of oncology. Our platform facilitates collaboration among different functional groups and feeds into early research to cultivate promising targets with clinical and commercial potential.

Our platform integrates all the necessary capabilities to streamline our target-to-market timeline. These capabilities are housed in five main functional units: research and development, CMC, regulatory affairs, manufacturing and commercialization. These individual functional units have been optimized, and great attention has been given to building cross-function integration at key points in the lifecycle of a product candidate.

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The following table summarizes certain technology-related aspects of our platform:

Products	Technologies/advantages from licensor	Technology development plan	Outcomes
Relma-cel (autologous)	Unique vector with high efficacy and safety	Developed unique manufacturing process resulting in manufacturing dependability; conducted pre-clinical research; developed clinical programs and conducted extensive clinical research to demonstrate safety and efficacy	Potential superior product
JWCAR129 (autologous)	Unique vector with high efficacy and safety	In IND-enabling study right now (pre-clinical research). Plan to leverage our unique manufacturing process (similar to relma-cel); plan to file an IND in China as early as the first half of 2021	Develop a differentiated CAR-T therapy to treat MM patients
JWATM203 (autologous)	AFP antibody screened from E-ALPHA platform, a highly diverse human-derived antibody phage library; CAR-T based on ARTEMIS 3.0 platform, a novel technology platform; unique approach to solid tumour; better infiltration and less side effects	In tech transfer right now; plan to leverage our knowledge and expertise in process, analytical development and clinical development to optimize the product and conduct clinical research; IND-enabling studies could initiate as early as first half of 2021	Optimized manufacturing process and clinical research programs; Advancing JWATM203 to clinical stage for patients with AFP HCC
JWATM204 (autologous)	GPC-3 antibody screened from E-ALPHA platform; CAR-T based on ARTEMIS platform; unique approach to solid tumour; better infiltration and less side effects	Plan to leverage our knowledge and expertise in process, analytical and clinical development to optimize the product and conduct clinical research; IND-enabling studies could initiate as early as second half of 2021	Optimized manufacturing process and clinical development programs; potential to be a promising treatment for patients with GPC3+ HCC
JWATM213 (autologous) JWATM214 (autologous)	Lyell T-cell technology applied on products targeting AFP and GPC3 in an ARTEMIS construct (JWATM203 and JWATM204) to increase T-cell functionality and reduce T-cell exhaustion to potentially improve the anti-tumor effects	Plan to leverage our knowledge and expertise in process, analytical development and clinical development to combine Lyell technology to develop products with enhanced T-cell function and improved efficacy	Potential first -in-class products designed to have enhanced T-cell functions, persistence and infiltration into solid tumours with an improved safety profile

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RESEARCH AND DEVELOPMENT

R&D is a core part of our overall platform, and our capabilities span across the entire spectrum from discovery to clinical development and in both products and processes. Our proprietary R&D processes have been instrumental in enabling relma-cel to be the first anti-CD19 CAR-T product to be IND-approved by the NMPA for clinical trials in China in June 2018, before obtaining an acceptance from the NMPA to review our NDA application for relma-cel as a third-line treatment for DLBCL in less than two years. In addition, we focus substantial R&D efforts on improving our processes, and on using those improved processes to develop next-generation product candidates. We believe that such R&D efforts are key to maintaining our competitiveness in the biopharmaceutical industry, and we are dedicated to enhancing our pipeline by leveraging our world-class in-house R&D capabilities.

As of the Latest Practicable Date, our research and development team consisted of 70 employees, which includes our clinical development team of approximately nine employees. Our R&D projects have cross-disciplinary expertise in a variety of fields, including chemistry, biology, pharmacology, toxicology, pharmacovigilance, and translational and clinical research. We have established a range of in-house R&D capabilities, including metabolism and pharmacokinetic analysis, *in vivo* assessment of product efficacy, PK/PD properties and toxicity. Going forward, as our business continues to grow, we intend to increase our R&D headcount by approximately 20% to 25% annually in 2021 and 2022. We plan to hire R&D personnel with expertise and experience in cell therapy in the areas of process development, clinical operation, translational research and other areas as per the Company’s needs.

Our Zhangjiang R&D center in Shanghai spans approximately 2,404.35 square meters (including an ancillary office area) and is equipped with viral vector and cell therapy process development platform, analytical platform with molecular, flow cytometry lab, biochemical and physical-chemical lab, and cell-based assay lab. It houses our Process Development (“PD”) operations, which include (i) process transfer-in/out; process development and optimization; process and product characterization; and bringing new technologies and platforms for plasmids, viral vector and cell therapy products, as well as (ii) an analytics platform consisting of a PCR/qPCR lab, flow cytometry lab, biochemical and physical-chemical lab and cell-based assay platform, aiming to support in-process testing and product characterization of plasmids, vector and cell therapy as well as to bring in new characterization measurement to improve the understanding of the process and our product. For further information on our PD capabilities, including our analytics platform, see “— Chemistry, Manufacturing and Controls.”

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Moreover, the manufacturing processes for our lead product relma-cel (JWCAR029) and second product, JWCAR129, were developed at our Zhangjiang R&D center, and our Nex-G process as well as our pipeline products JWATM203, JWATM213, JWATM204, and JWATM214 are also being developed at the Zhangjiang R&D center.

For the years ended December 31, 2018 and 2019 and the six months ended June 30, 2020, our R&D expenses were RMB76.0 million, RMB136.1 million and RMB82.3 million, respectively.

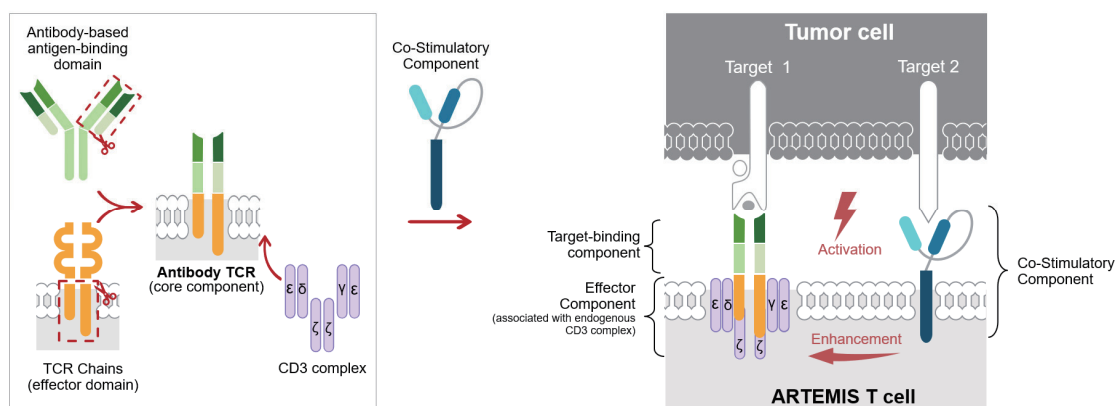
Research and Development for In-Licensed Product Candidates

We promptly commenced research and development activities after in-licensing product candidates from our licensing partners. We have devoted a considerable amount of time and resources to the R&D of in-licensed product candidates, and such efforts include but are not limited to: (i) the design of the clinical trials to be implemented in China and proactive communication with relevant regulatory authorities to obtain IND approvals and (ii) the preparation of clinical trials, which includes analyzing data on clinical needs, conducting central lab preparation, developing and validating the methodology, setting up electronic data capturing system, finalizing statistical analysis plan, risk management plan, and medical monitoring plan, conducting site selection, applying for necessary approvals, and conducting meetings with principal investigators. We have set up standards of project management and clinical operations, and give detailed instructions and guidance to such third parties. Additionally, we invite leading CAR-T experts and arrange training sessions for potential investigators in preparation for the clinical trials.

