OVERVIEW

We are an RNA therapeutics biopharmaceutical company with product candidates in pre-clinical and clinical stages that focuses on the discovery and development of innovative drugs for indications with medical needs and large market opportunities. We are the first company to achieve positive Phase IIa clinical outcomes in oncology for an RNAi therapeutics for our core product, STP705, and the first clinical-stage RNA therapeutics company to have a strong presence in both China and the U.S. We were founded in 2007 with the establishment of US Sirnaomics and currently have a presence in both China and the U.S., with research and development centers in both countries. Our core product STP705 demonstrated efficacy and safety in an oncology Phase I/II clinical trial for non-melanoma skin cancer and we have further advanced STP705 in a Phase IIb clinical trial for squamous cell carcinoma in situ (isSCC), a Phase II clinical trial for treatment of skin basal cell carcinoma (BCC), a Phase II clinical trial for treatment of keloid and a Phase I/II clinical trial for treatment of hypertrophic scar (HTS). In addition, we initiated a Phase I clinical trial using STP705 for treatment of hepatocellular carcinoma (HCC) through a local injection based on an independent IND approval from US FDA.

Our proprietary delivery platforms for administration of RNA-based therapeutics are the foundation of our product pipeline, including our polypeptide nanoparticle (PNP) delivery platform optimizable for local or systemic administration of RNAi therapeutics and targets beyond liver hepatocyte cells, our GalNAc-based delivery platforms for systemic administration and liver-targeting RNAi therapeutics, and our polypeptide lipid nanoparticle (PLNP) delivery platform useful for administration of mRNA vaccines and therapeutics. Delivery platforms, including our proprietary delivery platforms, are considered by the FDA to be excipients, or non-active ingredients, in the formulation of the RNAi therapeutic drug product. No additional regulatory approval is required for the delivery platforms separate from the regulatory approvals required for the drug products utilizing the delivery platforms.

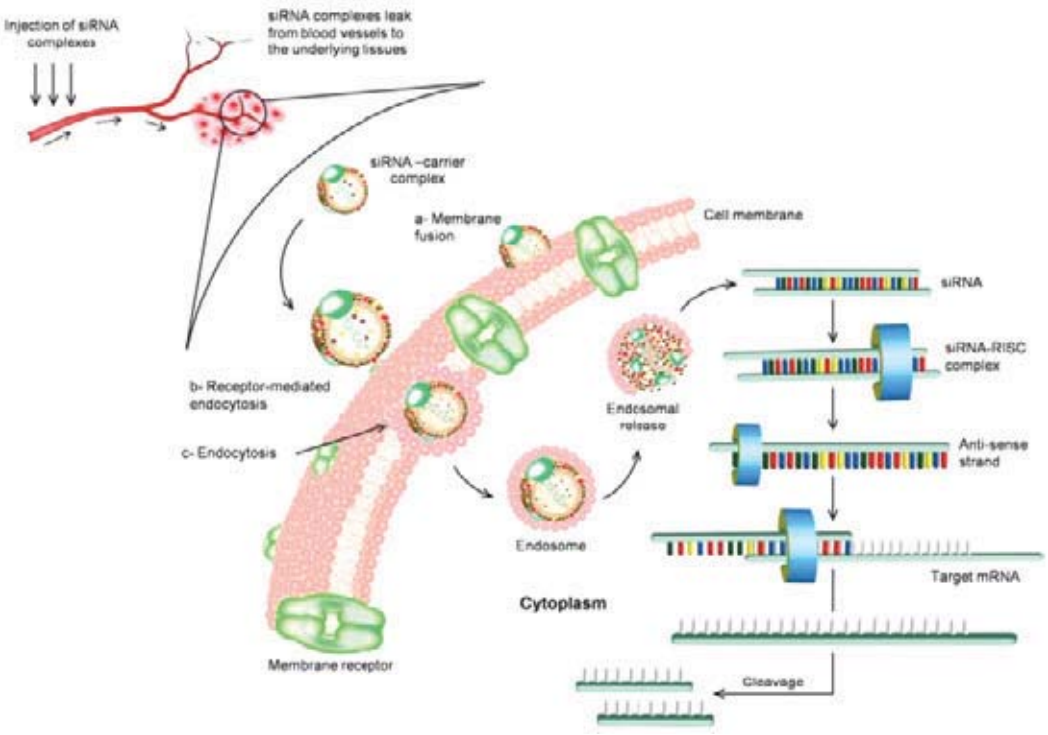
Our product pipeline has over a dozen product candidates for a range of therapeutic indications across rare and large market diseases and its product candidates currently span all stages between preclinical research and IND-enabling studies to Phase I and Phase II clinical trials, creating an extended timeline of product candidates. We strategically focus our product development efforts on indications with growing needs and market opportunities for accelerated development by leveraging the synergies from accelerated regulatory approvals from U.S. FDA to NMPA and using results obtained from clinical trials in the U.S. in the clinical trials in China. Our antiviral and cardiometabolic diseases pipeline products are strategically selected based on clear scientific rationales for targets suitable for our delivery platforms. NMSC and dermal fibrosis, for which the non-surgical treatments have only limited efficacy, are our initial targets. We are developing STP705 for NMSC, dermal fibrosis and solid liver tumors using our PNP delivery platform optimized for local administration. As of the Latest Practicable Date, we owned two issued patents in the U.S. and seven pending patent applications, including two in China and five in the U.S., covering our core product candidate,

STP705, while our other clinical stage product candidate, STP707, is covered by one of the same issued U.S. patents that covers STP705, as well as 13 pending patent applications (which do not also cover STP705) including one in China, two in the U.S., one in Europe and nine in other jurisdictions. We are developing STP707 using our PNP delivery platform optimized for systemic administration. STP705 and STP707 are also covered by three pending patent applications covering aspects of our PNP delivery platform.

- **STP705**. Our core product candidate, STP705, is a dual TGF-ß1/COX-2 inhibitor. TGF-ß1 and COX-2 are known in the scientific literature as gatekeeper targets for oncology and fibrosis disease drug development. TGF-ß1 regulates a broad range of cellular processes, including cell proliferation, differentiation, apoptosis, extracellular matrix production, angiogenesis, inflammation and immune response, while COX-2 is a proinflammatory and proliferative mediator. STP705 leverages our PNP delivery platform in a locally administered formulation for direct administration to diseased tissue. We are developing STP705 for NMSC, dermal fibrosis and solid liver tumors. We are conducting clinical trials for the development of STP705 and our other product candidates. Clinical trials are generally divided into three different stages, but in some cases can be combined (e.g., Phase I/II combined) or subdivided (e.g., Phase IIa or Phase IIb) where appropriate and in consultation with U.S. FDA. Phase IIa clinical trials are generally pilot studies designed to demonstrate clinical efficacy or biological activity, whereas Phase IIb clinical trials are used to determine the optimal dose at which the drug shows biological activity with minimal side-effects. See "Regulatory Overview – Overview of laws and regulations in the United States – Laws and regulations in relation to new drug."

  Mechanism of Action. STP705 is comprised of two distinct siRNA oligonucleotides, which target each of the TGF-ß1 and COX-2 genes through their design as a copy of short regions of each of those genes, and a histidine-lysine polypeptide (HKP). The HKP self-assembles into a polypeptide nanoparticle (PNP) that encapsulates the siRNA and ensures that the siRNA cargo is neither degraded by nucleases nor filtered out by the kidney prior to reaching the intended tissue in the body. The siRNA, which comprise the drug substance, target the TGF-ß1 and COX-2 genes by way of RNA interference, as illustrated in the figure below. When administered to the body, the PNP-siRNA molecules are gradually taken up by the target cells through endocytosis, a cellular process by which substances are brought into the cell. The PNP is initially engulfed in an endosome within the cytoplasm, but the HKPs disrupt the endosome to aid the escape of the siRNA into the cytoplasm. The siRNA may then activate the RNA-Induced Silencing Complex, or RISC. RISC processes the double-stranded siRNA to release one strand and use the other strand as a guide to locate regions of the mRNA for the TGF-ß1 and COX-2 genes. Ultimately, the entire mRNA for the TGF-ß1 and COX-2 genes is cleaved and the protein that would have been produced from the mRNA is not produced, thereby

"silencing" the gene. Silencing of TGF-ß1 and COX-2 expression results in the downregulation of multiple tumor promoting and pro-fibrotic factors. Importantly, simultaneous silencing of TGF-ß1 and COX-2 in the same cell results in increased efficacy compared to silencing of either alone.



Source: Draz, M. et al. Theranostics, 2014:4(9), 872–892.

NMSC. STP705 successfully completed a combined Phase I/II clinical trial in the U.S. for the treatment of NMSC, specifically in isSCC, in October 2020, where the Phase II portion of our clinical trial was a Phase IIa clinical trial. We initiated a Phase IIb clinical trial for isSCC in May 2021 in the U.S. with interim results expected in the first half of 2022. The Phase IIb for isSCC clinical trial is a standalone trial, meaning that U.S. FDA will not require revision of the clinical trial report issued for the completed Phase I/II clinical trial based on the results of the Phase IIb clinical trial. We also initiated Phase II clinical trials for the treatment of non-melanoma basal cell carcinoma (BCC) in the U.S. in December 2020 pursuant to a supplement to the IND covering isSCC. We filed an IND for an isSCC Phase IIb clinical trial in China, where the trial will be part of global multicenter clinical trials, meaning that the study is comprised of clinical trials conducted at multiple sites. We are currently awaiting approval of the IND by NMPA.

NMSC, including squamous cell carcinoma (SCC) and BCC, comprise the most common forms of neoplasia in the U.S. Conventional and standard treatments for BCC and isSCC are standard surgical excision, Mohs micrographic surgery, topical

cream treatments, cryosurgery, laser therapy, electro-desiccation and radiation therapy. Currently, there are two drugs approved by U.S. FDA for pre-metastatic BCC patients, both of which are used off-label for pre-metastatic SCC patients: 5'-fluorouracil and imiquimod topical creams. According to the CIC Report, both can cause skin reactions in some patients. The annual incidence of new cases of BCC and SCC grew by 33% from 2015 to 2020 and is expected to reach over ten million new patients by 2030, representing a substantial financial burden in the U.S. according to the CIC Report. These incidence increases are associated with several factors, including raised awareness of NMSC, improved registration, transition of patient population toward the elderly, increased exposure to UV radiation, and, for SCC, improved diagnosis. The market size of NMSC treatment in the U.S. is expected to increase from US$6.5 billion in 2020 (the isSCC segment was US$1.5 billion, or over 20%) to US$22 billion in 2030. In China, the market size of NMSC treatment was US$38 million in 2020 (the isSCC segment was US$4.3 million, or approximately 11%) and is also expected to grow faster in the coming years, reaching US$149 million in 2030. The value proposition of STP705 for isSCC and BCC is that treatment with STP705 shows benefits in cosmetic appearance, especially for patients with lesions on the head, face or neck, and clinical results demonstrate that STP705 has a high histological clearance compared with currently available topical treatments. According to the CIC Report, the estimated demand for STP705 is expected to be around US$43 million in the U.S. solely with respect to isSCC in the anticipated launch year of 2023 and is projected to reach approximately US$68 million in China with respect to multiple indications including isSCC, BCC, HTS and keloids in the anticipated launch year of 2024. See "Industry Overview – Non-Melanoma Skin Cancer, Liver Cancer and Non-Small Cell Lung Cancer Pharmaceutical Markets – Non-Melanoma Skin Cancers (NMSCs)."

Dermal Fibrosis. With respect to dermal fibrosis, we initiated Phase I/II clinical trials with STP705 for the treatment of keloid scarless healing in the U.S. in April 2021 and expect to file an IND for a Phase II clinical trial in China. We initiated a Phase I/II clinical trial for HTS in the U.S. in 2017; however, after a modification to the clinical trial protocol was recommended, we elected to divert funding to other programs with the intent to move forward the Phase II clinical trial for HTS at a later date. We expect to file an IND for a Phase II clinical trial for HTS in China in the second half of 2022. Our studies for keloid scarless healing and HTS in the U.S. are conducted pursuant to a supplement to the same IND (IND-124844) covering the NMSC studies. HTS and keloids are common dermatological conditions affecting more than 16 million patients in the U.S. and China annually, which can result in permanent functional loss and disfiguring scarring. While there is no standard of treatment for HTS and keloids, the available treatment options are intralesional injection, cryotherapy, bleomycin, laser therapy and surgical excision. The combined market size for HTS and keloids treatments in the U.S. is projected to grow from

US$10.3 billion in 2020 to US$18.6 billion in 2030, and in China from US$2.9 billion in 2020 to US$5.9 billion in 2030. The value proposition of STP705 for HTS and keloids is that there is no complete cure of HTS and keloid currently and clinical trial results demonstrate that STP705 inhibited TGF-ß1 and COX-2 expression and activated fibroblasts apoptosis within scars, which can effectively reduce HTS.

Liver Cancer. In addition to our initial target indications, we are developing STP705 for treatment of hepatocellular carcinoma and cholangiocarcinoma (HCC/CCA). We initiated a Phase I clinical trial in March 2021 in the U.S. to develop STP705 for the treatment of HCC/CCA using intra-tumoral injection via computerized tomography guided treatment. Our studies for liver cancer are conducted pursuant to a separate IND from that which covers the NMSC and dermal fibrosis indications. We are also developing combination therapies with STP705 and immune checkpoint inhibitors for liver cancer where the proposed therapy would involve separate administration of STP705 and the immune checkpoint inhibitor pharmaceutical product. As of the Latest Practicable Date, there were approximately 13 drugs approved by U.S. FDA for treatment of HCC or CCA; however, five-year survival rates for liver cancer in China and the U.S. are 12% and 18%, respectively. In addition, many patients suffer systemic side effects from the approved drugs. Other available treatment options for liver cancer are surgical excision, liver transplant, ablation therapy, embolization therapy, targeted therapy, immunotherapy and radiation therapy. China alone accounts for more than half of worldwide liver cancer cases with an annual incidence of more than 500,000 new HCC/CCA patients annually according to the CIC Report. The combined market size for HCC/CCA pharmaceuticals in China is projected to grow from US$1.5 billion in 2020 to US$8.5 billion in 2030, and in the U.S. from US$2.2 billion in 2020 to US$6.3 billion in 2030. The value proposition of STP705 for liver cancer is threefold: first, there is no standard target therapy for advanced CCA, so that a large need exists for systemic therapy of advanced CCA; second, STP705 demonstrates inhibition of tumor growth in CCA tumor cell line xenograft models, which is expected to satisfy the needs for CCA treatment; and third, pre-clinical study results demonstrate that STP705 show inhibition of tumor without loss in body weight compared to chemotherapy.