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Early Research Capabilities — Eureka ARTEMIS Platform

The ARTEMIS (Antibody Redirected T-cells with Endogenous Modular Immune Signaling) platform is a novel proprietary technology platform that was designed to utilize the natural biology of T-cells to fight cancer. The following diagram illustrates the key elements of the ARTEMIS platform:



Source: Eureka Information

The ARTEMIS receptor has two core functional components: (i) the antibody-based antigen binding domain and (ii) the TCR-based effector domain. The antigen-binding domain of the ARTEMIS receptor, selected using the E-ALPHA platform (as described below), is a targeting component such as a Fab fragment derived from a human antibody. The effector domain of the ARTEMIS receptor comprises portions of the γ (gamma) and δ (delta) TCR chains. This antibody-TCR, or AbTCR, core design serves as the universal backbone of the ARTEMIS platform to which additional modular components can be added to optimize the T-cell activation and expansion, enabling customization for different tumor types. The ARTEMIS receptor forms a multimeric receptor with the endogenous CD3 complex, which feeds into a network of signaling pathways that regulate T-cell activation. This ARTEMIS receptor-CD3 complex association is what allows the ARTEMIS receptor to use intrinsic cellular response and regulation mechanisms that have naturally evolved for immune cell signaling.

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Furthermore, the utilization of $\gamma\delta$ TCR chains in the ARTEMIS receptor may afford an advantage over current TCR-T therapy. To generate an engineered $\alpha\beta$ TCR-T-cell, exogenous α and β chains have to be introduced into $\alpha\beta$ T-cells, which may result in an exogenous α chain pairing with an endogenous β chain (and vice versa). This can lead to the generation of mispaired $\alpha\beta$ TCRs, which could bind to unintended targets. In contrast, the effector domain of the ARTEMIS receptor comprises portions of the $\gamma\delta$ TCR chains. $\gamma\delta$ TCR chains do not bind or pair with endogenous $\alpha\beta$ TCR chains. Thus, we believe introducing the ARTEMIS receptor into $\alpha\beta$ T-cells should not result in the formation of mispaired receptors with unknown cross-reactivity.

Currently marketed CAR-T therapies include a boxed warning citing fatal or life-threatening risks of CRS and NT. We believe this is due to hyperactivation of T-cells expressing CAR constructs that directly fuse or couple CD3 signaling domains to T-cell co-stimulatory domains. Through the utilization of pathways naturally evolved for immune cell signaling and the avoidance of receptor mispairing, we believe the ARTEMIS platform have the potential to enable the development of safer T-cell therapies. Two of our programs (JWATM203 and JWATM204) were built upon the ARTEMIS platform.

Pre-clinical Research

We have conducted extensive pre-clinical research to meet the CDE’s requirement for IND-enabling studies in pharmacodynamics, pharmacokinetics and toxicology. We have expertise in house to conduct, manage, and analyze pre-clinical studies necessary for IND filing enablement with regulatory authorities in China and the rest of the world. Specifically, for relma-cel, we have successfully completed and filed as part of both IND and NDA submissions to CDE, *in vitro* pharmacology (such as cytolytic activity, proliferation, cytokine release assays, tissue (tumors vs normal) and species cross-reactivity analysis, integration site analysis, as well as assessment of ScFv-Fc binding profile using membrane protein arrays), *in vivo* pharmacology plus pilot toxicology studies for 13 weeks, and *in vivo* PK-bio-distribution study for 8 weeks. We also have the needed expertise to conduct, manage and analyze *in vivo* studies in tumor-bearing immune-compromised mice to demonstrate effective anti-tumor activity of our early stage product candidates, and we have conducted such studies for relma-cel. We have begun to conduct similar pre-clinical testing for other product candidates, such as JWCAR129, and we intend to conduct such studies for future product candidates as well. In addition, we have the expertise to conduct, manage and analyze long-term (26 weeks) toxicity, which the CDE believes can serve the purpose of assessing the potential for malignant transformation during long-term persistence of CAR-T in patients. This remains a requirement for late phase clinical trials and future marketing authorization, and we have submitted such data for relma-cel to the CDE as part of our NDA submission.

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More specifically, our extensive pre-clinical research conducted to date has included the following elements:

- Developing and validating Next-Gen RNAseq methods for clinical analysis to monitor tumor micro environment at transcriptomic levels;
- Validating other assays at genomic, protein and cellular levels and implementation into clinical studies to monitor pharmacodynamics, pharmacokinetics, safety, and surrogate biomarkers;
- Conducting in-vitro functional assays and demonstrating the specificity of cytotoxicity, cytokine release, proliferation and activation of our CAR-T products;
- Conducting in vivo pharmacology studies as a proof of concept and demonstrating the effectiveness of our CAR-T products in appropriate disease animal models, i.e. xenografted immunocomprised mice;
- Performing pharmacokinetic and tissue distribution studies in animal models of disease;
- Completing definitive toxicity studies (short- and long-term toxicity to support IND and BLA, respectively), and evaluating the potential toxicity of our products in animal models (in particular, the risk of tumorigenicity as well as carcinogenicity following infusion were also evaluated in these studies); and
- Conducting insertional assessment and evaluating the risk of insertional genotoxicity and carcinogenicity of our CAR-T vectors.

Clinical Development

Our clinical development unit is led by Dr. Hongxia Zheng, M.D., Ph.D.. The clinical development unit of our platform manages substantially all stages of clinical trials, including clinical trial design, implementation, production of product candidate samples used, and the collection and analysis of trial data. As of the Latest Practicable Date, our clinical development team consists of approximately nine employees, including three holding doctorate degrees and six holding master’s degrees.

We conduct all of our clinical operations in-house to ensure quality and execution efficiency. As of the Latest Practicable Date, we have involved more sites in our clinical trial in China, than any other CAR-T company, according to Frost & Sullivan.

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Our clinical development unit is responsible for the selection of trial sites. We select trial sites based on multiple factors, including suitability of onsite facilities, availability of qualified staff and availability of research subjects. We have entered into agreements with numerous hospitals and principal investigators located in China that can support our clinical trials of different indications at different stage. We believe the size and geographic diversity of these facilities provide us with a significant advantage in implementing large-scale clinical trials and also enable us to conduct multiple clinical trials concurrently. We believe our expertise in recruiting clinical trial patients helps us optimize our drug development timeline. With the support of our partner hospitals, we are capable of recruiting participants from specific populations for studies that would otherwise be difficult to fulfill enrollment.

Except for clinical translational laboratory work and statistical analysis, we do not use CROs for our clinical research.

CHEMISTRY, MANUFACTURING AND CONTROLS

Based in our facilities in Zhangjiang and Shanghai Waigaoqiao, China, our CMC team provides pre-clinical and clinical support throughout the product development process. This aspect of our fully-integrated platform covers CMC functions including process development, analytical development and quality control and quality assurance. Each of these functions is seamlessly coordinated with one another, and this group also supports our manufacturing capability.

Our CMC capability includes the following functions:

- Our *Process Development capabilities* include process transfer-in/out; process development and optimization; process and product characterization; and bringing new technologies and platforms for plasmids, viral vector and cell therapy products. Our process development capabilities consist of three main platforms: cell therapy process platform, microbial/plasmid platform and viral vector platform.
 - The cell therapy process platform is designed based on autologous T-cell process as a basic platform, with the flexibility to adapt to other processes. The platform process was designed based on technology transferred from Juno with internal development and optimization. Our lead product relma-cel has been extensively characterized and validated; through which we have established process robustness and accumulated extensive manufacturing experience.

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The current platform process is based on a unit operations concept with an automated and standardized device for each unit operation. The operations are automated to minimize human error, with closed processing to minimize contamination and cross-contamination, which enables a high run-rate while keeping operation costs low at a commercial scale. As part of our “2.0” strategy (described below), part of the T-cell process platform is under further development to a next-generation process that targets simultaneously improvement in cost of goods, manufacturing cycle time, and potentially clinical outcomes.

- The viral vector platform consists of packaging (adhesion or suspension) and purification platform, with capabilities for process development and vector production to support cell therapy product/process development up to pre-clinical studies. Clinical manufacturing capabilities are being developed and are anticipated to be online by the end of 2021.
- The microbial/plasmid platform consists of fermentation and plasmid purification platform, with capabilities for process development and plasmid production to support viral vector development and production.
- Our *Analytics Platform* consists of a PCR/qPCR lab, flow cytometry lab, biochemical and physical-chemical lab and cell-based assay platform, aiming to support in-process testing and product characterization of plasmids, vector and cell therapy as well as to bring in new characterization measurement for better understanding of the process and our product. Our assay development and optimization efforts are focused on improving process robustness, strengthening understanding to the product mechanism of action (“MOA”), to provide product characterization in addition to release testing, to inform quality target product profile (“QTPP”) and product specification setting, and to develop a well-informed, data-driven raw material and process control strategy.
- Our established *Quality System* meets Chinese health authorities and ICH requirements. We implement a holistic quality control strategy including raw material control, in-process, and release testing designed for gene and cell therapy products with high specificity, sensitivity and fast turnaround. We have built capabilities to improve, validate and transfer analytical methods from Process Development and both internal and external collaborators in assay platform such as: flow cytometry for identity and immunophenotyping; cell biological assays (cell viability and cell count, cytolytic potency); molecular biology (qPCR for vector copy number, replication-component lentivirus, and mycoplasma); ELISA-based impurity panel; infectious titer and vector functional test; and a battery of microbial testing including rapid sterility.

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There was no material issue related to CMC or manufacturing in our development of relma-cel. Six batches of product during our Phase I clinical trial relating to relma-cel did not meet the pre-defined specifications. This did not cause any safety related issue. The cause was subsequently rectified, and no similar issue arose during our subsequent clinical trials. The release criteria consist of safety, identity, purity, and potency categories of specifications, and they have not been changed over the past two years since the beginning of Phase I manufacturing. The release criteria are being reviewed by CDE, and they may change per CDE requests.

REGULATORY AFFAIRS

Our regulatory affairs team is responsible for the regulatory approval process of our product candidates, including assembling application dossiers for IND applications and NDAs, addressing inquiries from relevant authorities and monitoring our R&D projects to ensure their compliance with relevant regulations.

We believe that we are viewed by regulators as one of the key players in providing input from a commercial perspective on the development of China’s cell therapy regulatory environment. We provided input on the development of cell therapy regulatory guidance by the NMPA’s Center for Drug Evaluation (“CDE”), and we regularly communicate with the CDE on issues related to cell therapy. We also provided feedback to the CDE on the Drug Administration Law and the CAR-T GMP inspection guide. Our feedback and input to the CDE on these matters have typically taken the form of participation in workshops convened by the CDE, to which regulators, academics and industry representatives have been invited. Our primary goal in providing such feedback and input was to promote the consistency of emerging PRC industry regulatory standards with existing international standards. Moreover, as founding chair of the Shanghai CAR-T Alliance and as a member of the China Pharmaceutical Innovation and Research Development Association (PhIRDA), we are one of the key players in building the CAR-T industry in China.

Material Regulatory and Industry Communications

In the course of the pre-clinical and clinical development of relma-cel, we have engaged in the following material communications with the CDE (in addition to filing an IND application in December 2017, obtaining approval of our IND application in June 2018, and submitting and receiving acceptance of our NDA in June 2020 relating to relma-cel). The CDE did not raise any objections or material concerns with respect to the development of relma-cel.

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Communication Type	Form of Communication	Date	Content of Communication	Communication Result
Pre-IND Meeting	Face-to-face meeting	November 8, 2017	Consultation on the design of pharmacological and toxicological tests, cell production technology and clinical trial protocols.	CDE agreed with our proposed design for pharmacological and toxicological tests and clinical protocols, and responded to CMC questions.
End of Phase I Meeting	Face-to-face meeting	January 22, 2019	Report the results of the Phase I clinical trial of relma-cel; discuss and determine the plan of the registrational/pivotal Phase II clinical study of relma-cel; discuss technical CMC issues related to the clinical development of relma-cel.	<ol style="list-style-type: none"> 1. Discussed and reached a consensus on the design of the Phase II trials, including dosage, primary efficacy endpoint and sample size. 2. CDE agreed to our CMC proposals, including recommendations on viral vectors, production media, and release testing methods.
Pre-NDA Meeting	Written response	April 27, 2020	Consultation on clinical, pharmacological, toxicological, and CMC issues before NDA filing.	<ol style="list-style-type: none"> 1. Clinical issues: A separate meeting was held on May 7, 2020 with the CDE on the clinical issues. 2. Pharmacological and toxicological issues: CDE provided clear feedback on and acknowledged our responses to the questions. 3. CMC issues: CDE gave suggestions or answers to the questions on which we consulted.
Pre-NDA Meeting	Telephone conference	May 7, 2020	Report the results of the registrational/pivotal Phase II clinical trials of relma-cel, and consultation on whether the clinical data that we proposed to provide to CDE in the NDA is acceptable.	CDE gave clear confirmation on our proposed clinical data set to be included in the NDA submitted by us and agreed to our submission of the NDA in accordance with the proposal.
Pre-NDA Meeting	Telephone conference	June 11, 2020	Presentation of the results of our CMC research on relma-cel, and responses to questions previously raised by CDE.	CDE heard our presentation and accepted and acknowledged our responses to various questions raised.

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In addition to the foregoing material regulatory communications, in the course of our clinical trials of relma-cel, we engaged in close communications with principal investigators and ethics committees at each of the 11 hospitals and research institutes at which we conducted our Phase I and registrational/pivotal Phase II clinical trials over a two-year period between June 2017 and June 2019, and received approval for our proposed clinical trials at such institutions from the relevant ethics committees. For further information on the data that we gathered from our clinical trials at these institutions, see “— Our Product Pipeline — Our Core Product Candidate — relmacabtagene autoleucel (“relma-cel”) — Clinical Data Related to Relma-cel.”

As a result of the foregoing material regulatory and industrial communications, we developed extensive training materials for physicians on the administration of relma-cel, as well as a comprehensive introduction to CAR-T therapy for patients as part of the process of obtaining informed patient consent to the administration of CAR-T therapies. Our communications with physicians at the hospitals and research institutes where we conducted clinical trials of relma-cel contributed significantly to the formation of our commercialization strategy for relma-cel. Since these institutions have established treatment or disease management procedures and supporting medical resources developed during the administration of relma-cel as part of our clinical trials, these institutions are expected to also be our initial commercial target sites. As set forth in greater detail under “— Our Strategies — Drive full-scale commercialization of relma-cel and build upon our significant first mover advantage” above and under “— Commercialization” below, our commercialization strategy for relma-cel involves i) building a focused in-house sales team to cover, initially, approximately 50 of the top hospitals in China with the best hematological and transplantation centers and ii) designing our marketing and academic education strategy around close and continued engagement with physicians (including those at the hospitals and research institutes where we have conducted clinical trials). Once we have gained a foothold at such top hospitals in China, all of which are located in major urban centers, we plan to use them as reference sites to influence/educate hospitals in second-tiered regions for mid-term commercial development.

Aside from the foregoing material regulatory and industrial communications, we do not believe that our communications with other third parties (such as oncologists, other KOLs, patient groups, consultants or scientific advisors) had a material impact on the design of our clinical trial plans or commercialization plans with respect to relma-cel. We have regularly updated our significant shareholders on the implementation of our clinical development plan.