- **STP707**. Our key product candidate STP707 is, like STP705, a dual TGF-ß1/COX-2 inhibitor that uses our PNP delivery platform. Whereas STP705 uses a formulation of our PNP delivery platform optimized for local administration (i.e., directly to the site of disease), STP707 uses a formulation of our PNP delivery platform optimized for systemic administration. Thus, STP707 may be administered intravenously for treatment systemically, including solid tumors or fibrotic tissue in the liver or lung. We are developing STP707 for the treatment of liver and other cancers and fibrosis of the liver and lung via systemic administration. Our preclinical studies with non-human primates have shown clear efficacy in silencing the target genes and

demonstrate a good safety and tolerability profile. A safety window observed from this study provides a 30-fold safety margin over the proposed clinical doses. We initiated a Phase I clinical trial for solid tumors in November 2021 in the U.S. and plan to submit an IND in China for Phase I clinical trials for HCC as part of the global multicenter clinical trials. We also filed an IND for PSC, a rare form of liver fibrosis, in November in the U.S. Depending on the response we see in our solid tumor basket study Phase I clinical trial as well as efficacy data obtained in preclinical studies in various tumor models, we could potentially follow the Phase I clinical trial with Phase II clinical trials in multiple tumor types such as metastatic cutaneous squamous cell carcinoma, non-small cell lung cancer (NSCLC), HCC and CCA. Fibrotic disorders affect nearly all tissues and organ systems. The annual incidence of NSCLC in 2020 is larger in China (approximately 757,000 new cases) than in the U.S. (approximately 176,000 new cases), while the market for NSCLC targeted drugs is expected to increase by 13.9% and 13.1%, respectively, in the next ten years to US$12.1 billion in China and US$26.1 billion in the U.S. The prevalence of PSC in China was 194,000 patients in 2020 and in the U.S., 45,000 patients in 2020. We are also developing combination therapies with STP707 and immune check point inhibitors and other novel oncology drugs currently used as treatments for liver cancer, metastatic cSCC and NSCLC.

- **STP122G**. Another key product candidate is STP122G, formulated using our GalAhead™ platform and targeting Factor XI, which is being developed for anticoagulant therapy for use in the many different therapeutic settings where anti-thrombotic therapeutics are needed. We plan to file an IND with U.S. FDA in the first half of 2022.

- **RIM730**. Instead of applying RNAi technology like the candidates described above, RIM730 is being developed by RNAimmune as a prophylactic mRNA vaccine candidate for prevention of COVID-19 using LNP technology to target certain mutations of the SARS-CoV-2 virus.

- **Other Pipeline Candidates**. In addition to those key products, we have a pipeline of at least 12 other products currently in preclinical studies covering a range of therapeutic indications, including treatments for influenza, hepatitis B, HPV and COVID-19 infections; treatments for cardiometabolic disease; pancreatic cancer, colon cancer and other cancer treatments; and fat sculpting for medical aesthetics. Based on the company's strategic planning, we are trying to form licensing-out partnerships with MNCs and China pharma companies. In April 2021, we entered into a licensing-out agreement with Walvax for an exclusive China right of our siRNA product candidate STP702, which comprises siRNA targeting conserved gene sequences of influenza virus. Multiple RNAi therapeutic programs within our product pipeline are currently undergoing negotiations for potential licensing-out partnerships.

The following chart illustrates our pipeline and summarizes the development status of our clinical-stage drug candidates and selected IND-enabling stage candidates as of the Latest Practicable Date:

Notes：* denotes our core product

** denotes orphan drug

Abbreviations: isSCC= squamous cell carcinoma in situ; BCC= basal cell carcinoma; cSCC= metastatic cutaneous squamous cell carcinoma; NSCLC= non-small cell lung cancer; CRC= colorectal carcinoma; BC= bladder cancer; PSC= primary sclerosing cholangitis; PNP= our polypeptide nanoparticle (PNP) RNAi delivery platform; PNP-IT= PNP platform formulated for intratumoral administration; PNP-IV= PNP platform formulated for intravenous administration; GalAhead™= our GalNAc RNAi delivery platform that conjugates GalNAc moieties to RNAi triggers; PDoV-GalNAc= our GalNAc RNAi delivery platform that conjugates GalNAc moieties to Peptide Docking Vehicle (PDoV) peptide linkers and up to two siRNAs to the peptide; LNP = lipid nanoparticle (LNP) formulation for delivery of mRNA; HPV= human papilloma virus; HBV= hepatitis B virus; OL China= out licensed mainland China, Hong Kong, Macau and Taiwan rights under agreement with Walvax but we retain the rights for rest of the world; and MRCT= multi regional clinical trial in which we will be the sponsor for all clinical trial sites.

1. Liver cancer (basket) includes cholangiocarcinoma, hepatocellular carcinoma, liver metastases etc.

2. We filed our IND in China in June 2021, which is currently awaiting approval from NMPA, for study sites in China. The study sites will be part of a global multicenter clinical trials for our Phase IIb clinical trial for isSCC.
3. We expect to file the IND in China as part of the global multicenter clinical trials.
4. We expect to file the IND solely for HCC in China as part of the global multicenter clinical trials.
5. Studies in combination with anti-PD-(L)1 inhibitors conducted pursuant to collaborations with Innovent and Shanghai Junshi.
6. Research and development conducted by our subsidiary RNAimmune.

RNA therapeutics comprise a rapidly expanding and disruptive category of drugs that is expected to dramatically reshape therapeutic interventions, by using various approaches to suppress or to enhance expression of genes by targeting messenger RNA (mRNA), the intermediate between the gene encoded in DNA and the protein that is coded for by that gene. Among the approaches to suppress gene expression is RNAi therapeutics, which comprise small interfering RNA (siRNA) that direct the reduction or silencing of the expression of genes associated with disease by targeting mRNA. Whereas conventional therapeutics typically function by directly targeting the proteins implicated in causing disease, RNAi therapeutics instead act by silencing the genes that encode proteins, thus preventing the disease-associated proteins from being produced, and minimizing or eliminating their potentially negative effects. Our leading pipeline candidates are primarily directed to the RNAi therapeutics approach. mRNA therapeutics and vaccines, on the other hand, are intended to deliver mRNA to cells for expression in order to compensate for a defective gene or supply a therapeutic protein. Through our subsidiary RNAimmune, we are also developing mRNA therapeutics and vaccines for a wide range of infectious diseases, rare diseases and oncology indications.

Although the biological mechanism of RNA interference that underlies RNAi therapeutics was discovered in 1998, the wide-scale development of RNAi therapeutics has been limited by a number of factors, including inefficient biodistribution, poor cellular uptake and off-target effects. Naked RNAi triggers are prone to nuclease degradation, and may activate the immune system, while also being too large and negatively charged to passively cross the cell membrane and must, therefore, rely on additional means of cellular entry to access the cytoplasm.

The primary challenge in creating effective RNAi and mRNA therapeutics and vaccines is formulating an effective platform to deliver the respective RNA to both the desired cell type and the site of action inside that cell, as well as to protect the RNA from degradation prior to it reaching the target cell. According to the CIC Report, it is difficult to develop drugs for a wide number of indications deploying LNP delivery platforms. In addition, LNPs are chemically synthesized lipid formulations whose manufacture requires multiple base ingredients and are limited by complex manufacturing processes. GalNAc RNAi platforms are based on GalNAc, or N-acetylgalactosamine, a sugar molecule that binds to a cell surface receptor found on liver hepatocytes. GalNAc RNAi platforms, exhibit higher delivery efficiency, reduced side effects and simpler manufacturing compared to LNP delivery platforms, but are limited to delivery to liver hepatocytes.

According to CIC, the global market size of RNAi therapeutics across all indications is estimated to grow from US$362 million in 2020 to reach US$25 billion in 2030. The key global players in RNAi therapeutics, according to the CIC Report, other than us, include

Alnylam Pharmaceuticals, Arrowhead Pharmaceuticals, Dicerna Pharmaceuticals, Silence Therapeutics, Sylentis, Quark and Brii Biosciences. Most of these competitors rely on GalNAc-based delivery platforms, except for Alnylam which also relies on both lipid nanoparticle (LNP) and GalNAc-based delivery platforms. Alnylam is the only developer with commercialized products, three of which it commercializes in the U.S. and are directed to rare diseases, and one, which is licensed to Novartis and commercialized in Europe is used for the treatment of elevated cholesterol levels. The first RNAi therapeutic was approved in 2018. As of the Latest Practicable Date, there was no commercialized RNAi therapeutics commercialized in China.

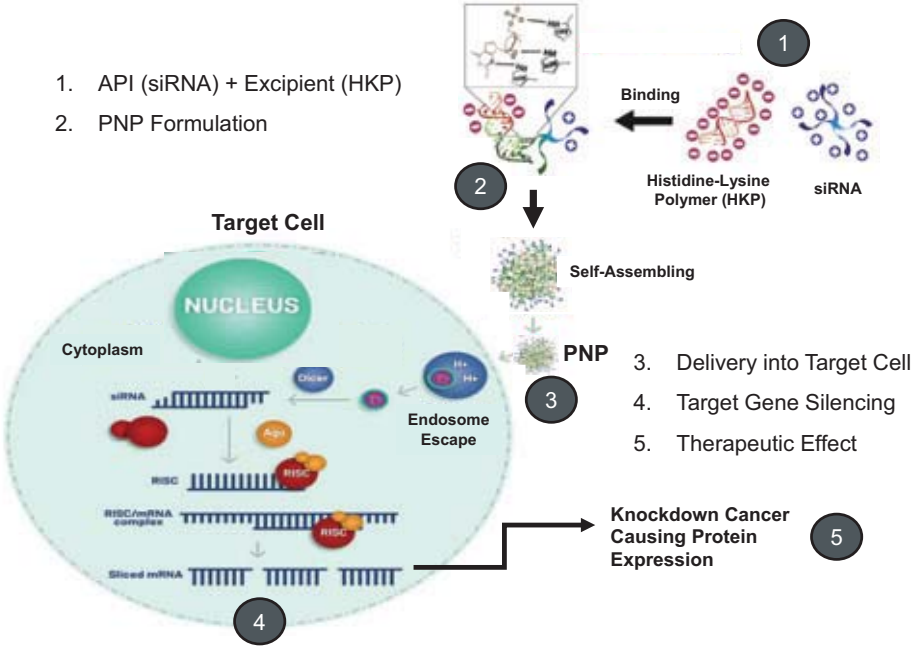
We believe our proprietary polypeptide nanoparticle (PNP) and novel GalNAc RNAi delivery platforms have distinct competitive advantages over the delivery platforms used by our competitors. Our PNP delivery platform allows delivery of both siRNA and mRNA to diseased cells via local or systemic administration with distinct advantages in low toxicity, easy manufacturing and the capability to reach many more targeted organs other than the liver, while our novel GalNAc RNAi delivery platforms enable specific delivery to liver hepatocytes with high potency. Both our PNP and novel GalNAc RNAi delivery platforms are distinguished based on their capabilities to knockdown two distinct target genes for a synergistic effect that improves therapeutic potential against diseases. Our technology-driven platforms for drug delivery, drug discovery and drug development enable us to create new opportunities for RNA therapeutics. We are currently developing potential first-in-class therapeutics for non-melanoma skin cancer (NMSC), liver cancer, other solid tumors and dermal fibrosis in the near term, with a pipeline encompassing a wide array of indications, including a broad spectrum of oncology and fibrosis-related diseases as well as antiviral and cardiometabolic diseases.

Our proprietary PNP delivery platform, designed to resolve the bottleneck of LNP and conventional GalNAc RNAi delivery platforms and used in our STP705 and STP707 product candidates, has the potential to expand the reach of RNAi technology. The results of our Phase IIa clinical trial in oncology study validates both the effectiveness of our PNP delivery platform and the therapeutic targets for isSCC, positioning us to expand our pipeline of products and facilitate our research and development of those pipeline products using the same PNP delivery platform. We believe that our PNP-formulated siRNA has improved delivery efficiency based on its effective cellular uptake and efficient endosomal release into the cytoplasm, which are crucial characteristics for RNAi delivery platforms.

The PNP is comprised of a branched histidine lysine polypeptide (HKP) that is readily synthesized in the laboratory. The HKP acts an excipient, a non-active ingredient that enhances the delivery of the siRNA active ingredient. The HKP wraps around the siRNAs, binding to the siRNA through both electrostatic and hydrogen bond interactions, and self-assembles into PNPs. Each PNP can encapsulate multiple distinct siRNAs, on the order of thousands of siRNAs in a single 100 nm PNP. The PNP-siRNA formulation can be injected for local administration, for example, in the skin or a tumor, or systemically administered, for example, by intravenous or subcutaneous injection or inhalation. The PNP protects the siRNA from the surrounding environment while in the bloodstream, including protection from nucleases and immune system activation. On reaching the target cell, the PNP enters the cell

either through receptor-mediated endocytosis or non-specific endocytosis via an endosomal pathway, where the PNP is initial held in the endosome. Once in the target cell, the histidine groups protonate and allow release of the siRNA payload from the endosome into the cytoplasm where the siRNAs may act to induce gene silencing. The escaped siRNAs are further processed by a Dicer protein, such that the antisense strand of the double-stranded sRNA binds to and activates the intracellular protein complex referred to as the RNA-Induced Silencing Complex, or RISC. RISC uses the antisense sequence to locate the complementary sequence in the targeted mRNA, and recruits RNA nucleases to cleave and break down the mRNA, preventing the translation of that mRNA molecule into protein and thus resulting in silencing or knockdown of the target gene.

Mechanism for Operation of the PNP Delivery System for RNAi Therapeutics



Source: Company

Our PNP delivery platform seeks to overcome the challenges of developing effective RNAi therapeutics. Our manufacturing process utilize microfluidic technology to mix the siRNA active ingredient and HKP excipient with an established process at defined scale. The microfluidic technology enables consistent sizing of the PNP nanoparticles and consistent loading of those nanoparticles with siRNA for consistent drug concentrations between batches. The PNP effectively protects the siRNA from nucleases prior to reaching the target cell. When injected intravenously in animals, the PNP is rapidly observed in the liver – specifically it is internalized in cells with importance for fibrosis treatment and oncology indications, such as stellate cells and hepatocytes, the indications we are currently developing with our core product STP705 and the closely related STP707. The research indicates that the PNP can home in on tumors and deliver siRNAs to inhibit tumor growth via the enhanced permeability and retention (EPR) effect, which is characterized by an increased accumulation of macromolecules, such as liposomes, drugs, and NPs in tumors versus in normal tissues.

In addition, we seek to address the problems of target selection in oncology with our PNP delivery platform. For example, cancer can become resistant to drugs that target only a single molecular target by upregulating other pathways. Our PNP delivery platform can carry multiple siRNAs within the same particle for delivery to the same cell at the same time to silence more than one target gene. Simultaneous delivery of multiple siRNAs can produce a synergistic effect in cancer cells, providing a better therapeutic capability and reducing the likelihood for the cancer cell to evade the therapeutic pressure. Our PNP delivery platform has low toxicity since it is comprised of polypeptides that are biodegradable within the cell after siRNA delivery. Our PNP delivery platform can be used for both local delivery or systemic administration for selective targeting of multiple tissue and cell types. Our core product candidate, STP705, as well as our other clinical stage product candidate, STP707, and at least eight other preclinical product candidates utilize our PNP delivery platform. RNAimmune also applies our innovative PNP delivery platform, and a related proprietary delivery platform based on polypeptide-lipid nanoparticles (PLNP), to formulate mRNA-based therapeutics and vaccines. RNAimmune's novel PLNP platform has presented advantages such as lower toxicity and higher efficiency in certain applications.

Our novel GalNAc-conjugate delivery platforms rely on peptide conjugates and/or unique RNA structures that allow knockdown of single or multiple distinct mRNA targets. Our GalAhead™ delivery platform conjugates GalNAc moieties to unique RNAi trigger structures that can target one or more genes simultaneously. Particularities of the structures also reduce the complexity of their manufacturing compared to conventional GalNAc RNAi triggers. We have three pipeline products utilizing our GalAhead™ platform quickly approaching the IND-enabling studies. In our PDoV-GalNAc RNAi platform, GalNAc is conjugated to a Peptide Docking Vehicle (PDoV) peptide linker and up to two siRNAs are also conjugated to the same peptide. While GalNAc directs delivery to the liver, the PDoV peptide is designed to improve cellular uptake and endosomal escape compared with conventional GalNAc RNAi platforms. The PDoV peptide linker allows dual gene targeting by conjugating two siRNAs. The ability to deliver multiple siRNAs per molecule can provide improved delivery efficiency relative to conventional GalNAc RNAi platforms, or allow synergistic therapeutic effect when two distinct siRNAs are used to target multiple genes. We are actively seeking patent protection for the novel structures incorporated into our proprietary, in-house developed GalNAc RNAi platforms in the U.S., China, Europe and other potentially significant markets, which, if granted, will confer protection through 2039.

Apart from our PNP and novel GalNAc RNAi delivery platforms, we believe we also derive growth potential based on a number of innovative delivery platforms we are currently developing, including different approaches of siRNA/chemo-drug conjugates, peptide ligand tumor targeting and respiratory virus treatment via airway delivery. Our technology platform includes a proprietary algorithm to drive early discovery efforts to identify promising siRNA candidate sequences, and high throughput processes to design, screen and rigorously test future pipeline products. We are committed to investing in research and development in our delivery platforms to enable the expansion and refinement of the range of organs and tissues that can be targeted by our pipeline products and to drive future growth opportunities.

While advancing our product candidates and platform technology, we have developed manufacturing processes that are capable of large, commercial-scale GMP-compliant manufacturing of our product candidates. Our manufacturing technology uses microfluidic technology that is scalable from research and development level to commercialization, delivering high-quality products at low cost. We have sufficient capacity in the U.S. for our current and anticipated needs through our well-established network of contract manufacturers and have built a manufacturing facility in Guangzhou to further enhance our in-house manufacturing capacity and provide flexibility for optimizing our clinical strategy in China by adapting production to our then-current needs. Our manufacturing facility in Guangzhou will commence operations in the first quarter of 2022. Our Guangzhou manufacturing facility will be capable of GMP-compliant manufacturing of our pipeline product candidates, including formulation, fill and finish, test and release for clinical applications. The supplies from this facility will be sufficient to support our Phase II clinical trials in China, and potentially to supply our Phase III clinical trials in China and our clinical trials globally.

Our clinical development strategy is to initiate and conduct clinical trials primarily in the format of a global multi-center study, meaning that the studies are comprised of clinical trials conducted at multiple sites. For our current product pipeline, including STP705, STP707, STP122G and RIM730 as well as other product candidates, we intend to rely primarily on clinical readouts in the U.S.-based trials for further development, although we will also results from clinical sites in other countries and areas, including China. For STP705, our Phase I/II clinical trial for the treatment of isSCC was conducted in the U.S., and our Phase IIb clinical trial for the treatment of isSCC, our Phase II clinical trial for BCC, our Phase I/II clinical trial for keloid scarless healing and our Phase I clinical trial for solid liver tumors are all initiated in the U.S. For STP707, we also intend to initiate our Phase I clinical trials first in the U.S. In circumstances where it is appropriate for the specific indication, we plan to initiate the clinical trial first in China and may rely on clinical trial readouts primarily from clinical sites in China. For example, for HTS, because the demand for the treatment of the condition is stronger in China, our clinical trial strategy is to initiate the clinical trial in China led by a Chinese principal investigator.

We are an RNA therapeutics company with product candidates in pre-clinical and clinical stages with a strong research and development presence in both China and the U.S. We aim to capture both the largest market in the world (U.S.) and one of the fastest growing markets in the world (China) (in terms of revenue for therapeutic treatment of human disease). Our dual presence in China and the U.S. allows us to leverage complementary regulatory systems to gain a fast to market advantage, where U.S. FDA approval expedites review by NMPA in China. Because our executive leadership and scientific advisory board members are top-tier scientists and biopharmaceutical professionals in both China and the U.S., we are able to attract top talents and build strong teams across markets.

OUR STRENGTHS

We believe the following strengths differentiate us from other biopharmaceutical companies.

Major player in rapidly growing and transformative RNA therapeutics market with strong presence in China and the U.S.

RNAi therapeutics have the potential to transform global healthcare as a new major class of drugs alongside small molecules and antibodies by treating diseases that were once considered undruggable according to the CIC Report. RNAi has several innate advantages over small molecular therapeutics and antibody drugs:

- **Wide scope of targets**. Because RNAi targets mRNA directly to regulate the expression of the target protein, RNAi can reach a wide range of potential targets in the body, both intracellular protein targets not typically 'druggable' to small molecule or antibody therapeutics as well as extracellular protein targets that are more typically reached by these conventional therapeutics, thereby providing therapeutic access to virtually any endogenous protein in the body with a known mRNA sequence.

- **Precise and personalized therapeutics**. RNAi executes its function by simple base pairing with the target mRNA, whereas small molecule and antibody drugs typically require binding through complex spatial conformation of certain proteins. RNAi therapeutics can be algorithmically designed with high specificity to target any known gene for silencing for higher success rates with lower off-target rates. Consequently, RNAi therapeutics can potentially treat many diseases that cannot be treated by small molecule and antibody drugs because no target molecule with high activity, affinity and specificity has been identified, or because no small molecule or antibody drug has been designed or can be delivered to the target protein.

- **Favorable safety profiles**. Since RNAi therapeutics exploit natural biological processes, they have lower immunogenicity than antibodies, and lower toxicity compared to some small molecule drugs.

- **Long lasting effect**. The effects of gene silencing through RNAi can last from days to months after administering the therapeutic, compared to small molecule or antibody therapeutics which last from hours or a few days for small molecules and up to several weeks for antibodies. RNAi therapeutics are thus well-suited for treatment of various chronic diseases.

- **Faster and higher development success rate and relatively low manufacturing cost**. Whereas small molecule and antibody therapeutics are developed by screening

pools of potential candidates, with RNAi therapeutics, at least in theory, any gene of interest can be targeted since only the appropriate nucleotide sequence of the targeted mRNA needs to be selected, resulting in potentially a higher likelihood of approval and shorter time for completing new product design than small molecule or antibody drugs. RNAi therapeutics have the potential for relatively low manufacturing costs due to reduced manufacturing complexity and RNAi therapeutics companies have a higher gross profit margin than many competitors.

More broadly than RNAi, we are also developing other RNA therapeutics, including mRNA vaccines. mRNA vaccines have advantages over conventional vaccines, which have already been validated by the success of the COVID-19 vaccines, allowing for precise therapeutics, a wide scope of potential targets with faster and higher development success rates. mRNA vaccines also demonstrate the following advantages over conventionally developed vaccines:

- **Rapid process development**. mRNA vaccines work by delivering a transcript made of RNA that encodes an antigen or immunogen. Synthesis of the mRNA transcript can be accomplished using existing technology as soon as the desired sequence is available. The process can be easily scalable and is cell-free, requiring minimal change to the delivery platform during mRNA formulation and manufacturing.

- **Simpler manufacturing**. Production requirements are directed to the single mRNA sequence of the target antigen, producing significant time and cost savings since no cell culture, virus / antigen extraction or purification steps are required, thus improving production capacity.

- **Simplified quality control during production**. Since the mRNA vaccine is produced through enzymatic in vitro transcription, and not by growth and expansion of living cell cultures, in addition to time savings from simplified manufacturing procedures, quality control is significantly simplified.

- **High potency of immune response.** mRNA vaccines are capable of inducing both humoral immunity and cellular immunity at the same time, affording the body protection through multiple mechanisms.

- **Favorable safety profiles**. Since mRNA vaccines express the target protein in the cytoplasm and do not enter the nucleus, there is reduced risk of nuclear integration or insertional mutagenesis by the mRNA, and potentially fewer side effects since mRNA vaccines do not include the entire viral genome, are non-infectious, and are free of protein and virus-derived contamination during production. mRNA can be quickly degraded in the cytoplasm of transfected cells after immunization, which can reduce the risk of its safety issues.

Technological breakthroughs, including by our research and development team, are increasing the number of indications for RNAi therapeutics and mRNA vaccines, including through improved RNA delivery platforms for efficient delivery, and identification of numerous gene targets for rapid development of highly specific therapeutics. Actions taken by applicable government regulators have also created a favorable environment for development of RNAi therapeutics, such as guidelines issued by the NMPA, the listing of RNAi therapeutics in the key development fields in the 13th Five-Year Plan for the Development of the Biological Industry, and the approval of RNAi drugs in recent years by the U.S. FDA. Specifically, the global market size for RNAi therapeutics has increased from US$12 million in 2018 to US$362 million in 2020 with CAGR of 449%, and is estimated to reach US$21 billion by 2030. Leading global pharmaceutical companies are increasingly investing in and partnering with RNAi therapeutics companies, with accumulated investment tripling from US$8.5 billion in 2017 to US$35 billion in 2020. Although currently mainly focused on rare diseases, the market size of RNAi therapeutics for common disease and oncology are expected to increase and account for 49% of the total market size by 2030.

We are the first company globally to achieve positive Phase IIa clinical outcomes in oncology for an RNAi therapeutic. We believe our novel and innovative delivery platforms have the potential for better therapeutic results and less complex manufacturing than our competitors and can enable us to expand rapidly, capturing market opportunities ahead of the competition.

As an early entrant and leader in the RNA therapeutics market in China, and particularly as the only clinical-stage RNA therapeutics company with presence in both China and the U.S., we are in a position to gain commercial access to the largest as well as the fastest markets in the world. We utilize the complementary regulatory systems in China and the U.S. to accelerate development and attain regulatory approvals, including by pursuing candidates and indications where orphan drug designation can be achieved in the U.S., which can shorten the review period from 1-2 years to 6-12 months, through enhanced priority review by the NMPA in China even where the indication does not qualify for orphan drug status in China. The review period can be further shortened as U.S. FDA approval may serve as an endorsement of the IND to NMPA and may in turn expedite the process. In addition, U.S. FDA approved drugs can be prescribed before approval in China in certain designated hospitals; while Real-World-Data (RWD) can be generated from the pilot prescription scheme, which could facilitate the drug registration process into hospitals. Our positioning also gives us better access to talent in the research ecosystems of both countries.

Empowered by our leading industry position and unique geographic footprint, we have a strong track record of collaboration with biopharmaceutical and biotechnology companies in China as well as academic research institutions in China and the U.S. We are collaborating with Innovent and Shanghai Junshi on the development of combination therapies using STP705 and immune checkpoint inhibitors where the proposed therapy would involve separate administration of STP705 and the immune checkpoint inhibitor pharmaceutical product. We entered an agreement with Walvax to co-develop anti-influenza therapeutics, which includes

an out-license for certain rights in mainland China, Hong Kong, Macau and Taiwan. We also benefit from our collaborations with renowned universities, including the University of Maryland on the enhancement of our technology and Boston University on preclinical research and development.

We are in preparations for future commercialization. Our current in-house and externally contracted manufacturing capacity is sufficient to support currently planned clinical trials and to initiate our commercialization of our product candidates. We have established GMP-compliant manufacturing processes in the U.S. with contract manufacturers that are accredited by the U.S. FDA, and these contract manufacturers will contribute, in total, an annual capacity of at least two million vials per year to our manufacturing process. This is sufficient, for example, for at least 2,000,000 doses of STP705 for isSCC. We recently built our own manufacturing facility in Guangzhou that will be capable of GMP-compliant manufacturing of PNP-based RNAi therapeutics. Our Guangzhou facility will be ready to supply our clinical trials in early 2022, and we believe it will be easy to scale up manufacturing based on our previous experience. We are also planning to build an in-house sales and marketing team to commercialize our products once approved.

RNA delivery platforms, including well-validated platforms that solve principal challenges to RNAi therapeutics and an alternative platform with tremendous potential for mRNA therapeutics and vaccines

We believe our highly innovative RNAi delivery platforms set us in a class by ourselves. The primary challenge and the key to success in developing RNA therapeutics is the delivery platform used to protect the RNA from degradation in the blood and deliver the RNA into a cell where it acts. Our proprietary PNP and novel GalNAc delivery platforms confer advantages over conventional delivery platforms.

Our proprietary PNP delivery platform is the basis of our STP705 and STP707 product candidates and is based on a peptide that is capable of self-assembly into a nanoparticle that encapsulates the siRNA to protect it in the bloodstream and promote cellular uptake and delivery to the target within the cell. Early efforts in RNAi therapeutics utilized LNP technology to encapsulate and deliver siRNAs, which is difficult to use to produce drugs for a wide number of indications, requires multiple base ingredients and greater manufacturing complexity, and in some cases has demonstrated relatively high toxicity. Our proprietary PNP delivery platform, on the other hand, generates products having low immunotoxicity and high efficiency of delivery into the cell for therapeutic action, and its manufacturing process is less complex and more controllable than LNP manufacturing processes. For example, our PNP delivery platform requires fewer ingredients and process steps, and has aqueous solubility enabling efficient lyophilization. Our PNPs also have very high RNA payload packing efficiency (>97%) and can carry multiple RNA molecules directed to different targets. GalNAc RNAi delivery platforms are the predominant delivery platforms used by our competitors, and while they have lower toxicity and easier manufacturing than conventional LNP delivery, they

are limited in their scope since the GalNAc RNAi platforms deliver RNAi trigger cargo only to hepatocyte cells in the liver. In contrast, our PNP delivery platforms can be used for local delivery to the skin or tumors, as well as other parenteral administration routes for systemic delivery to target a variety of cell and tissue types other than liver hepatocytes, including tumor cells, lung cells, and non-hepatocyte liver cells. Unlike the LNP synthesis process, which is highly complex, the synthesis process for our PNP delivery platform is relatively easy, well-controlled and scalable. Our ability to load multiple RNAi therapeutics in a single PNP means that we can simultaneously target multiple target genes for synergistic effects and increased treatment efficacy.

Our in-house developed manufacturing process for our proprietary PNP delivery platform uses microfluidic technology that has successfully enabled commercial-scale GMP-compliant manufacturing of our product candidates. Our manufacturing process generates high quality products. We have demonstrated consistency in loading nanoparticles with siRNA as well as homogeneity of nanoparticles size. Consistent nanoparticle RNA loading results in consistent drug concentrations between batches, even in products where multiple different siRNAs are used. Narrow particle size distribution is emphasized by FDA as a critical quality attribute and an essential component of stability studies of nanoparticle products.