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Prior to CDE approval of our NDA relating to relma-cel, we expect to engage in the following additional material communications with the CDE, all of which are part of the ordinary course approval process for new products. First, we expect to receive queries from the CDE regarding our NDA, including potential requests for additional information, and we will respond to such queries and requests. Thereafter, the CDE would schedule inspections of our clinical trial sites and manufacturing facilities, which we currently expect to occur during the fourth quarter of 2020. After our facilities have passed such inspections, the CDE would approve our NDA relating to relma-cel, which we currently expect to occur during the first half of 2021.

To date we have not conducted clinical trials, or engaged in material regulatory or industry communications with third parties, with respect to any of our product candidates other than relma-cel.

MANUFACTURING

Overview

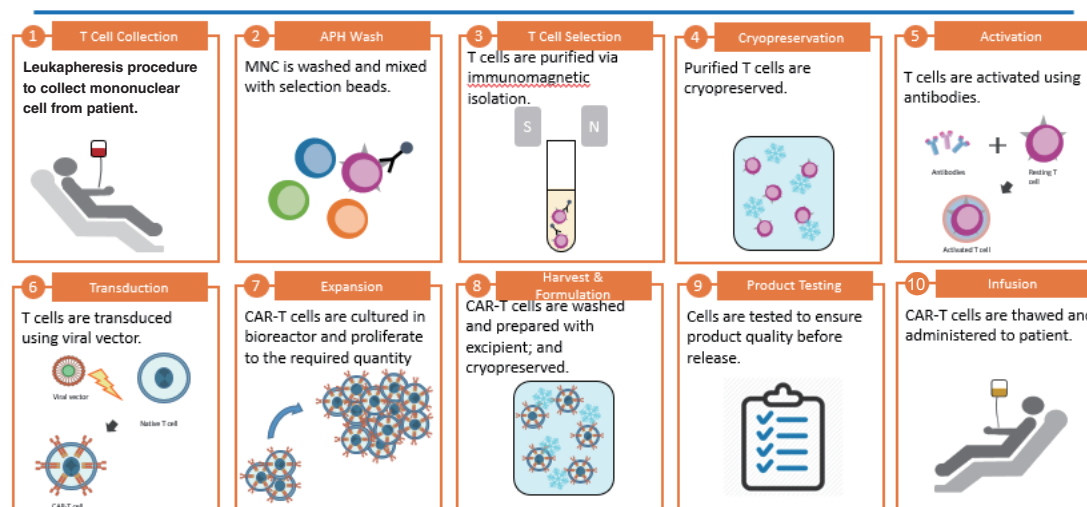
Since we commenced clinical trials of relma-cel in 2018, we have carried out clinical manufacturing at our Waigaoqiao and Zhangjiang facilities in Shanghai, which covers approximately 600 square meters. We have a 100% success rate for the manufacture of relma-cel throughout our DLBCL registrational clinical trial.

In June 2020, we received a production license from Jiangsu province authorities for our new commercial manufacturing facility in Suzhou. This facility provides approximately 9,976 square meters for commercial and clinical manufacturing in compliance with cGMP and QMS standards. It is designed to house four independent modules. Currently, two modules are constructed, qualified, and in full GMP operations. The design of the modules can be adapted to support all cell platforms, including those using gene-modified autologous T-cells and NK cells, gene-modified or non-gene-modified TIL and gene-modified allogeneic immune cells, as well as facilities to produce clinical grade viral vectors that are used to genetically modify these cells. It currently has the capacity to support autologous CAR-T treatment of up to 2,500 patients per year. This facility is designed to address all of the major challenges associated with scaling up from clinical scale to commercial scale manufacturing, which represents a paradigm shift in which product quality, regulatory compliance, process reliability, scalability and cost of goods all become critical factors. We believe the degree of automation that we have designed into our commercial manufacturing processes positions us as a leader in terms of CAR-T manufacturing in China. There are no material differences between our clinical and commercial manufacturing. However, the CDE may request that we tighten our product release specifications (typically based on our already demonstrated process capabilities). We do not anticipate any problems with meeting more tightened product release specifications.

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Manufacturing Process

The following diagram provides an overview of the manufacturing process for a CAR-T therapy for an individual patient:



Our cell therapy process platform is designed based on autologous T-cell process as a basic platform, with a flexibility to adapt to other processes. The current platform process is based on unit operations concept with automated and standardized device for each unit operations. Our lead product relma-cel has been extensively characterized and validated; and has established process robustness and accumulated extensive manufacturing experience.

Moreover, we have designed our commercial manufacturing capabilities to include the following features:

- *One common process for the manufacture of different doses to ensure consistency in product quality attributes.* Many CAR-T development companies face the common challenge of trying to produce enough CAR-T in order to meet the dose requirements, due to the large variability in each patient’s starting materials in terms of cell numbers and characteristics. In our manufacturing process, we design a series of in-process controls to ensure the variability in the incoming patient materials is progressively reduced towards the final cell drug product. Furthermore, we design our process to have the capability to produce the highest dose anticipated and then use different infusing volumes to achieve different doses, throughout Phase I and registrational Phase II of our DLBCL clinical trials, while maintaining consistent manufacturing cycle time and consistent product quality attributes.

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- *Closed processing to prevent contamination and cross-contamination, which allows concurrent processing of multiple patient samples in a large clean room with lower grade of clean room requirements.* Many other CAR-T companies use “open-processing” manufacturing operations, which involves processing each patient’s starting material and intermediates in an isolated, small “clean room” with a higher grade of clean room classifications requirements. Since the materials being processed are exposed to the atmosphere, there is a higher risk of contamination. In contrast, our closed-processing operations use aseptic connection techniques that ensure materials being processed are not exposed to the atmosphere. This enables us to process multiple patient samples and intermediates concurrently in a large clean room with lower grade of clean room classification requirements. As a result, we can achieve higher quality and reliability, at higher output with the same area, which means lower capital and operational costs.
- *Highly automated systems to ensure consistent, error-free operations and to control labor costs.* The manufacturing process of many other CAR-T companies involve manual operations that rely on highly experienced and highly trained operators. They also rely on SOPs that need to comprehensively capture the knowhow of expert operators. Any human errors, no matter how small, could potentially lead to severe consequences that may result in a failed batch. In addition, the number of labor hours and costs for training, qualifications, and operations are quite significant. In contrast, our manufacturing process is highly automated and requires significantly less labor hours and costs. In addition to ensuring consistent and error-free operations, our highly automated operations do not rely on personnel with specific knowhow.
- *Implementation of computerized MES (manufacturing execution system) to ensure robust traceability/chain of identity.* In CAR-T manufacturing, it is essential to ensure a robust traceability/chain of identity, so that each patient receives CAR-T derived from that patient’s starting material. Failure to maintain a robust chain of identity could be fatal, since if a patient receives CAR-T derived from a different patient’s starting material, it would likely give rise to a severe allergic reaction. Accordingly, we have implemented a computerized MES to ensure a robust chain of identity, in compliance with regulatory requirements for CAR-T manufacturing in China.

Our computerized MES was developed on a platform supplied by a well-established international MES developer. Our vendor’s MES platform specializes in the pharmaceutical and biopharmaceutical industry. Our MES implementation follows international GMP standards for computerized system development and validation. The MES has been successfully implemented and validated, and currently in GMP operations. As this is an important system for our operations, hardware system redundancy and manual paper emergency backup procedure have been implemented to

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mitigate risks of potential failure to maintain a robust chain of identity. We believe, however, that many potential CAR-T competitors in China will find implementation of a similar system to be a significant barrier to entry.

Our CAR-T product consists of >99% CD3+ T cells. Our process includes a proprietary T-cell selection step that selects CD3+ T-cells simultaneously prior to activation with high level purity.