We believe our GalNAc RNAi delivery platforms, for which we are actively pursuing patent protection in key jurisdictions, have potential competitive advantages for delivery to the liver, allowing for dual- and multi-gene targeting. Our GalAhead™ platform conjugates the GalNAc sugar moieties to unique RNA structures, capable of delivering one or more different RNAi triggers. Our GalAhead™ platform utilizes smaller RNAi triggers than other GalNAc RNAi platforms, creating potentially easier synthesis and manufacturing compared to other GalNAc RNAi platforms. Our PDoV-GalNAc platform utilizes a uniquely structured peptide linker that is compatible for both single and dual targeted siRNAs and that also enhances gene silencing potency through improved endosomal escape efficiency.

We have also initiated research into PLNP and PNP formulations for mRNA, both of which are exclusively licensed to our RNAimmune subsidiary to facilitate the development of mRNA therapeutic and vaccine applications. Our proprietary PLNP platform combines polypeptides and lipids to generate nanoparticles comprised of both to provide encapsulation of both non-amplifying and self-amplified mRNA, allowing for efficient cellular delivery through better endosomal escape for novel mRNA vaccines and therapeutics. Our PLNP platform has less complex manufacturing than LNP delivery platforms due to fewer components, and does not include polyethylene glycol (PEG), which is used in current LNP delivery platforms and is thought to cause severe adverse effects in some patients. Products formulated using our PLNP platform are stable at ambient temperatures, thus eliminating distribution costs associated with cold chain storage of LNP-based products.

Our investment in further development of novel RNAi delivery technology provides us with growth potential in the future. We are currently developing siRNA-chemo drug

conjugates and peptide-drug conjugates to investigate the combinatorial power of both siRNA and small molecule drugs for enhancement of the antitumor activity of each on its own. We are developing novel targeted siRNA platforms, targeting tumor cells with our PNP delivery platform and modified liposomes for airway delivery for inhalation administration to the lungs. Our focus in developing novel delivery platforms demonstrates our commitment to future growth in the RNA therapeutics field and our determination to achieve and maintain a preeminent position in the field.

Broad and deep product pipeline with candidates intended to breach the limitations on conventional RNAi indications to further address current clinical needs

Leveraging our proprietary technologies and know-how in drug discovery and development, we have discovered and are developing an innovative pipeline of product candidates. These product candidates currently span all stages between preclinical research and IND-enabling studies to Phase I and Phase II clinical trials, creating an extended timeline of product candidates. Conventional RNAi therapeutics that have been approved for commercialization or which are in late clinical stage studies are directed to diseases or conditions with a genetic etiology, and typically limited to delivery to hepatocytes in the liver. Our portfolio of product candidates is intended to address a wider variety of clinical needs, particularly our initial target indications for oncology and dermal fibrosis.

We strategically select our RNAi therapeutics to target genes that have the potential to treat multiple indications and disease states. One of the indications of our core product candidate STP705 is directed at the oncology indication NMSC, which has no effective non-surgical options in current practice according to the CIC Report. Cosmetic appearance remains a key need for NMSC, for which surgery, curettage and electrodesiccation form the cornerstone for NMSC treatment and for which the risk of scarring remains high. NMSC has a high incidence in the United States, with more than five million new patients in 2020. According to the CIC Report, due to the relatively late launch of molecularly targeted drugs and biologics in China, a significant number of patients with cancer, including NMSC, cannot be adequately treated through the use of conventional chemotherapeutic drugs. The success of our Phase IIa clinical trial for treatment of NMSC with STP705 validates the effectiveness of our PNP delivery platform for application in treating oncology indications. STP705, as well as our clinical stage key product candidate STP707, each comprise dual targeted siRNAs against TGF-ß1 and COX-2, which have broad applicability across tumor types and fibrotic diseases. We are in Phase II clinical trials for STP705 in NMSC indications. We have commenced Phase I clinical trials for STP705 in liver cancer in the U.S. and plan to file an IND in China. We initiated a Phase I clinical trial for STP707 for solid tumors in the U.S. in November 2021. Our STP355 product candidate comprises dual siRNAs against TGF-ß1 and VEGFR2 (a target gene well-validated for its involvement in tumor angiogenesis and metastasis), that is being progressed in IND-enabling studies for the treatment of multiple tumor types. STP705, STP707 and our other oncology product candidates are well-positioned to fill the needs for new and better cancer treatments.

We have applied our platform technologies to the selection of other non-oncology target indications. We are studying other product candidates for treatment of other diseases which have clinical need. We are also developing STP705 and STP707 for the treatment of fibrosis indications. We have initiated Phase II clinical trials with STP705 for the treatment of dermal fibrosis indications, including HTS and keloid scarless healing. We have completed IND-enabling stage studies for STP707 in liver fibrosis (PSC) and filed an IND in the U.S. in November 2021. We are also exploring STP707 for treatment of lung fibrosis. Our STP122G product candidate is being developed for anticoagulant therapy, and STP144G and STP133G are undergoing preclinical research for use in complement-mediated diseases and cardiometabolic diseases, respectively.

In addition to our RNAi research programs and product candidates, our subsidiary RNAimmune has several preclinical mRNA product candidates under development, including for a vaccine directed against COVID-19. Our preclinical candidate RIM730 comprises mRNA that codes for SARS-CoV-2 viral proteins formulated with LNP delivery technology for intramuscular administration as a prophylactic vaccine for the prevention of COVID-19. RNAimmune is also developing other mRNA product candidates directed against infectious disease, as well as certain oncology indications and rare diseases.

Our pipeline includes products with both nearer term and longer horizon time to market. STP705 and STP707 exemplify our near term strategy to focus on therapeutic indications where orphan drug designations are available or early clinical trials can be accelerated by use of combined Phase I/II trials. We are simultaneously progressing development in Phase I and pre-IND studies for broader indications in oncology for STP705 and STP707. We are also developing STP705 in preclinical trials for the medical aesthetics market for fat sculpting. We are also pursuing preclinical studies for other product candidates for cardiometabolic indications using PCSK9 siRNA, including both dyslipidemia and hypercholesteremia, as well as for complement-mediated diseases and viral diseases, including COVID-19, flu and hepatitis B. Even with our long term clinical trials, we have focused on indications where proof of concept can be achieved first in indications with orphan drug designations or other accelerated regulatory pathways, allowing us to pivot resources to the most promising candidates.

The strength and diversity of our pipeline is further fueled by our product candidates that are capable of targeting more than one gene simultaneously and exploration of the combinatorial potential of use with established immune-oncology therapies. We are currently exploring the efficacy of combination therapy with STP705 and anti-PD-1 targeted therapies as well as for our other lead product candidate STP707 in combination therapies with anti-PD-1/PD-L1 targeted therapies for liver cancer, metastatic cSCC and NSCLC.

Potential first-in-class dual-targeted RNAi therapeutics that inhibit both TGF-ß1 and COX-2 for high therapeutic potency in skin cancer, liver cancer and fibrosis indications

STP705 and STP707 are dual-targeting RNAi therapeutics based on more than a decade of our experience researching TGF-ß1 and its synergistic effects when combined with COX-2 for tumor suppression and fibroblast apoptosis (i.e., a form of programmed cell death). Fibroblast cells contribute to dermal scarring externally and fibrotic disease in a variety of tissues, including contributing to a fibrotic tumor microenvironment which can make tumors resistant to conventional therapeutic treatments. Reducing fibrosis in the tumor microenvironment can make the tumor more responsive to therapeutics. The mechanism of action for both TGF-ß1 and COX-2 in tumor biology and fibrotic disease is widely recognized. Both act as gatekeeper genes, where their inhibition blocks a downstream cascade of events that would otherwise lead to tumor cell proliferation, survival, invasion, angiogenesis and immune evasion. Although TGF-ß1 is an attractive target for antitumor drugs, its involvement in normal cellular processes across the body have limited the development of small molecule and antibody therapies because of the resulting systemic toxicity. Our PNP delivery platform enables delivery of our product candidates either locally or with preferential uptake in the liver to create cell- and tissue-selective targeting of the TGF ß1/COX 2 inhibitory activity provided by the siRNA therapeutic and avoiding whole body exposure. No currently marketed drug product utilizes this molecular targeting approach.

While silencing either TGF-ß1 and COX-2 alone induces downregulation of fibrotic activity, targeting both TGF-ß1 and COX-2 simultaneously using STP705 enables a synergistic response leading to fibroblast apoptosis and modification of the tumor microenvironment. In addition, simultaneous knockdown of TGF-ß1 and COX-2 by STP705 in our STP705 clinical trials resulted in increased infiltration of CD4+ and CD8+ T-cells to the tumor microenvironment suggesting increased T-cell responsiveness and the potential for use in combination therapy with immune checkpoint inhibitors. Moreover, by silencing TGF-ß1 and COX-2 simultaneously, our product candidates achieve a higher potency than inhibiting either alone. The therapeutic effectiveness for STP705 has been confirmed by our successful Phase IIa results.

Comprehensive intellectual property portfolio driven by independent research and development capability

Since our inception we have set strategic focus in developing innovative technologies and seeking protection using a comprehensive strategy for filing for patent protection across markets and technology areas. All of our pipeline products have been developed primarily in-house in our research centers in the U.S. and China such that the development of our product candidates is initiated and directed by our in-house team and we do not rely on third party in-licenses for our product pipeline. As of the Latest Practicable Date, we owned 20 issued patents (nine in China, nine in the U.S. and two in Europe) and have filed 119 patent applications that are currently pending (19 in China, 43 in the U.S., six in Europe, eight under

the Patent Cooperation Treaty and 43 in other jurisdictions). Our patent claims cover the siRNA and mRNA drug composition in our pipeline products, our delivery platforms, modes of delivery for our pipeline products, manufacturing technology, and methods of use in various therapeutic areas. Senior management and experienced outside intellectual property counsels collaboratively craft our globally-integrated intellectual property strategy with an eye to broad protection in China, the U.S., Europe and other key jurisdictions.

Our in-house research and development teams have conducted considerable research and development into our PNP delivery platform, expanding on the technologies that we initially in-licensed over a decade ago on an exclusive basis from Dr. A. James Mixson, a professor at the University of Maryland School of Medicine, that had achieved promising results in academic settings to develop a delivery platform useful and effective for pharmaceutical formulations. Our innovative development efforts established high purity manufacturing processes and pharmaceutical-level formulation technology that allow for the large scale production of uniformly sized nanoparticles formulated to contain more than one siRNA, including through the use of microfluidic technology. Through our research and development efforts, we have developed our PNP delivery platform into a pharmaceutical excipient system useful for novel RNAi therapeutics and validated by large scale manufacturing and human clinical testing include:

- Improved the purity of the histidine-lysine polymer (HKP) product, from 50-60% purity achieved in university labs to >99% in large scale industry production.

- Established a process for obtaining a lyophilized PNP-based drug product.

- Established a process with HKP and siRNA aqueous solutions for a local injectable formulation (STP705), achieving success in non-human primate GLP pharmacology/toxicity studies and entered into Phase II clinical studies.

- Established a process with HKP(+H) and siRNA aqueous solutions for a systemic injectable formulation (STP707), completed a 4-week preclinical non-human primate GLP pharmacology/toxicity study and entered into a Phase I clinical study.

- Completed seven large scale (about 3000 vial) GMP manufacturing rounds for STP705 and STP707 drug products.

- Achieved positive clinical readouts for the PNP-based formulation of STP705 for treatment of isSCC in a Phase 2a study.

- Conjugated a chemo-drug Gemcitabine with HKP to serve as a dual-function drug and excipient for siRNA delivery.

- Manipulated HKP with a HKC design for tumor targeted siRNA delivery with a RGD peptide.

- Completed 13-week preclinical non-human GLP pharmacology/toxicity study for potential long term use of the STP707 for treatments of chronical diseases, such as liver and lung fibrosis.

- Built a pilot plant for manufacturing PNP-siRNA formulations with a facility in Guangzhou for our clinical study applications.

While our PNP delivery platform is no longer protected by the initial patents, which have recently expired (and the subject matter of the patents has entered the public domain for anyone including us to use), our research and development efforts resulted in improvements and enhancements of the initially in-licensed technology, and therefore these initial patents are no longer material to the continuous research and development of our PNP delivery platform. We protect our PNP delivery platform by relying on our recently filed patent applications, as well as trade secret protection covering proprietary aspects of related manufacturing and pharmaceutical formulation technology in particular as they relate to our core product and other product candidates. We intend to continue to file patent applications to protect novel aspects of our PNP delivery platform as appropriate.

Our issued patents and pending patent applications protect key features of our core product STP705, as well as our related key product candidate STP707, including the RNA sequences targeting the TGFß1 and COX2 genes that comprise the drug substance, aspects of the pharmaceutical formulation containing those RNA sequences, and methods of using the combination of RNA sequences targeting the TGFß1 and COX2 genes for treatment of various therapeutic applications, including those that we are currently developing such as cancer treatments including skin cancer and fibrosis treatments including HTS and keloid scarless healing. STP705 also benefits from intellectual property protection in the PNP delivery platform, which is used in the STP705 formulation, including patent applications directed to manufacturing methods, and know-how and trade secrets covering manufacturing and pharmaceutical formulation technology. We believe the combination of patent protection directed to STP705 and our PNP delivery platform as well as the trade secrets and proprietary know-how in our manufacturing processes provide sufficient protection to prevent competitors from developing and commercializing RNAi therapeutics that comprise the same siRNA sequences and/or the same formulation technology.

Our robust intellectual property position is bolstered by our commitment to research and development internally, led by our Founder, President and CEO Dr. Lu, our Chief Scientific Officer Dr. David Mark Evans who has worked in the RNAi field since 2003, Dr. Dmitry Samarsky, our Chief Technology Officer who has been involved in scientific research in the RNAi field since 2001 and our Chief Medical Officer Dr. Michael V. Molyneaux. As of the Latest Practicable Date, our research and development team in China consists of 87 employees and consultant, 11 of whom hold doctorate degrees and 22 with masters degrees, while our U.S. team comprises 32 employees and consultant, 18 with doctorate degrees and seven members with masters degrees. Dr. David Mark Evans leads our teams focused on target gene

discovery, siRNA therapeutic design, development, and in vitro and in vivo testing and toxicology. Dr. Dmitry Samarsky's team focuses on our novel GalAhead™ platform technology and therapeutic programs. Dr. Michael V. Molyneaux's team focuses on clinical pipeline development.

We have research laboratory facilities in Suzhou, China and Gaithersburg, Maryland. Our facilities in Suzhou consists of approximately 1800 square meters of leased laboratory and office space, including biological laboratories, a chemistry laboratory and a GLP testing laboratory. Our facilities in Gaithersburg consist of approximately 1280 square meters of leased laboratory and office space with each representing about half of the space. The laboratory space includes a main biology laboratory, a tissue culture laboratory and a chemistry laboratory.

Seasoned management team and world-class industry expertise

We are led by our management team with deep experience and capabilities in discovering, developing and commercializing RNA therapeutics. In addition, our management team and scientific advisory board have on average more than 20 years of pharma research and development experience at the world's leading pharmaceutical companies and research institutions in China and the U.S. Our management team has built a scientifically-driven and collaborative culture that crosses borders and fosters both nimble and rational decision-making.

Dr. Lu, founder, Chairman of Board, President and CEO, has over 28 years of biopharma research and development experience in China and the U.S. After seven years working at Novartis gene therapy division, Dr. Lu co-founded Intradigm Corp. in 2001 in the U.S., serving as its executive vice president and leading the company's siRNA therapeutic research and development until early 2007. After leaving Intradigm, Dr. Lu founded US Sirnaomics in the spring of 2007 and then established Suzhou Sirnaomics (2008) and Guangzhou Sirnaomics (2012). Dr. Lu has led our teams building up a robust technology platform and an enriched RNA therapeutic product pipeline. Dr. Lu has authored over 55 scientific publications, is an inventor on 53 patents and has been recognized with multiple awards and grants in China and the U.S. for his innovative research and entrepreneurship.

Dr. Michael V. Molyneaux, our Chief Medical Officer, has over 20 years of experience in clinical medicine and the biopharmaceutical industry, and most recently served as (Public Company) Chief Medical Officer of Macrocure. Dr. Molyneaux has expertise in preclinical IND-enabling activities and product candidate development, clinical operations, medical affairs, and regulatory affairs in clinical stage biopharmaceutical companies. Dr. Molyneaux is currently responsible for Medical Affairs, Clinical Operations, and Regulatory Affairs activity within our company and will lead clinical activities for IND and NDA filings in multiple therapeutic targets and pipeline development.

Dr. David Mark Evans, our Chief Scientific Officer, has over 25 years of pharmaceutical drug discovery experience, primarily in oncology. Dr. Evans has worked in the RNAi field since 2003, holding senior management positions at Translational Genomics Research Institute (TGEN) and Dharmacon, Inc. (ThermoFisher Scientific, Inc.) prior to joining our company.

Dr. Dmitry Samarsky, our Chief Technology Officer, has over 20 years of experience in research and development. Dr. Samarsky has been at the inception of RNAi technology and drug development, starting in 2001 at Sequitur (later acquired by Invitrogen) and then working, with increasing responsibilities, at Dharmacon/ThermoFisher (U.S.), RXi Pharma (U.S.) and RiboBio (China). Most recently, he served as Chief Scientific Officer of Silence Therapeutics. Dr. Samarsky has authored more than 40 scientific papers, articles, book chapters, patents and patent applications, and has been an invited speaker at more than 100 international conferences.

Dr. Zhifeng Long, our Chief Development Officer, has more than 30 years of biopharmaceutical industry experience, including translational research, drug development, animal pharmacology and toxicology studies, and preclinical and clinical research. Dr. Long has played key roles in over 20 clinical trials from Phase I to III conducted in the U.S., Europe and Japan, across different therapeutic areas, including oncology, cardiovascular, inflammation, genetic disease and infectious disease.

Dr. Edward Yongxiang Wang, our Chief Production Officer, has more than 25 years of research experience. Dr. Wang has in-depth knowledge of biopharmaceutical research and the IND and NDA processes.

Our scientific advisory board is composed of key opinion leaders and renowned scientists with substantial industry experience. Our scientific advisory board includes members in both China, the U.S. and Europe, with experience in drug delivery and polymer design, regulatory strategy, oncology and oncology clinical trial design, liver diseases, dermatology, cardiometabolic diseases and surgical treatments.

OUR STRATEGIES

Our mission is to become a fully-integrated international biopharmaceutical company, leveraging our deep experience in RNA therapeutics and novel delivery platform technologies to rapidly discover, develop and, if approved, commercialize a portfolio of transformative therapeutics and vaccines for patients suffering from a wide range of both rare and large market diseases. We intend to solidify our leadership position in RNA therapeutics by expanding the capabilities of our proprietary delivery platforms to overcome the current barriers to the delivery of RNAi triggers and mRNA and unlock their therapeutic potential. We aim to focus initially on oncology and fibrosis, and then expand to anticoagulant therapies, cardiometabolic disease and viral infections, and ultimately unlock the full potential of RNA therapeutics to address as many patient populations as possible.

The key strategies to achieve our mission are as follows:

Enhance and apply our proprietary delivery platforms to advance the development of innovative therapeutic modalities for the treatment of a broad range of disease states and strengthen our intellectual property position

Our goal is to unlock the full potential of RNAi therapeutics to silence gene targets by improving on and moving beyond the successes of conventional GalNAc RNAi delivery platforms to hepatocytes in the liver, in order to specifically reach a broader range of tissue and cell types. Our current drug candidate pipeline validates the successful utility of our proprietary PNP delivery platform in achieving this goal. Notably, the value and promise of our proprietary delivery platforms have been recognized by our third party preclinical research partners, our current development partner, and are expected to continue to attract the interest of potential partners.

Our PNP delivery platform efficiently encapsulates siRNAs to protect the siRNA in the bloodstream and deliver the siRNAs to cells and tissue where the siRNA acts to silence the target genes. It is implemented into our two lead product candidates, STP705 and STP707, as well as our other oncology and fibrosis product candidates including STP355 and STP369 (as examples). Our GalAhead™ platform, with its novel RNA structures, is implemented into three of our preclinical stage programs to develop drugs for thrombosis, cardiometabolic and complement-mediated disease treatments. Our PDoV-GalNAc platform is also implemented in preclinical stage programs for improving endosomal escape for enhanced therapeutic potency. We believe our innovative GalNAc platforms will allow us to further enhance the therapeutic potency of liver hepatocyte-targeted RNAi therapeutics. RNAimmune has developed a PLNP platform featuring a unique peptide lipid nanoparticle structure for delivery of mRNA therapeutics and vaccines. We intend to advance our product candidates to and through clinical trials, and also to continue to add new targets to our delivery platforms, to further validate application of our platforms for use in a broad range of indications.

We also intend to keep our programs at the forefront of RNAi delivery by continuing to invest in other novel delivery platforms currently in our early discovery programs that will broaden the ability to selectively target a broader range of tissue types. Our continued research and development of novel and innovative technology will further strengthen our intellectual property position. Our early discovery programs include research into RNA-drug conjugates, PLNP mRNA formulation or tumor targeting delivery tools. By continuing these activities, we expect to make our product candidates and delivery platforms more attractive for partnering opportunities for new indications and new targets. We also intend to continue to improve our GMP processes and further enhance our proprietary microfluidic technology platform to develop robust large-scale manufacturing processes, disease- and tissue-specific formulations and diverse clinical applications.

Rapidly advance development of our core product candidate STP705 through clinical trials toward market approvals in a broad range of indications in China and the U.S.

We believe STP705 has strong therapeutic potential in a wide variety of oncology and fibrosis indications, and plan to pursue potentially expedited routes to market approval including by leveraging U.S. FDA orphan drug designations. We have achieved the first successful Phase II clinical results for oncology in our non-melanoma isSCC Phase IIa clinical trial in the U.S., with 19 of 25 patients showing complete tumor cell clearance, validating our approach and drug delivery platform. Our Phase IIb clinical trial for isSCC was initiated in May 2021 in the U.S. with interim results expected in first half of 2022 and we filed an IND in China for a Phase llb clinical trial for isSCC. We have also initiated a Phase II clinical trial to develop STP705 for the treatment of BCC, and Phase I clinical trials for the treatment of HCC/CCA for which we have orphan drug designation from the U.S. FDA. For fibrosis indications, we have initiated Phase I/II clinical trials for treatment of keloid scarless healing and for HTS in the U.S. We are also developing combination therapies with STP705 and conventional chemotherapy drugs, as well as novel oncology drugs such as immune checkpoint inhibitors, for solid tumors.

Develop and commercialize a diverse portfolio of transformative RNA products in a broad range of therapeutic areas, including both rare diseases and diseases with large patient populations

We are enhancing our diverse portfolio of product candidates, which we believe increases our likelihood of success in bringing novel RNA products and delivery modalities through development and, if approved, commercialization. The key highlights of our product pipeline beyond STP705 include:

- **STP707 (oncology and fibrosis)**. Our product candidate STP707 leverages a systemic PNP formulation with the same dual TGF-ß1/COX-2 inhibitor targeting siRNAs as STP705. We are developing STP707 for the treatment of liver cancer, multiple solid tumors and liver fibrosis indications as well as lung cancer and lung fibrosis indications. We initiated Phase I clinical trial for solid tumors in November 2021. We also filed an IND for PSC, a rare form of liver fibrosis, in November 2021 in the U.S. Depending on the response we see in our dose escalation Phase I clinical trials as well as efficacy data obtained in preclinical studies in various tumor models, we could potentially follow the Phase I clinical trial with Phase II clinical trials of STP707 in multiple tumor types, such as metastatic cutaneous squamous cell carcinoma, NSCLC, HCC and CCA in the first half of 2022 in the U.S. We are also developing combination therapies with STP707 and other oncology therapeutics for liver cancer, metastatic cSCC and NSCLC.

- **STP702 (anti-viral)**. Our product candidate STP702 is formulated for systemic delivery and comprises siRNA targeting the influenza virus. We entered into a license agreement with Walvax in April 2021 pursuant to which we out-licensed

commercialization rights for STP702 in mainland China, Hong Kong, Macau and Taiwan. We expect to file an IND in the U.S. pending successful completion of our toxicology and non-clinical studies in the second half of 2022.

- **STP122G (anticoagulant)**. Our product candidate STP122G is being developed for anticoagulant therapy. It leverages our GalAhead™ delivery platform, and is formulated for subcutaneous delivery, as with our other preclinical stage GalAhead™ product candidates. We expect to file IND in the U.S. in the first half of 2022.

- **Other RNAi therapeutics**. We intend to continue to advance our other product candidates (five in oncology, three antivirals, and two cardiometabolic diseases), and will add new product candidates into clinical proof-of-concept studies to our growing pipeline on an ongoing basis.

- **mRNA therapeutics**. RNAimmune is advancing development of our PLNP and PNP formulations for delivery of mRNA, which is intended to enable expression of desired genes in tissues of interest, in contrast to siRNA which is intended to decrease or eliminate expression of target gene sequences. RNAimmune is engaged in preclinical research development of prophylactic vaccines for influenza and COVID-19, as well as therapeutics and vaccines for certain oncology indications and rare diseases.

Build a fully integrated biopharmaceutical company by advancing our capabilities in product development, expanding our internal GMP manufacturing capabilities, and developing commercialization abilities, if our product candidates are approved

To achieve our long-term goal of becoming a fully integrated biopharmaceutical company, we are expanding on our research and development centers, our manufacturing facility in Guangzhou and our business development offices. We have built significant expertise and know-how by creating innovative delivery capabilities for RNA, as well as developing microfluidic formulation processes and GMP manufacturing capabilities. We plan to continue to invest in our technology and manufacturing processes with the goal of further establishing ourselves as the leader in developing and producing RNA therapeutics as well as developing innovative delivery platforms. In particular, we intend to further grow the robustness of our manufacturing processes from process development through to clinical-grade and commercial-scale GMP manufacturing to enable scaling for support of later stage clinical programs and indications and future commercialization of our products. In the future we intend to build commercialization capabilities, including sales and marketing.

With significant leadership and operational presence in both China and the U.S., we believe we are well positioned to take advantage of research and development and manufacturing benefits, speed to market efficiencies and the vast market potential of the

largest and fastest growing healthcare therapeutics markets in the world. Following the guidance of the NMPA, we will continue to pursue product candidates and indications where orphan drug designation can be achieved in the U.S., for which approval may enhance priority review by the NMPA, and shorten the review period from 1-2 years to 6-12 months to more quickly reach market approval in China.

To prepare for the anticipated commercialization of STP705 and STP707, we plan to build an in-house sales and marketing team to commercialize our products. We plan to recruit and train our sales and marketing team in accordance with the clinical development progress of our pipeline products, aiming to ensure the timely commercialization of our pipeline products once we obtain relevant approvals. RNA therapeutics 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 RNA therapeutics.

Selectively pursue synergistic collaboration opportunities to maximize the potential of our clinical product candidates

While we aspire to develop fully-integrated end-to-end biopharmaceutical operations, our near-term goals are to bring our product candidates to approval and commercialization as quickly as possible. We currently retain worldwide development and commercialization rights to all of our product candidates, with the exception of the rights to STP702 for influenza in mainland China, Hong Kong, Macau and Taiwan for which we have entered into a collaboration partnership with Walvax. Based on our discussions with potential partners on some of our pipeline candidates, including our PCSK9 and hepatitis B programs, both of which are developed on our PDoV delivery platform, we believe that our early stage programs are attractive for partnering.

We intend to explore business growth through investment in potential selective acquisition in China or in other global markets of suitable companies and in-licensing of suitable product rights or new technology. We plan to explore investment opportunities in product rights or new technology having broad indications with promising efficacy and safety profiles, well-validated mechanism of action, high barrier to entry in manufacturing or dosing, and/or strong needs without affordability issues.

As we have done with our current product pipeline, we will continue to seek to identify and initiate studies on targets for indications with clinical needs to demonstrate proof of concept in preclinical studies. Based on the results of proven feasibility, we plan to expand studies to include other therapeutic programs that we believe will be attractive to potential partners. We plan to selectively evaluate collaborations for our existing and new product candidates that we believe may complement our expertise, or help the geographical coverage of our future commercialization efforts.

OUR BUSINESS MODEL

We have built an international professional team for discovery and development of RNAi therapeutics and mRNA vaccines and therapeutics, based on our proprietary drug delivery technology platforms. Our target market is global with our current focus specifically on the U.S. and China markets, which are supported by our research and development facilities and manufacturing capabilities in both countries. We are adopting a clinical development strategy to conduct clinical trials for our product candidates initially in the U.S. and then to extend those trials into China, based on the differing medical needs of the two markets, for example, some orphan drug indications in the U.S. are more prevalent in the population in China.

Our initial focus is on oncology and fibrosis products, as well as antiviral products and products that leverage liver targeted drug delivery. We have developed in-house and own the global rights to STP705 and STP707, our lead product candidates, which demonstrates our capabilities in designing novel RNA therapeutics based on our proprietary delivery platforms and developing them into drugs to address medical needs. Our proprietary delivery platforms include our PNP delivery platform, useful for local or systemic administration of RNAi therapeutics to targets beyond liver hepatocyte cells, our GalNAc RNAi delivery platforms for systemic administration of RNAi therapeutics to the liver, and our PLNP delivery platform for administration of mRNA vaccines and therapeutics. We exclusively in-licensed core patents covering our PNP delivery platform at an early stage and have conducted research and development in-house to enhance our PNP delivery platform and adapt it for formulating novel RNA therapeutics to treat a range of therapeutic indications. We have developed in-house and own the global rights to GalNAc RNAi delivery platforms. Our GalAhead™ delivery platform conjugates GalNAc moieties to unique RNAi trigger structures while our PDoV-GalNAc delivery platform conjugates GalNAc moieties to Peptide Docking Vehicle (PDoV) peptide linkers and up to two siRNAs conjugated to the peptide linker. Our PNP and GalNAc RNAi delivery platforms serve as a basis to expand our pipeline of early-stage product candidates. Our subsidiary RNAimmune develops mRNA-based vaccines and therapeutics, including an mRNA SARS-CoV-2 vaccine program using Delta variant spike protein-coding mRNA as an antigen with LNP delivery formulation, which is undergoing pre-IND discussion with U.S. FDA and mRNA tumor vaccine and therapeutics programs, which use our proprietary PLNP delivery platform that we developed in-house and to which we own global rights.