Our primary improvement on the Juno manufacturing process is to employ a more cost-effective single-train process in which CD4+ and CD8+ T-cells are simultaneously selected and then processed through the activation, transduction, and expansion unit operations in a single train to produce the final product. In the Juno process, the CD4+ and CD8+ T-cells are selected separately and subsequently processed in a dual-train to produce separate CD4+ and CD8+ T-cell products before combining them to make a final product. We have also implemented a proprietary maximum limit of CD3+ T-cells to be activated and transduced to ensure that the durations of cell expansion are consistent throughout the entire Phase I and II clinical manufacturing, which is critical to ensure consistent T-cell characteristics (T-cell phenotype, such as memory type of T-cell) in the final product, which consequently contributes to a potential improvement in safety.

Our “Nex-G” Strategy

A key initiative of our manufacturing development includes our “Nex-G” strategy, which is aimed at reducing manufacturing costs, in order to make cell therapies accessible to a broader segment of the population, while maintaining and enhancing the efficacy, safety and overall quality of our products. This strategy includes:

- Leveraging our extensive clinical and CMC data derived from a single version of manufacturing process, we are building a proprietary data integration platform, and deploying machine learning approaches to develop critical insights for our autologous CAR-T therapy platform. We are developing our next-generation process to simultaneously improve cost of goods, manufacturing cycle time, and potentially clinical outcomes.
- Significantly reducing cost of raw materials by eliminating wastes and scraps; as well as pursuing substitutions with lower cost materials and eliminations where feasible.

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- Securing a world-class, high-quality and cost-effective supply network; and establishing long-term supply agreements to simultaneously achieve lower costs and high reliability.
- Leveraging economies of scale by expanding our scale through opening up additional modules for commercial use within our existing facilities; and
- Further enhancing our quality consistency through increased automation and optimization of production operations.

COMMERCIALIZATION

As CAR-T therapies are a new and comprehensive treatment process that is unlike any other treatment currently approved in the market, we expect that significant efforts will be necessary to educate physicians and patients on the potential benefits of CAR-T therapies, and to demonstrate the proper process in administering and monitoring the treatment (including timely and proportionate measures to mitigate adverse effects).

We plan to build a focused in-house sales and marketing team to market relma-cel across China. Our initial target is to create, at the initial commercialization of relma-cel, a sales team of approximately 60-70 people to cover approximately 50 of the top hospitals in China with the best hematological and transplantation centers, which are equipped with the technology and physicians to administer our CAR-T therapies. In particular, we plan to set up sales and operations teams at the target hospitals to facilitate and administer the use of our products. These teams will ensure our CAR-T therapies are executed in accordance with the applicable standards and provide advice to the medical team at the site. A significant number of these hospitals have acted as clinical trial centers for relma-cel, as a result of which many relevant physicians in those hospitals will already be familiar with relma-cel. As our business grows over the next three years, we anticipate expanding our sales force to approximately 100-120 people in order to support the administration of our CAR-T therapies across the top 100 oncology hospitals in China.

Because physicians are expected to play a key role in this process, not only in administering CAR-T therapies but also in educating patients about their potential benefits, we intend to design our marketing and academic education strategy around close and continued engagement with physicians. We believe that we have already established a strong rapport with a significant number of physicians and other KOLs across China through the extensive clinical trials that we have conducted, in terms of both gaining recognition of the merits of relma-cel and enhancing physicians’ familiarity with the product. In addition, we plan to be pro-actively involved in the policy making framework relating to cell therapy by actively participating in consultation sessions with the relevant authorities, particularly on improving medical procedures and standards.

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We plan to enhance our existing collaboration with these physicians and other KOLs through the establishment of a specialized team for medical affairs, which will oversee the training and support that we provide to physicians. In addition, we plan to develop a specialized, standardized training plan that will allow us to onboard and train physicians and treatment centers that have not been involved in our clinical trials, with the ultimate goal of gaining widespread acceptance of relma-cel across the medical community and the general public. We are also working with academic organizations in China to update the guidelines of lymphoma treatment to reflect the treatment results and promote awareness of relma-cel.

Our marketing plans are currently focused on r/r DLBCL and will expand to cover other indications as our clinical trials progress. Our marketing activities will include introducing our product candidates to physicians, educating KOLs about the competitive advantages of our product candidates and participating in industry and academic conferences and promoting brand awareness.

Prices of innovative drugs in China vary from product to product. In recent years, innovative drugs in China have been priced at a wide range of discounts to the price of the same drug in the U.S., often between 20% and 70% of the same drug in the U.S., according to Frost & Sullivan. For example, Ibrutinib, approved in 2017 in China, was priced at approximately 17.5% of the same drug in the U.S. While Durvalumab, approved in 2019 in China, was priced at approximately 69.2% of the same drug in the U.S. There are currently no commercialized CAR-T products in China and hence no CAR-T market price is available in China. However, the Company anticipates that its CAR-T products will be priced at a discount to U.S. CAR-T products under a similar trend, and that a number of factors, such as clinical value, product quality, product marketing, competitiveness, patient affordability and competitors’ pricing strategy will also affect its product pricing.

In the future, we may be subject to laws and regulations relating to drug distribution and tender process. For details, please refer to the section headed “Regulatory Overview — Regulations on Dual Invoicing System” in this document.

SUPPLIERS AND RAW MATERIALS

The principal raw materials that we use in our business include human albumin, human serum, activation beads, selection beads, culture media, lentiviral vector, among others. The principal types of equipment that we use in our business include controlled rate freezers, LN2 tanks, bioreactors, magnetic cell separation devices and automated cell processors. We procure these raw materials and supplies from a variety of suppliers around the world. We select our suppliers by considering their quality, industry reputation, compliance with relevant regulatory agencies according to company purchasing policy, among other factors.

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For the years ended December 31, 2018 and 2019 and the six months ended June 30, 2020, our purchases from our five largest suppliers in aggregate accounted for 23%, 20% and 12% of our total purchases, respectively, and purchases from our largest supplier alone accounted for 11%, 9% and 5% of our total purchases, respectively. Purchases include raw materials, third party contracting services for research and development purposes, equipment, construction and renovation, and administrative services. Save for WXAT Shanghai, all of our five largest suppliers during the Track Record Period are Independent Third Parties, and none of our Directors, their respective associates nor any shareholder who, to the knowledge of our Directors, owned more than 5% of our issued share capital as at the Latest Practicable Date, has any interest in any of our five largest suppliers during the Track Record Period.

In addition, as adequate alternative sources for such supplies exist, we have developed alternative sourcing strategies for these supplies. We will establish necessary relationships with alternative sources based on a periodic supply continuity risk assessment. Other than the agreements with certain CROs, we order supplies and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

COMPETITION

Our products will compete with novel therapies developed by biopharmaceutical companies, academic research institutions, governmental agencies and public and private research institutions developing therapies that target the indications which we are targeting, in addition to standard of care treatments for those indications.

Novartis International AG (“**Novartis**”) and Kite Pharma, Inc. (“**Kite**”) were the first to achieve FDA approval for autologous T-cell therapies. In August 2017, Novartis obtained FDA approval to commercialize Kymriah for the treatment of children and young adults with acute B lymphocytic leukemia or r/r ALL, and in May 2018, Kymriah received FDA approval for adults with r/r DLBCL. Kite obtained FDA approval to commercialize Yescarta, the first CAR-T product candidate for the treatment of adult patients with r/r large B-cell lymphoma, in October 2017, and accelerated approval for Tecartus, the world’s first CAR-T treatment for MCL, in July 2020. Kite also has published data on Yescarta in ALL. Juno has published data on its anti-CD19 CAR therapy, liso-cel. Bluebird bio, Inc. was the first company to publish data on an anti-BCMA CAR-T therapy, ida-cel, in MM. Legend Biotech Corporation (“**Legend**”) and Janssen Biotech, Inc. (“**Janssen**”) have jointly published data on their CAR-T product candidate, LCAR-B38M/JNJ-4528, for the treatment of MM.