Our long time (since 2008) and dual presence in the U.S and China allows us to navigate between both countries' regulatory systems. We are subject to the regulation of competent authorities from the U.S. and China in light of our dual presence in both countries. In China, NMPA is the primary regulatory agency for pharmaceutical products and businesses, and regulates across the life cycle of pharmaceutical products. In the U.S., FDA represents the counterpart of the NMPA regulating drugs and biologics. For details of relevant regulatory authorities, see "Regulatory Overview – Overview of Laws and Regulations in the PRC" and "Regulatory Overview – Laws and Regulations in the United States." As of the Latest Practicable Date, we had a regulatory and clinical team with five members in the U.S. and six in China with ample knowledge and experience with regard to regulatory filings in both

countries managing the regulatory submission process in the U.S. and China. We plan to commence clinical trials in China for isSCC, HTS, and liver cancer in 2022.

OUR DRUG CANDIDATES

By leveraging our proprietary delivery platform technologies and know-how in RNA drug discovery and development, we have built an innovative pipeline of product candidates. These product candidates have broad applicability across therapeutic indications, and thus allow us to de-escalate the inherent risk of developing innovative drug product candidates. Our key product candidates as of the Latest Practicable Date are set forth below:

Notes：* denotes our core product

** denotes orphan drug

Abbreviations: isSCC= squamous cell carcinoma in situ; BCC= basal cell carcinoma; cSCC= metastatic cutaneous squamous cell carcinoma; NSCLC= non-small cell lung cancer; CRC= colorectal carcinoma; BC= bladder cancer; PSC= primary sclerosing cholangitis; PNP= our polypeptide nanoparticle (PNP) RNAi delivery platform; PNP-IT= PNP platform

formulated for intratumoral administration; PNP-IV= PNP platform formulated for intravenous administration; GalAhead™= our GalNAc RNAi delivery platform that conjugates GalNAc moieties to RNAi triggers; PDoV-GalNAc= our GalNAc RNAi delivery platform that conjugates GalNAc moieties to Peptide Docking Vehicle (PDoV) peptide linkers and up to two siRNAs to the peptide; LNP = lipid nanoparticle (LNP) formulation for delivery of mRNA; HPV= human papilloma virus; HBV= hepatitis B virus; OL China= out licensed mainland China, Hong Kong, Macau and Taiwan rights under agreement with Walvax but we retain the rights for rest of the world; and MRCT= multi regional clinical trial in which we will be the sponsor for all clinical trial sites.

1. Liver cancer (basket) includes cholangiocarcinoma, hepatocellular carcinoma, liver metastases etc.
2. We filed our IND in China, which is currently awaiting approval from NMPA, for study sites in China. The study sites will be part of a global multicenter clinical trials for our Phase IIb clinical trial for isSCC.
3. We expect to file the IND in China as part of the global multicenter clinical trials.
4. We expect to file the IND solely for HCC in China as part of the global multicenter clinical trials.
5. Studies in combination with anti-PD-(L)1 inhibitors conducted pursuant to collaborations with Innovent and Shanghai Junshi.
6. Research and development conducted by our subsidiary RNAimmune.

OUR CORE DRUG CANDIDATE

STP705

STP705 is comprised of two siRNA nucleotides targeting TGF-ß1 and COX-2 mRNA formulated into nanoparticles using our PNP delivery platform for local intratumoral delivery. TGF-ß1 is a cytokine well-recognized as a key driver of fibrosis that also acts to promote tumor growth, angiogenesis, immune-escape and metastasis. COX-2 is well known to be involved in inflammation and its expression is elevated in many tumor tissues as well as fibrotic tissues. STP705 simultaneously silences the expression of TGF-ß1 and COX-2 for a synergistic effect to both promote tumor suppression and downregulate genes involved in fibrotic effect. STP705 is well-positioned to meet medical needs for non-surgical treatment of NMSC and skin fibrosis indications and provide effective treatment for liver cancer.

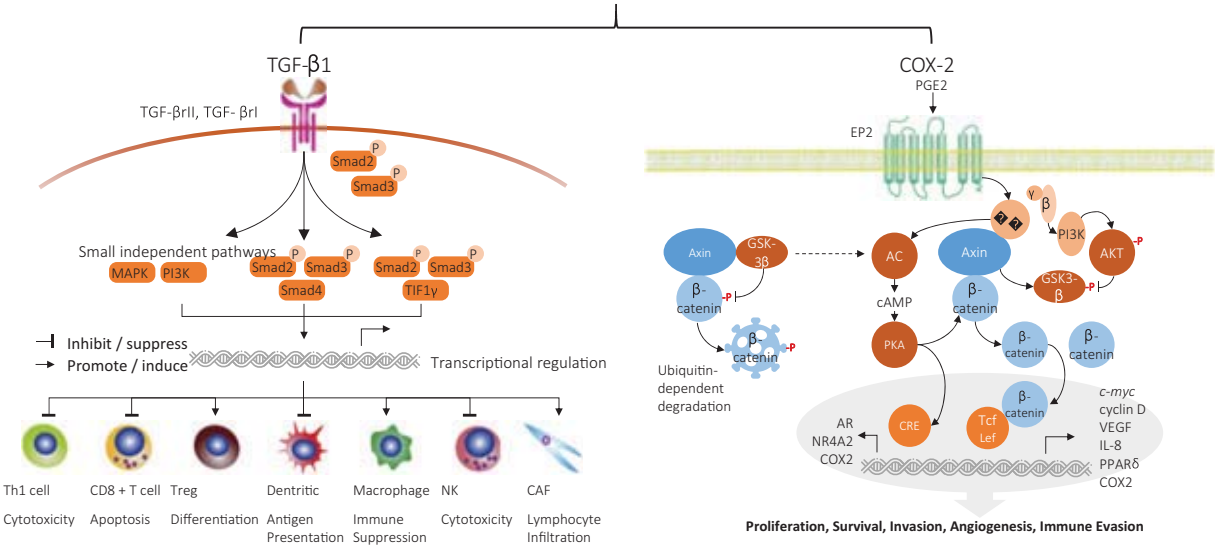
We are currently evaluating STP705 in Phase II trials for NMSC and skin fibrosis indications and have commenced Phase I trials in liver cancer in the U.S. STP705 has received Orphan Drug Designations in the U.S. for the treatment of certain liver cancers and liver fibrosis including: primary sclerosing cholangitis (PSC), cholangiocarcinoma (CCA), and hepatocellular carcinoma (HCC). In 2017, we achieved IND approval for hypertrophic scarring (HTS), which was the first in China for a class 1.1 drug for an RNAi therapeutic, although we did not commence clinical trials in China. Based on our two-pronged development approach for leveraging regulatory synergies in China and U.S., we strategically elected to pursue Phase I/II clinical trials in the U.S. for HTS rather than commencing a Phase I clinical trial in China, and permitted our IND in China for HTS to lapse. While we initiated Phase I/II clinical trial for HTS in the U.S., after a modification to the clinical trial protocol was recommended we elected to focus our resources on NMSC and to re-initiate clinical trials in HTS at a later date. In our recently completed U.S.-based Phase IIa clinical trials for non-melanoma squamous cell carcinoma *in situ* (isSCC), STP705 demonstrated encouraging efficacy and safety results. We initiated the Phase IIb clinical trial for isSCC in May 2021 in the U.S. and also filed an IND in China for a Phase IIb clinical trial that would be part of a global multicenter study.

We hold patents and patent applications related to STP705 in the U.S., China and other markets. We hold the rights to develop and commercialize STP705 globally.

Mechanism of Action

TGF-ß1 signaling regulates a broad range of cellular processes including cell proliferation, differentiation, apoptosis, extracellular matrix production, angiogenesis and inflammation and immune response. COX-2 is a potent proinflammatory and proliferative mediator. COX-2 is the rate-limiting enzyme in prostanoid synthesis, including Prostaglandin E2 (PGE2), the predominant prostaglandin. PGE2 is known to be involved in tumor growth, resistance to apoptosis, immunosuppression and angiogenesis. STP705 silences the expression of both TGF-ß1 and COX-2 genes, resulting in the downregulation of multiple pro-fibrotic and tumor promoting factors. Importantly, simultaneous silencing of TGF-ß1 and COX-2 in the same cell results in increased efficacy compared to silencing of either alone. As set out in the figure below, STP705 is designed to reduce the negative effects of both TGF-ß1 and COX-2 in oncology and fibrosis by silencing their expression in affected tissues.

TGF-ß1 and COX-2 Pathways



Sources: *Bai, X., et al. OncoTargets and Therapy, 2019: 12, 9527–9538.*

Hashemi Goradel N, et al. J Cell Physiol. 2019: 234, 5683-5699.

Oncology

TGF-ß1 has been identified as a major factor that promotes epithelial cell proliferation and is a critical regulator of development and progression of certain cancers in humans. The cell surface receptor for TGF-ß1 is a complex of TGF-ßl type I and type II transmembrane receptors (TßRI and TßRII), both of which are serine threonine kinases. Binding of TGF-ß1 recruits TßRI into a heterotetrameric complex, resulting in phosphorylation and activation of

the cytoplasmic domain of TßRI by TßRII kinase. This activates the kinase activity of the TßRI towards its substrates the R-(receptor activated) Smads, which for TGF-ß1 are Smad2 and Smad3. Once phosphorylated, Smad2 or Smad3 form a complex with the co-Smad, Smad4, and translocate to the nucleus to regulate TGF-ß responsive genes, through either specific Smad-binding element, other suppressive elements, or through interaction with other transcription factors. TGF-ßs can also activate members of the mitogen-activated protein (MAP) kinase signaling molecules including JNK, p38, ERKs, and the PI3 K/AKT pathway.

TGF-ß1 overexpression has been reported in various cancers, including both skin and liver cancers. Chronic elevation of TGF-ßl has been reported to contribute in chronic liver inflammation, liver fibrosis, and cirrhosis and is considered to be the main pro-fibrogenic cytokine in the liver that induces fibrosis by activating hepatic stellate cells (HSCs). Additionally, current data suggests that TGF-ß1 overexpression may have a tumor promoting effect even at the early stages of skin carcinogenesis if overexpressed in proliferative cells of the epidermis/tumor epithelia. The expression of TGF-ß has been significantly correlated with tumor progression, tumor invasiveness, lymph node metastasis, distant metastasis, and tumor recurrence, and epithelial-mesenchymal transition at the later stages of carcinogenesis. The tumor promotion role is associated with TGF-ß1's effect on the loss of epithelial cell adhesion, extracellular matrix remodeling, and enhanced angiogenesis. Given the critical role of TGF-ßl in tumor progression, it has been acknowledged as an attractive target for preventive and therapeutic approaches against NMSC and liver cancer development.

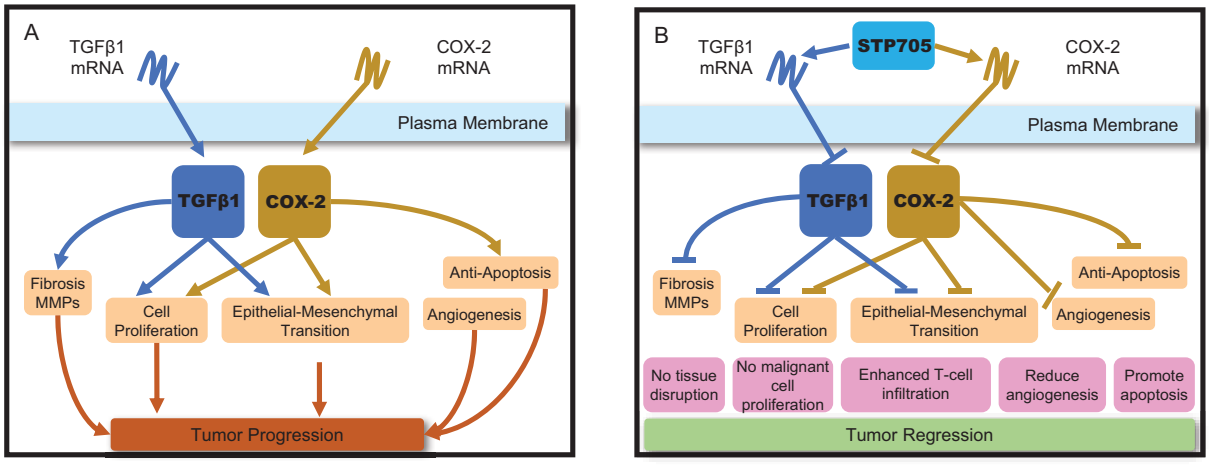
TGF-ß1 is also a well-known regulator of immune cells. TGF-ß1 has been shown to have an inhibitory effect on T-cell proliferation, activation and effector function. Elevated TGF-ßl levels at a tumor site are associated with a reduction in the ability for T-cells to respond to tumors. In published studies in mouse models where tumor T-cell exclusion was observed, simultaneous inhibition of TGF-ß and PD-1 or PD-L1 resulted in improved T-cell infiltration of the tumor. Thus, the evidence strongly suggests that inhibition of TGF-ßl may improve the efficacy of immune checkpoint inhibitors such as anti-PD-1/PD-L1 antibodies as cancer therapeutics.

Cyclooxygenase (COX), also known as prostaglandin-endoperoxide synthase (PTGS), is an enzyme that is responsible for the formation of prostanoids, including thromboxane and prostaglandins such as prostacyclin. COX-2 is one of the members of the PTGS family. COX-2 is expressed in many types of cancers and exerts a multifaceted role in promoting tumorigenesis and cancer cell resistance to therapy. Chronic elevation of COX-2 has been reported to contribute to chronic liver inflammation, liver fibrosis and cirrhosis and its overexpression has also been reported in skin cancer (both SCC and BCC) patients. While the precise molecular mechanism of COX-2 is still under investigation, several possible mechanisms of COX-2 that could play a role in the development of cancer have been postulated. COX-2 can act as a proliferative factor for malignant cells by promoting the synthesis of prostaglandin E2 (PGE2). COX-2 also mediates antiapoptotic effects on cells through induction of Mcl-1 and Bcl-2 expression. Bcl-2 is a known antiapoptotic factor and

Mcl-1 upregulation is involved in c-Myc and IL-6 mediated apoptotic effects. COX-2 is also required by the myeloid suppressor cells to produce the immunosuppressive molecule arginase-1 that promotes invasion and angiogenesis in human carcinoma cells. Additionally, studies have reported that COX-2 could promote epithelial-mesenchymal transition (i.e., weakens intercellular adhesions) that enhances the motility of carcinoma cells allowing them to penetrate surrounding tissues and metastasize. Inhibition of COX-2 has been shown to suppress cell migration and induces apoptosis. Indeed, administration of COX-2 inhibitors in a preoperative setting may reduce the risk of metastasis in cancer patients and COX-2 inhibition may also sensitize cancer cells to chemotherapy and radiation treatment. Clinical and preclinical studies have demonstrated that the COX-2 inhibitor celecoxib was highly effective in preventing NMSC in subjects who were at high risk of developing skin cancers due to either a large number of actinic keratoses, or having already developed one or more skin cancers. Epidemiological studies also demonstrate that COX-2 inhibitors are associated with decreased risk of cutaneous SCCs. In vitro cell culture studies and in vivo mouse studies show association between increased COX-2 expression and resistance to apoptosis and induction of angiogenesis. Overall, the positive correlation with COX-2 overexpression and both NMSC and liver inflammation and fibrosis renders it as an attractive therapeutic target.

The figure below shows the hypothesized mode of action of STP705 and demonstrates that treatment with STP705 promotes tumor suppression through silencing of TGF-ß1 and COX-2. (A) outlines the proposed mechanism of TGF-ß1 and COX-2 in cancer cells that induces tumor progression by promoting tissue disruption, cell proliferation, epithelial-mesenchymal transition, angiogenesis and anti-apoptosis. (B) outlines the proposed mechanism of STP705-mediated inhibition of TGF-ß1 and COX-2 in cancer cells that suppresses tumor progression by (i) inhibiting tissue disruption, cell proliferation, and angiogenesis; (ii) maintaining cellular integrity of healthy cells; and (iii) promoting apoptosis of cancer cells. Overall, the figure demonstrates that STP705 treatment, by inhibiting TGF-ß1 and COX-2 expression, would promote tumor suppression.

Mechanism of Action for STP705



Source: Company

Fibrosis

Fibrosis is defined by the excessive accumulation of extracellular matrix (ECM) in and around damaged tissue, which can lead to permanent scarring. Both keloid scarring and HTS result from a disrupted balance between ECM protein deposition and degradation during dermal wound healing and are characterized by persistent inflammation. Prolonged inflammation leads to increased vascularization, hypercellularity and excessive collagen deposition. Keloid scars are considered benign tumors. Simultaneous silencing of TGF-ß1 and COX-2 results in the downregulation of fibrogenic markers such as α-smooth muscle actin (α-SMA), hydroxyproline, Collagen 1 and Collagen 3, as well as pro-apoptotic effects in fibroblasts. The synergistic effect of simultaneous silencing of TGF-ß1 and COX-2 may reverse fibrotic scarring through minimizing inflammation and activating fibroblast apoptosis.

Market Opportunity and Competition

Treatment of Non-Melanoma Skin Cancer

We have completed Phase IIa clinical trials of STP705 for the treatment of squamous cell carcinoma *in situ* (isSCC) and have initiated Phase II clinical trials for basal cell carcinoma (BCC). BCC and squamous cell carcinoma (SCC) are the two major subtypes of non-melanoma skin cancer (NMSC), which is the most common form of cancer in the U.S. SCCs arise from hair follicle stem cells and account for 16% of all skin cancers. In contrast to BCCs, SCCs are more aggressive and may metastasize. Squamous cell carcinoma of the skin (cutaneous squamous cell carcinoma, or SCC) is characterized by developing from a precursor lesion called actinic keratosis (AK) which most commonly forms on skin damaged by chronic exposure to UV light. While a minority of AKs are thought to develop into skin cancer, most SCC develops from AKs. isSCC is an early-stage form of SCC that is localized to the surface of the skin and has not spread to deeper tissues or other organs.

According to the CIC Report, in the U.S., 2.4 million people and 3.2 million people were diagnosed with BCC and SCC, respectively, in 2020 and in China, 76 thousand people and 28 thousand people, respectively, diagnosed in 2020. The number of deaths in 2020 globally from NMSC was almost 64 thousand people, where the mortality of Asian NMSC patients represented 43.6% of the global total, significantly more than Northern America (8.4%). The incidence of BCC and SCC increased by 33% from 2015 to 2020 in the U.S., making NMSC an increasingly substantial economic burden. These increases are associated with several factors, including raised awareness of NMSC, improved registration, transition of the patient population toward the elderly, and increased exposure to UV radiation. SCC is believed to be increasing at a faster rate. In the past many squamous cell carcinoma in situ (isSCC) may have been misdiagnosed as AKs (over 60 million people in the U.S. have AK lesions) and now, "diagnostic drift" to isSCCs may be contributing to the increased incidence of SCC.

According to the CIC Report, the market size of SCC and BCC treatment for pre-metastatic patients in the U.S. is expected to grow faster in the years ahead, rising from

US$6.5 billion in 2020 to US$22.1 billion in 2030, with a CAGR of 13.0% primarily driven by the increase in the number of addressable patients and emerging new approaches to treatment. The market size of the SCC treatment will grow faster than BCC in the U.S. The market size of SCC and BCC treatment in China is also expected to grow faster, rising from US$38 million in 2020 to US$149 million in 2030, with a CAGR of 14.6%.

The current standard of care for pre-metastatic high-risk isSCC and BCC patients is surgical excision of the lesions. There is both growing evidence for the high rate of residual BCC and SCC after surgical lesion removal and dissatisfaction with surgical treatment from patients due to a high risk of scarring at the excision site. In a study of 233 shave biopsies of BCC or SCC, 58% of BCC specimens had residual tumor and 27% of SCC specimens had residual tumor. Additionally, surgery renders patients with the risk of infection, hematoma, and scar development and is often not a treatment option for immunocompromised patients. Other treatment options include pharmacotherapy, cryotherapy, photodynamic therapy, laser and radiotherapy. There is, however, evidence in the literature demonstrating that current non-surgical options lead to the development of resistance since these modalities usually require multiple administrations. A meta-analysis of several NMSC treatments including photodynamic therapy, surgical excision, cryotherapy, imiquimod, radiotherapy, and 5-fluorouracil concluded that surgical excision was the optimal treatment option for NMSC in terms of both efficacy and safety. Cosmetic appearance remains one of the key needs for NMSC treatment and has a large influence on patient preferences, especially for those with lesions on the head or neck. Current treatments focused on surgical excision are unable to satisfy this special need due to a high risk of scarring.

As of the Latest Practicable Date, there are two drugs approved by U.S. FDA for pre-metastatic BCC patients, both of which are used off-label for pre-metastatic SCC patients: 5'-fluorouracil and imiquimod. Both are administered topically, and according to the CIC Report, both can cause skin reactions in some patients. In addition, neither is a preferred option over surgical excision in terms of efficacy and safety.

Efficacy and Side Effects for Drug Products Approved for Pre-Metastatic BCC

Drug name	Generic name	Approved markets	Indication	Efficacy	Side effects
Adrucil	5'-fluorouracil	China, US	BCC	With isolated, easily accessible basal cell carcinomas, the success rate with fluorouracil cream and solution is approximately 93%	Burning, crusting, allergic contact dermatitis
Aldara	Imiquimod	China, US	BCC	Superficial BCC imiquimod vs vehicle clearance rate is 75% vs 2%	Headache, back pain, burning

Source: the CIC Report

There remains needs for new therapeutics for pre-metastatic NMSC that effectively treat disease, have a favorable safety profile and low risk of scarring. While surgical treatments are effective at treating disease, those treatments have a higher risk of infection, bleeding and scarring, which are particularly concerning to patients with early stage disease, particularly for those with lesions on the head, face or neck. Despite substantial deal activity and investments by biopharmaceutical companies in the development of NMSC therapies over the years, many drug candidates have failed to show significant clinical efficacy.

Treatment of Keloid Scarless Healing and Hypertrophic Scarring

We are evaluating STP705 in a Phase I/II clinical trial for the treatment of keloid scarless healing. Keloid disorders constitute an abnormal fibro-proliferative wound healing cascade where raised scar tissue grows excessively and invasively beyond the original wound borders. Keloids are an example of a fibrogenic disease, which also include skin hypertrophic scarring, and liver, lung and kidney fibrosis. Localized keloids and raised hypertrophic scars can represent an excessive tissue response to dermal injury and are characterized by local fibroblast proliferation and overproduction of collagen matrix. Hypertrophic scar formation is a major clinical problem in the developing and industrialized worlds. Burn injuries, traumatic injuries, and surgical procedures can give rise to exuberant scarring that result in permanent functional loss and the stigma of disfigurement. Each year, approximately 42 million surgical procedures are performed in the U.S. resulting in about 62 million scars. Furthermore, many patients experience hypertrophic scarring and keloids after surgery—with higher percentages observed in developing countries. By causing pain, pruritis and contractures, excessive scarring significantly affects the patient's quality of life, both physically and psychologically.

According to the CIC Report, in 2020 more than seven million patients were affected by HTS or keloids in China and eight million patients in the U.S.. Although the incidence of HTS following traumatic skin injuries is not known, it is an outcome that creates a problem of enormous magnitude. According to the CIC Report, the market size for hypertrophic scarring and keloid treatment is expected to grow between 2020 and 2030 from US$2.9 billion to US$5.9 billion in China and US$10.3 billion to US$18.6 billion in the U.S.

Fibrogenic diseases including liver, lung and kidney fibrosis, as well as keloids and skin hypertrophic scarring, are diseases with limited therapeutic options. Intralesional injections of corticosteroids are first line therapy for keloids and second line therapy for hypertrophic scarring. Combination therapy of corticosteroids with surgery, photodynamic therapy and cryotherapy is also performed. Common adverse effects for corticosteroid treatment include skin and subcutaneous fat atrophy and telangiectasias, or spider veins. Cryotherapy, scar revision, radiotherapy and laser therapy are also utilized for treatment. Most therapeutic approaches remain clinically unsatisfactory at reducing or preventing keloid or hypertrophic scarring.

Treatment of Liver Cancer

We are evaluating STP705 in a Phase I clinical trial for the treatment of liver cancer, specifically, hepatocellular carcinoma and cholangiocarcinoma (HCC/CCA), using intra-tumoral injection via computerized tomography (CT) guided treatment. Liver cancer is a global health problem, with liver neoplasms representing the second-most frequent cause of cancer-related death. There are many different types of liver cancers including HCC, CCA, liver angiosarcoma, hepatoblastoma and others. Additionally, the liver is a highly metastasis-permissive organ. It is the most frequently afflicted organ by metastasis, and liver metastases are much more common than primary hepatic tumors. The distinctive biology of the liver renders it intrinsically susceptible to metastases. This includes (i) liver's significant role in the circulatory system and the liver-specific microcirculation provides increased access of disseminated tumor cells carried in the blood, (ii) the regenerative capability creates a favorable environment for survival and growth of tumor cells, and (iii) regional immune suppression due to its constant exposure to inflammatory stimuli results in a tolerant microenvironment permissive of tumor cell survival and growth. Liver involvement in metastasis is frequently overlooked and under-investigated as lesions are often symptomless, as even extensive infiltration by metastatic tumors may not alter liver function or homeostasis until late stage of the disease. The true prevalence of liver metastasis is unknown, but between 30% and 70% of patients dying of cancer have liver metastases and most patients with liver metastases will die of their disease.

According to the CIC Report, China alone accounts for more than half of worldwide liver cancer cases, with more than 400,000 new HCC patients and more than 100,000 new CCA patients diagnosed in 2020. As of 2016, more than 279,000 people die of liver cancer annually in China. In the U.S., approximately 36,000 new HCC patients and 5,000 new CCA patients were diagnosed in 2020. According to the CIC Report, the market size of HCC and CCA in the U.S. is expected to climb from US$2.2 billion in 2020 to US$6.3 billion in 2030, while the market size of HCC and CCA in China is expected to rise from US$1.5 billion in 2020 to US$8.5 billion in 2030.

Frontline therapies for liver cancer all have limited efficacy. Liver cancer has one of the lowest survival rates among common cancers in both China and the U.S., with five-year survival rates of 12% and 18%, respectively, according to the CIC Report. Early stage HCC is typically treated by surgery while treatment of advanced HCC typically uses chemoembolization and radioembolization, targeted therapy and immunotherapy. The current standard of treatment for early stage CCA includes surgery and radiation therapy while advanced CCA is usually treated with chemotherapy using gemcitabine and cisplatin, targeted therapy and immunotherapy. New treatment modalities have attracted much attention for research and development to solve what remains a need for effective treatment, including oncolytic viruses and RNAi therapeutics.

Efficacy and Side Effects for Drug Products Approved for HCC and CCA

Drug name	Generic name	Approved markets	Indication	Efficacy (experimental cohort, placebo or other cohorts)	Side effects (control: % of all grades, % of grades 3-4; placebo: % of all grades, % of grades 3-4)
Tecentriq	Atezolizumab	China, US	HCC	Median OS (NE, 13.2; hazard ratio, 0.58) Median PFS (Tecentriq in combination with Bevacizumab: 6.8, 4.3; hazard ratio, 0.59)	Hypertension (Tecentriq in combination with bevacizumab: 30%, 15%; sorafenib: 24%, 12%)
					Fatigue/asthenia (Tecentriq in combination with bevacizumab: 26%, 2%; sorafenib: 32%, 6%)
					Proteinuria (Tecentriq in combination with bevacizumab: 20%, 3%; sorafenib: 7%, 0.6%)
Avastin	Bevacizumab	China, US	HCC	Median OS (Avastin in combination with Atezolizumab: NE, Sorafenib: 13.2; hazard ratio, 0.58)	Hypertension (Avastin in combination with atezolizumab: 30%, 15%; sorafenib: 24%, 12%)
				Median PFS (Avastin in combination with Atezolizumab: 6.8, Sorafenib: 4.3; hazard ratio, 0.59)	Fatigue/asthenia (Avastin in combination with atezolizumab: 26%, 2%; sorafenib: 32%, 6%)
					Proteinuria (Avastin in combination with atezolizumab: 20%, 3%; sorafenib: 7%, 0.6%)
Cabometyx	Cabozantinib-S-Malate	US	HCC	Median OS (10.2, 8.0; hazard ratio, 0.76)	Diarrhea (54%, 10%;19%, 2%)
					Fatigue (45%, 10%; 30%, 4%)
					Decreased appetite (48%, 6%; 18%, <1%)

Drug name	Generic name	Approved markets	Indication	Efficacy (experimental cohort, placebo or other cohorts)	Side effects (control: % of all grades, % of grades 3-4; placebo: % of all grades, % of grades 3-4)
Keytruda	Pembrolizumab	China, US	HCC	Single arm, ORR 17%	Fatigue, Rash, vitiligo, arthralgia, ascites (8% Grades 3-4) Immune-mediated hepatitis (2.9%)
Lenvima	Lenvatinib Mesylate	China, US	HCC	Median OS (Lenvima: 13.6, Sorafenib: 12.3; hazard ratio: 0.92)	SAE Total (Lenvima: 43.07%, sorafenib: 30.32%) Hypertension (45%, 24%) Cardiac dysfunction (NA, 3%) Arterial thromboembolic (2%, NA)
Opdivo	Nivolumab	China, US	HCC	Cohort 4 (in Combination with Ipilimumab), ORR 33%	Cohort 4 (in Combination with ipilimumab): Rash (53%, 8%); Pruritus (53%, 4%); Musculoskeletal pain (41%, 2%)
Pemazyre	Pemigatinib	US	CCA	Single arm, ORR 36%	Hyperphosphatemia (60%, 0%) Alopecia (49%,0) Diarrhea (47%,2.7)
Cyramza	Ramucirumab	US	HCC	Median OS (8.5, 7.3; hazard ratio 0.71) PFS (2.8, 1.6; hazard ratio 0.45)	Fatigue (36%, 5%; 20%,3%) Peripheral edema (25%,2%; 14%,0%), Decreased appetite (23%, 2%; 20%, 1%)
Stivarga	Regorafenib	China, US	HCC	Median OS (10.6, 7.8; hazard ratio 0.63) PFS (3.4,1.5, hazard ratio 0.43)	Skin and subcutaneous tissue disorders (51%, 12%; 7%, <1%) Pain (55%, 9%; 44%, 8%) Asthenia/Fatigue (20%, 0%; 7%, 0%)

Drug name	Generic name	Approved markets	Indication	Efficacy (experimental cohort, placebo or other cohorts)	Side effects (control: % of all grades, % of grades 3-4; placebo: % of all grades, % of grades 3-4)
Nexavar	Sorafenib Tosylate	China, US	HCC	Median OS (10.7,7.9; hazard ratio 0.69)	Gastrointestinal (98%, 45%; 96%, 32%), Fatigue (46%, 10%; 45%, 13%), Diarrhea (55%, <11%; 25%, 2%)
Truseltiq	Infigratinib Phosphate	US	CCA	Single arm, ORR 23%	Nail toxicity (57%, 2%), Stomatitis (56%, 15%), Dry Eye (44%, 0)
Gemcitabine	Gemcitabine hydrochloride injection	China, US	HCC	Single arm, Median survival for all 30 patients was 6.9 months (95% confidence interval, 4.5-13.5) and the 1-year survival rate was 40%	10% patients experienced grade 3-4 adverse reaction. 7% patients developed Grade 4 neutropenia and 3% patients experienced Grade 3 thrombocytopenia.
Platinol	Cisplatin	China, US	HCC	(cisplatin, sorafenib) Median survival time: 14.0 vs. 12.3 months	There were few noticeable adverse events leading to discontinuation of treatment. One patient had anaphylactic shock as an adverse event that led to discontinuation of treatment.