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Due to the promising therapeutic effect of cell therapies in clinical trials, we anticipate increasing competition from existing and new companies developing these therapies. We expect to compete in China with Fosun Kite, which filed a NDA with the NMPA in February 2020 for approval to market (axicabtagene ciloleucel), a CD19-directed CAR-T product, as a third-line treatment for r/r large B-cell lymphoma (including DLBCL). Although both relma-cel and Fosun Kite’s axicabtagene ciloleucel are anti-CD19 CAR-T products, they are distinct products for several reasons. First, they use different CAR constructs: relma-cel uses a 4-1BB costimulatory domain, while axicabtagene ciloleucel uses a CD28 costimulatory domain. In addition, they are manufactured using different processes. Moreover, they have different characteristics, including safety and efficacy profiles.

We also expect to compete in China with Legend Biotech, which is in a Phase II trial for approval to market a BCMA-directed CAR-T product, as a treatment for r/r MM. In addition, other potential CAR-T therapy competitors include:

- Other companies developing CD19-directed cell therapies for the treatment of B-NHL;
- Companies developing BCMA-targeted cell therapies for the treatment of MM; and
- Companies developing cell therapies for treatment of HCC in China.

We also expect to compete with other companies seeking to develop and commercialize cell therapies in China, including for trial sites, for enrollment in our trials and with respect to indications that we are targeting and may target in the future.

Please see below table on the profiles of some of the Company’s competitors:

Company Name	Established Time	Headquarter	Major Industry Expertise in Cell Therapy
Fosun Kite	2017	China	Fosun Kite is a cell therapy company that has brought in the CAR-T therapy axicabtagene ciloleucel (U.S. trade name Yescarta) from Kite Pharma (project name FKC876) in China. The product is a CD19 targeted CAR-T, aiming to target r/r B-cell NHL. Fosun Kite has completed the clinical trials for the product in China and has submitted the NDA to the NMPA.
Legend Biotech	2014	US	Legend Biotech is focused on discovering and developing cell-based therapy, and its leading CAR-T product LCAR-B38M is currently undergoing Phase II clinical trial in China. LCAR-B38M targets BCMA and is being developed to treat patients with r/r MM.

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Company Name	Established Time	Headquarter	Major Industry Expertise in Cell Therapy
Novartis	1996	Switzerland	Novartis is a global pharmaceutical company and is a pioneer in cell therapy that developed the first CAR-T cell therapy tisagenlecleucel (U.S. trade name Kymriah) approved for r/r B-cell acute lymphoblastic leukaemia (ALL). Currently, it is carrying out a Phase III clinical trial in China for its CD19 targeted CAR-T for the treatment of r/r B-cell NHL.

Many of our competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, pre-clinical testing, clinical trials, manufacturing, and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors. Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than products that we may develop. Our competitors also may obtain NMPA or other regulatory approval for their products more rapidly than we obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. The key competitive factors affecting the success of all of our programs are likely to be efficacy, safety, convenience and pricing. These competitors may also vie for a similar pool of qualified scientific and management talent, sites and patient populations for clinical trials, as well as for technologies complementary to, or necessary for, our programs.

EMPLOYEES

The following table sets forth a breakdown of our employees by function as of the Latest Practicable Date:

Function	Number	% of Total
Technical operations	118	45.7
Quality	60	23.3
Medical	38	14.7
Business development and general administrative	10	3.9
Commercial	9	3.5
Support	23	8.9
Total	258	100.0

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As at the Latest Practicable Date, we had 167 employees in Shanghai, 75 employees in Suzhou, 14 employees in Beijing, one employee in Tianjin and one employee in Zhengzhou. We currently have a 70-member R&D team; and we plan to increase the size of our R&D team to 89 members by the end of 2020 to support the further development of our pipeline candidates. In anticipation of the launch of our pipeline candidates, we plan to further expand our commercialization team to 54 members, including marketing and sales representatives by the end of 2020. For further details, please see “— Commercialization” in this section.

Employment Agreements with Key Management and Research Staff

We enter into standard confidentiality and employment agreements with our key management and research staff. The contracts with our key personnel typically include a standard non-compete agreement that prohibits the employee from competing with us, directly or indirectly, during his or her employment and for up to one years after the termination of his or her employment. The contracts also typically include undertakings regarding assignment of inventions and discoveries made during the course of his or her employment. For further details regarding the terms of confidentiality and employment agreements with our key management, see “Directors and Senior Management” in this document.

We believe that we maintain a good working relationship with our employees. We believe we have not experienced any significant labor disputes or any significant difficulty in recruiting staff for our operations. None of our employees are currently represented by labor unions.

Training and Development

We provide formal and comprehensive company-level and department-level training to our new employees, followed by on-the-job training. We also provide training and development programs to our employees from time-to-time to ensure their awareness and compliance with our various policies and procedures. Given our emphasis on operating an integrated platform for our product development processes, some of the training is conducted jointly by different groups and departments serving different functions but working with or supporting each other in our day-to-day operations.

Employee Benefits

Our employees’ remuneration consists of salaries, bonuses, employees’ provident fund, and social security contributions and other welfare payments. In accordance with applicable PRC laws, we have made contributions to social security insurance funds (including pension plan, unemployment insurance work-related injury insurance, medical insurance and maternity insurance) and housing funds for our employees. As at the Latest Practicable Date, we had complied with all statutory social security insurance fund and housing fund obligations applicable to us under PRC laws in all material aspects.

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INTELLECTUAL PROPERTY

Intellectual property rights are important to the success of our business. Our future commercial success depends, in part, on our ability to obtain and maintain patent and other intellectual property and proprietary protection for commercially important technologies, inventions and know-how related to our business, properly practice and enforce our in-licensed patents, prosecute, maintain and enforce patents that we may own in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. We have a two-pronged intellectual property strategy: (i) in-licensing, which has been demonstrated by our agreements with Juno and Eureka (as disclosed above under “— Collaboration and License Agreements”), and (ii) our intention to patent our newly-developed knowledge in process development and clinical trials. We expect this strategy to provide a high barrier for our products and processes against other CAR-T developers at both the R&D stage and the commercial stage.

All our material patents are in-licensed from third parties. We do not own any material patents for our Core Product Candidate and the other products in our pipeline, nor have we filed any material patent applications with any authority. The patents we have in-licensed from third parties are pending approval from their respective authority. As of the Latest Practicable Date, we have in-licensed or have the exclusive option to in-license two PRC granted patents, 27 PRC patent applications and 10 patent applications under the PCT from our strategic partners in connection with our product candidates as well as our in-licensed platforms. For further details regarding the terms by which we have obtained rights to these patents and patent applications, please see “— Collaboration and License Agreements” in this section.

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The following table summarizes the details of the material filed patent applications we have rights to in connection with each of our material product candidates:

Product	Title of Invention	Jurisdiction	Patent Status	Applicant	Patent Expiration ¹	Our Market Commercial Rights
JWCAR029	Method for Transduction and Cell Processing	China, Hong Kong	Pending	Juno	2035.11.04	China, Hong Kong and Macau
	Methods and Compositions for Dosing in Adoptive Cell Therapy	China, Hong Kong	Pending	Juno	2035.10.20	China, Hong Kong and Macau
	Method and Compositions for Cellular Immunotherapy	China, Hong Kong	Pending	Fred Hutchinson; SCH	2033.08.20	China, Hong Kong and Macau
JWCAR129	Method for Transduction and Cell Processing	China, Hong Kong	Pending	Juno	2035.11.04	China, Hong Kong and Macau
	Methods and Compositions for Dosing in Adoptive Cell Therapy	China, Hong Kong	Pending	Juno	2035.10.20	China, Hong Kong and Macau
	Antibodies Targeting B-Cell Maturation Antigen and Methods of Use	China, Hong Kong	Pending	MSK; Eureka	2035.12.04	China, Hong Kong and Macau
	Chimeric Antigen Receptors Targeting B-Cell Maturation Antigen and Uses thereof	China	Pending	MSK; Eureka	2035.12.04	China, Hong Kong and Macau
	Chimeric Antigen Receptors Specific for B-Cell Maturation Antigen (BCMA)	PCT application	Pending	Juno; MSK	2038.01.11	China, Hong Kong and Macau

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Product	Title of Invention	Jurisdiction	Patent Status	Applicant	Patent Expiration ¹	Our Market Commercial Rights
JWACE002; JWACE055	DNA-Cell Conjugates	China ²	Pending ³	Univ. of California	2030.04.08	China, Hong Kong and Macau
	A Novel CD16+ Natural Killer Cell and a Method of Culturing CD16+ Natural Killer Cell	PCT application	Pending ³	Acepodia	2040.01.16	China, Hong Kong and Macau
JWATM203; JWATM204	Constructs Targeting AFP Peptide/MHC Complexes and Uses thereof	China, Hong Kong, Taiwan	Pending	Eureka	2036.04.01	China, Hong Kong, Macau, Taiwan and the member countries of ASEAN.
	Constructs Specifically Recognizing Glypican 3 and Uses thereof	China, Taiwan	Pending	Eureka	2038.04.24	China, Hong Kong, Macau, Taiwan and the member countries of ASEAN.
	Antibody/T-cell Receptor Chimeric Constructs and Uses thereof	China, Hong Kong, Taiwan	Pending	Eureka	2036.10.21	China, Hong Kong, Macau, Taiwan and the member countries of ASEAN.
	Cells Expressing Chimeric Activating Receptors and Chimeric Stimulating Receptors and Uses thereof	China, Taiwan	Pending	Eureka	2038.04.24	China, Hong Kong, Macau, Taiwan and the member countries of ASEAN.
ARTEMIS Platform	Chimeric Antibody/T-cell Receptor Constructs and Uses thereof	China, Taiwan	Pending	Eureka	2038.04.24	China, Hong Kong, Macau, Taiwan and the member countries of ASEAN.
	Cells Expressing Chimeric Antigen Receptors and Secondary Effectors and Uses thereof	Taiwan	Pending	Eureka	2038.04.24	China, Hong Kong, Macau, Taiwan and the member countries of ASEAN.

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Product	Title of Invention	Jurisdiction	Patent Status	Applicant	Patent Expiration ¹	Our Market Commercial Rights
JWATM213; JWATM214	Compositions and Methods for Inhibiting T-cell Exhaustion	PCT application	Pending	Stanford Univ.	2038.12.14	China, Hong Kong, Macau, Taiwan, and the member countries of ASEAN

Notes:

- ¹ For pending patent applications, patent expiration date is estimated based on current filing status and assumes patents will issue from such applications.
- ² The parent patent application CN201080021350.6 has been abandoned.
- ³ This patent application is currently only subject to our exclusive option to obtain a license under the Option and License Agreement with Acepodia. As of the Latest Practicable Date, we have not exercised this option. For further details, please see “— Collaboration and License Agreements — Acepodia Option and License Agreement” in this section.

The term of individual patents depends on the legal term for patents in the jurisdictions in which they are granted. In most jurisdictions, the patent term for inventions is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable jurisdiction.

We may rely, in some circumstances, on trade secret and/or confidential information to protect aspects of our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our consultants, scientific advisors, contractors, and invention assignment arrangements with our employees. We have entered into confidentiality agreements with our senior management and certain key members of our research and development team and other employees who have access to trade secrets or confidential information about our business. Our standard employment contract, which we enter into with each of our employees, contains an assignment clause, under which employees assign us the rights to all inventions, technology, know-how and trade secrets derived during the course of such employee’s work. The contracts with our key management personnel typically include a standard non-compete agreement. However these agreements may not provide sufficient protection of our trade secrets and/or confidential information. For further details, please see the section headed “Risk Factors — Risks Relating to Our Intellectual Property Rights — We rely substantially on our trade secrets and other confidential information, including unpatented know-how, and if we are unable to successfully protect such trade secrets, information and know how, our business and competitive

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position would be harmed. We may be subject to claims that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their former employers or claims asserting ownership of what we regard as our own intellectual property.” in this document.

We conduct our business under the tradename “JW Therapeutics.” As of the Latest Practicable Date, we had registered 59 trademarks in the PRC and had applied for four trademarks in Hong Kong, and we own one key domain name registration, which was in the process of being transferred from an agent to our Group.

As of the Latest Practicable Date, we were not involved in any proceedings in respect of, and we had not received notice of any claims of infringement of, any intellectual property rights that may be threatened or pending, in which we may be a claimant or a respondent.

For further details, please see the section headed “Appendix V — Statutory and General Information — Further Information about Our Business” to this document.

LAND, PROPERTIES AND FACILITIES

We rent a total 3,658.21 square meters of combined office and laboratory space in Waigaoqiao in Shanghai. The relevant rental agreements provide rental terms that expire on May 15, 2021 and August 31, 2021. We have the right of first refusal to renew the lease, provided that we notify the lessor sixty days before the expiration of the rental agreements. We also rent another combined office and laboratory space with a total of 2,404.35 square meters in Zhangjiang in Shanghai. The relevant rental agreement provides rental terms that expire on March 31, 2023. We have the right of first refusal to renew the lease, provided that we notify the lessor six months before the expiration of the rental agreement.

We rent a total of 10,177 square meters of combined office and laboratory space in Suzhou Industrial Park. The relevant rental agreements provide rental terms that expire on August 26, 2021 and June 17, 2022. We have the right of first refusal to renew the lease, provided that we notify the lessor at least three months before the expiration of the rental agreements.

We rent a total of approximately 640.52 square meters of office space in Beijing. The relevant rental agreements provide rental terms that expire on October 31, 2020, March 31, 2021 and May 31, 2021. We also rent a total of approximately 450 square meters of laboratory space in Beijing. The relevant rental agreement provides rental terms that expire on December 26, 2020. Five leased properties have failed to provide the land use right certificate and/or the building ownership certificates.

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As of the Latest Practicable Date, all of these lease agreements had not been registered with relevant authorities. Our PRC Legal Advisor is of the view that the non-registration of lease agreements will not affect the validity of the lease agreements, but the relevant local housing administrative authorities can require us to complete registrations within a specified timeframe and if we fail to so rectify, we may be subject to a fine of between RMB1,000 and RMB10,000 for each of these leasing properties. For further details, please see the sections headed “Risk Factors — Risks Relating To Our Doing Business In China — We may be subject to fines due to the lack of registration of our leases” and “Risk Factors — Risks Relating To Our Doing Business In China — Some of our properties are subject to a title deficiency, and we could be required to vacate any such leased property” in this document.

ENVIRONMENTAL MATTERS AND WORKPLACE SAFETY

We are committed to operating our business in a manner that protects the environment, provides a safety workplace for our employees and performs our social liabilities. We have implemented company-wide environmental, health and safety (EHS) manuals, policies and standard operating procedures that include management systems and procedures relating to general waste treatment; process safety management; handling, use, storage, treatment and disposal of hazardous substances; and worker health and safety requirements.

Our EHS function is responsible for monitoring and enforcing the compliance of our operations with environment, health and safety laws and regulations. This responsibility is executed through formulation and implementation of strategies, policies, standards and metrics; communication of EHS policies and procedures; EHS audits; and incident response planning and implementation through a team of volunteer first responders.

Certain specialized areas of responsibility are assigned to teams with relevant expertise and experience. For instance, our biosafety subject matter experts are responsible for biosafety training, compliance of our operations with biosafety-related legal requirements, biosafety risk assessment and review of corrective actions and preventative actions that we will take upon the occurrence of any biosafety emergency.

In light of the recent COVID-19 outbreak, we have endeavored to provide a safe work environment by implementing company-wide self-protection policies for employees to either work remotely or on-site with protective masks and sanitization. Our employees have to observe strict social distancing requirements when working on-site. If any employees are found to be noncompliant with on-site COVID-19 policies, inspectors are authorized to issue an oral warning or impose a monetary fine. For further details related to the impact of COVID-19 outbreak on our business, please see the section headed “Financial Information — Impact of the COVID-19 Outbreak” in this document.

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Our Board has the collective and overall responsibility for establishing, adopting and reviewing the EHS vision, policy and target of our Group, and evaluating, determining and addressing our EHS-related risks at least once a year. Our Board may assess or engage independent third party(ies) to evaluate the EHS risks and review our existing strategy, target and internal controls. Necessary improvement will then be implemented to mitigate the risks.

We have not had any significant workplace accidents in the history of our Company.

PERMITS, LICENSES AND OTHER APPROVALS

As at the Latest Practicable Date, we had obtained all requisite licenses, approvals and permits from relevant authorities that are material to our current operations.

LEGAL PROCEEDINGS AND COMPLIANCE

As at the Latest Practicable Date, we were not a party to any actual or threatened material legal or administrative proceedings. We are committed to maintaining the highest standards of compliance with the laws and regulations applicable to our business. However, we may from time to time be subject to various legal or administrative claims and proceedings arising in the ordinary course of business.

INSURANCE

We maintain insurance policies that we consider to be in line with market practice and adequate for our business. Our insurance policies cover adverse events in our clinical trials. We do not maintain property loss insurance, product liability insurance or key-person insurance.

RISK MANAGEMENT AND INTERNAL CONTROL

Risk Management

We recognize that risk management is critical to the success of our business operation. Key operational risks faced by us include changes in general market conditions and the regulatory environment of the Chinese biologics market, our ability to develop, manufacture and commercialize our product candidates, and our ability to compete with other pharmaceutical companies. See “Risk Factors” for a discussion of various risks and uncertainties we face. We also face various market risks. In particular, we are exposed to credit, liquidity and currency risks that arise in the normal course of our business. See “Financial Information — Market Risk Disclosure” for a discussion of these market risks.

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We have adopted a series of risk management policies which set out a risk management framework to identify, assess, evaluate and monitor key risks associated with our strategic objectives on an ongoing basis. The following key principles outline our approach to risk management:

- Our audit committee will oversee and manage the overall risks associated with our business operation, including (i) reviewing and approving our risk management policies to ensure that it is consistent with our corporate objectives; (ii) reviewing and approving our corporate risk tolerance; (iii) monitoring the most significant risks associated with our business operation and our management’s handling of such risks; (iv) reviewing our corporate risk in light of our corporate risk tolerance; and (v) monitoring and ensuring the appropriate application of our risk management framework across our Company.
- Our chief finance officer, Mr. Xin Fu, will be responsible for (i) formulating and updating our risk management policy and targets; (ii) reviewing and approving major risk management issues of our Company; (iii) promulgating risk management measures; (iv) providing guidance on our risk management approach to the relevant departments in our Company; (v) reviewing the relevant departments’ reporting on key risks and providing feedback; (vi) supervising the implementation of our risk management measures by the relevant departments; (vii) ensuring that the appropriate structure, processes and competencies are in place across our Group; and (viii) reporting to our audit committee on our material risks.
- The relevant departments in our Company, including but not limited to the finance department, the legal department and the human resources department, are responsible for implementing our risk management policy and carrying out our day-to-day risk management practice. In order to standardize risk management across our Group and set a common level of transparency and risk management performance, the relevant departments will (i) gather information about the risks relating to their operation or function; (ii) conduct risk assessments, which include the identification, prioritization, measurement and categorization of all key risks that could potentially affect their objectives; (iii) continuously monitor the key risks relating to their operation or function; (iv) implement appropriate risk responses where necessary; and (v) develop and maintain an appropriate mechanism to facilitate the application of our risk management framework.

We consider that our Directors and members of our senior management possess the necessary knowledge and experience in providing good corporate governance oversight in connection with risk management and internal control.

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Internal Control

Our Board of Directors is responsible for establishing and ensuring effective internal controls to safeguard our Shareholder’s investment at all times. Our internal control policies set out a framework to identify, assess, evaluate and monitor key risks associated with our strategic objectives on an ongoing basis.

Below is a summary of the internal control policies, measures and procedures we have implemented or plan to implement:

- We have adopted various measures and procedures regarding each aspect of our business operation, such as protection of intellectual property, environmental protection, and occupational health and safety. For more information, see “— Intellectual Property” and “— Environmental Matters and Workplace Safety.” We provide periodic training on these measures and procedures to our employees as part of our employee training program. We also constantly monitor the implementation of those measures and procedures through our on-site internal control team for each stage of the product development process.
- Our Directors (who are responsible for monitoring the corporate governance of our Group), with help from our legal advisors, will also periodically review our compliance status with all relevant laws and regulations after the [REDACTED].
- We plan to establish an audit committee in connection with the [REDACTED], which (i) makes recommendations to our Directors on the appointment and removal of external auditors; and (ii) reviews the financial information and renders advice in respect of financial reporting as well as oversee internal control procedures of our Group.
- We have engaged Guotai Junan Capital Limited as our Compliance Advisor to provide advice to our Directors and management team until the date on which we distribute our annual report in respect of our financial results for the first full financial year after the [REDACTED] regarding matters relating to the Listing Rules. Our Compliance Advisor is expected to, upon our consultation, provide advice and guidance in respect of compliance with the applicable laws and Listing Rules including various requirements of directors’ duties and internal control in a timely fashion.
- We plan to engage a PRC law firm to advise us on and keep us abreast of PRC laws and regulations after the [REDACTED]. We will continue to arrange various trainings sessions to be provided by external legal advisors from time to time when necessary, and/or any appropriate accredited institution to update our Directors, senior management and relevant employees on the latest PRC laws and regulations.

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- We have established procedures to protect the confidentiality of clinical trial data. Access to clinical trial data has been strictly limited to authorized personnel only according to the GCP and relevant regulations. Both external parties and internal employees involved in clinical trials have been required to comply with confidentiality requirements. Data are to be used only for the intended use, as agreed by the patients and consistent with the Informed Consent Form (the “ICF”). We will obtain consent from patients if any use of data falls outside the scope of ICF.
- Our code of conduct and compliance policies (especially healthcare and business ethics standard operating procedures such as sponsorship, donation, meal/travel/hospitality, fee-for-services, anti-bribery, anti-money laundering, etc.) are standard for our industry and apply to all of our employees. For example, we maintain strict anti-corruption policies on personnel with external communication functions. We will also ensure that our commercialization team complies with applicable promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations and limitations on industry-sponsored scientific and educational activities. All of these compliance policies can be readily applied to our future in-house sales and marketing team.
- We will comply with the Corporate Governance Code, except for the deviation from the code provision A.2.1 of the Corporate Governance Code. We have established three board committees, namely, the Audit Committee, the Nomination Committee and the Remuneration Committee, with respective terms of reference in compliance with the Corporate Governance Code. For further details, please see the section headed “Directors and Senior Management” in this document.
- Our Directors believe that compliance creates value for us and dedicate to cultivating a compliance culture among all of our employees. To ensure such compliance culture is embedded into everyday workflow and set the expectations for individual behaviour across the organisation, we regularly conduct internal compliance checks and inspections, adopt strict accountability internally and conduct compliance training.

During the Track Record Period, we have regularly reviewed and enhanced our internal control system.