Abbreviation: NE = Not estimable
Source: the CIC Report

Competitive Advantages

We believe that STP705 has the following major competitive advantages:

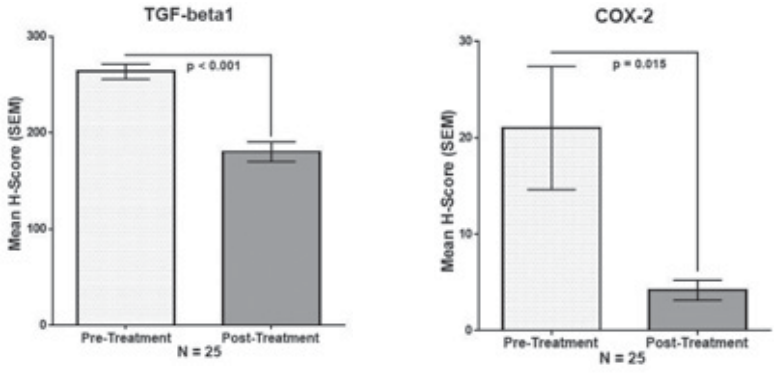
First Clinical Proof of Concept for Targeting TGF-ß1 and COX-2 in Cancer

Our clinical trial results demonstrate a promising therapeutic efficacy profile for STP705, providing proof of concept that dual targeting of TGF-ß1 and COX-2 has strong potential as an effective strategy for treatment of certain cancers. Our Phase IIa clinical trial results in isSCC show positive efficacy results for treatment of non-melanoma skin cancer, showing a high rate of histological clearance of tumor, with 19 out of 25 subjects achieving histological clearance of the lesion and subjects exhibiting improved local skin response (LSR) objective scoring, which suggests improved cosmetic appearance of the skin. Administration of STP705 achieved

both knockdown of TGF-ß1 and COX-2, the direct molecular targets of STP705, as well as downregulation of molecular biomarkers for tumor cell proliferation, progression and invasiveness.

Our clinical trial results showed significant silencing of both TGF-ß1 and COX-2 after treatment was completed, as shown in the figure below. Immunohistological analysis was performed on biopsies of tumor and tumor microenvironment prior to treatment and again seven days after the last treatment on residual tumor or surface epithelium and on adjacent non-tumor/scar tissue in all 25 subjects.

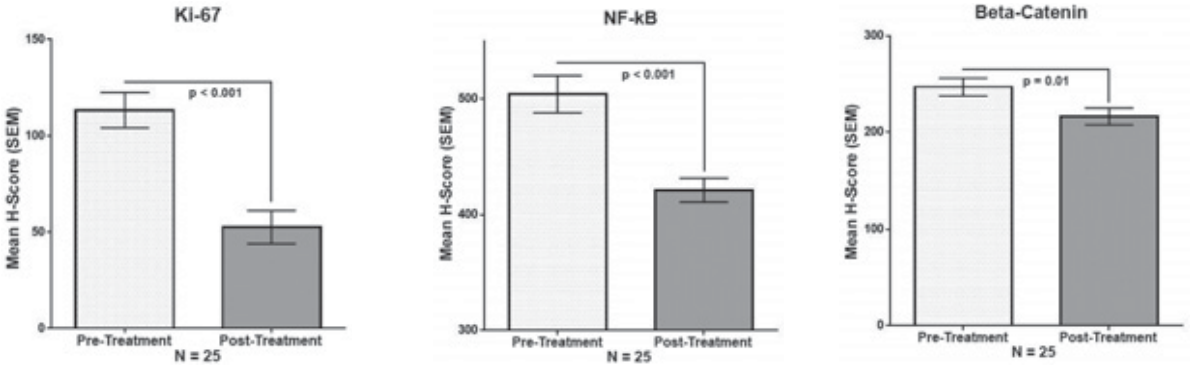
Silencing of TGF-ß1 and COX-2 Expression by STP705



Source: Company data

Our immunohistology analysis investigating biomarkers for downstream biological effects of STP705 in our clinical trial patients showed suppression of multiple cancer-related factors, including Ki-67, NF-κB and ß-Catenin, as illustrated in the figure below. Ki-67 is a protein marker for cellular proliferation and thus tumor growth, and its reduced expression after treatment with STP705 as compared to pre-treatment demonstrates STP705 significantly suppressed cellular proliferation. NF-κB expression is frequently enhanced in cancer cells and it is also a marker for inflammation and tumor progression. High expression of NF-κB has been associated in certain cancers with poor overall survival of patients, while its inhibition may inhibit tumor cell migration, invasion and proliferation. ß-Catenin is a marker for tumor invasiveness. Suppression of ß-Catenin was observed particularly in patients administered higher doses of STP705.

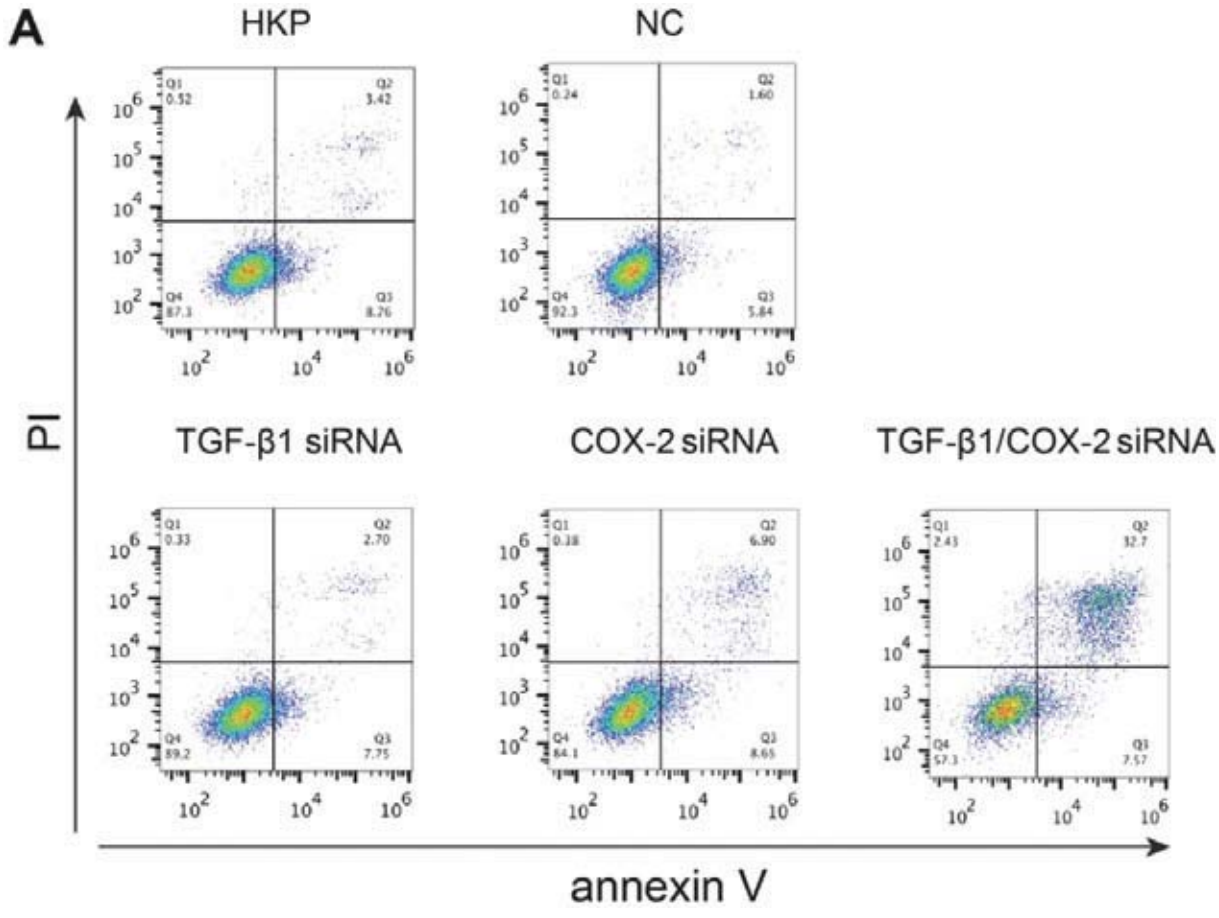
Suppression of Downstream Cancer Biomarkers after Administration of STP705



Source: Company data

Synergistic Effects of Dual Inhibition of TGF-ß1 and COX-2 for Tumor Suppression and Fibroblast Apoptosis

The ability of STP705 to simultaneously silence both TGF-ß1 and COX-2 in the same cell provides greatly improved therapeutic capabilities through synergistic effects. STP705 has clear therapeutic benefits in achieving histological clearance of tumors. In vitro studies demonstrate that simultaneous silencing of TGF-ß1 and COX-2 is more effective than silencing of either target alone. In studies using human fibroblast cells isolated from HTS tissue, cells were transfected with siRNAs targeting either TGF-ß1 or COX-2 individually or in combination, the combination resulted in additive effects. Targeting of either TGF-ß1 or COX-2 alone resulted in downregulation of the pro-fibrotic factors α-SMA, Collagen 1, Collagen 3 and hydroxyproline; however, induction of apoptosis was not observed. Only combined targeting of both TGF-ß1 and COX-2 induced apoptosis in the fibroblasts, as illustrated in the figure below, which shows the results of FACS analyzes of the fibroblasts treated with the TGF-ß1/COX-2 siRNA combination compared to those treated with siRNAs targeting either TGF-ß1 or COX-2 individually. Similar studies using human cutaneous squamous carcinoma cells showed similar results where silencing of either TGF-ß1 or COX-2 alone resulted in downregulation of pro-fibrotic markers, but simultaneous knockdown of both TGF-ß1 and COX-2 induced a marked increase in cellular apoptosis.



Source: Zhou, J. et al.. Oncotarget, 2017: 8(46), 80651–80665.

Apoptotic activity of human fibroblasts is induced when both TGF-ß1 and COX-2 are simultaneously silenced. The lower right panel shows a significant shift in the apoptotic cell population in human fibroblast cells treated with both TGF-ß1 and COX-2 targeting siRNAs compared to human fibroblast cells treated with TGF-ß1 targeting siRNA alone (lower left) or COX-2 targeting siRNA alone (lower middle). Cells were also treated with and without non-targeting siRNA loaded into the PNP platform as controls (top row).

Combination therapy is a key strategy in cancer therapies to combat development of drug resistance by tumor cells. Inhibition of one molecular pathway puts pressure on the tumor cell to upregulate alternative pathways. By simultaneously delivering siRNAs that silence two distinct targets in the same cell, there is decreased opportunity for tumor cells to escape the therapeutic effects of STP705. The increase in apoptotic cells due to the simultaneous knockdown of both TGF-ß1 and COX-2 further validates the combination therapy approach by showing synergistic effects resulting from simultaneous dual inhibition that are not seen in individual targeting.

Favorable Safety Profile

STP705's favorable safety profile is supported by both our Phase IIa clinical trial results and our preclinical studies in mice and non-human primates showing favorable toxicity data and low immunogenicity. See " – Our Core Drug Candidate – STP705 – Summary of Clinical Trial Results". The currently available drug products for the treatment of SSC and BCC are both associated with a high risk of reaction to surrounding normal skin tissue. Similarly, surgical excision is associated with a high risk of scarring. Our clinical results with treatment with STP705 demonstrated that the administration was well-tolerated, with the majority of subjects experiencing no or low-grade local skin responses. In addition, there were no adverse events occurring in dose-dependent patterns, demonstrating that the higher doses pose no more safety risk to subjects than lower doses of STP705. While histological analysis showed that treatment increased immune cell infiltration within tissues with residual tumor, notably the tissue without tumor did not show any increase in immune cell infiltration. Further, a GLP 28-day repeat dose toxicity in non-human primates with once daily subcutaneous dosing did not result in the observation of any abnormalities, thus demonstrating no apparent immunotoxicity from repeated dosing of STP705. While anti-drug antibodies were detected in a minority of animals, there was no resulting effect on safety or effect on gene silencing.

Lower Cost and Complexity of Manufacture

The manufacturing process for STP705 has relatively low complexity and therefore potential for reduced costs of manufacture compared to manufacture of protein-based biologic drugs, including antibody drugs, other marketed siRNA-based drug products, and in some cases small molecule drugs. Protein-based biologics require production of the proteins from living organisms and require stringent quality control measures. The cost and complexity of small molecule manufacture can vary greatly based on the complexity of both the small molecule and its formulation. While siRNA therapeutics are typically simpler than protein-based biologics, the manufacturing process for STP705 is lower complexity and therefore potentially lower cost than LNP-based siRNA therapeutics. The manufacturing process for STP705 relies on two ingredients—nucleic acids and peptides. Both ingredients can be generated by commonly used chemical synthesis processes and there are no chemical modifications required. In comparison, LNP-based products are the result of multiple ingredients and complex processes. STP705 benefits from an easy, controllable and scalable manufacturing process. In addition, the PNP delivery platform used for STP705 permits lyophilization of the finished dosage form and is stable at room temperature, with no cold chain storage requirement, thus reducing storage and distribution costs.

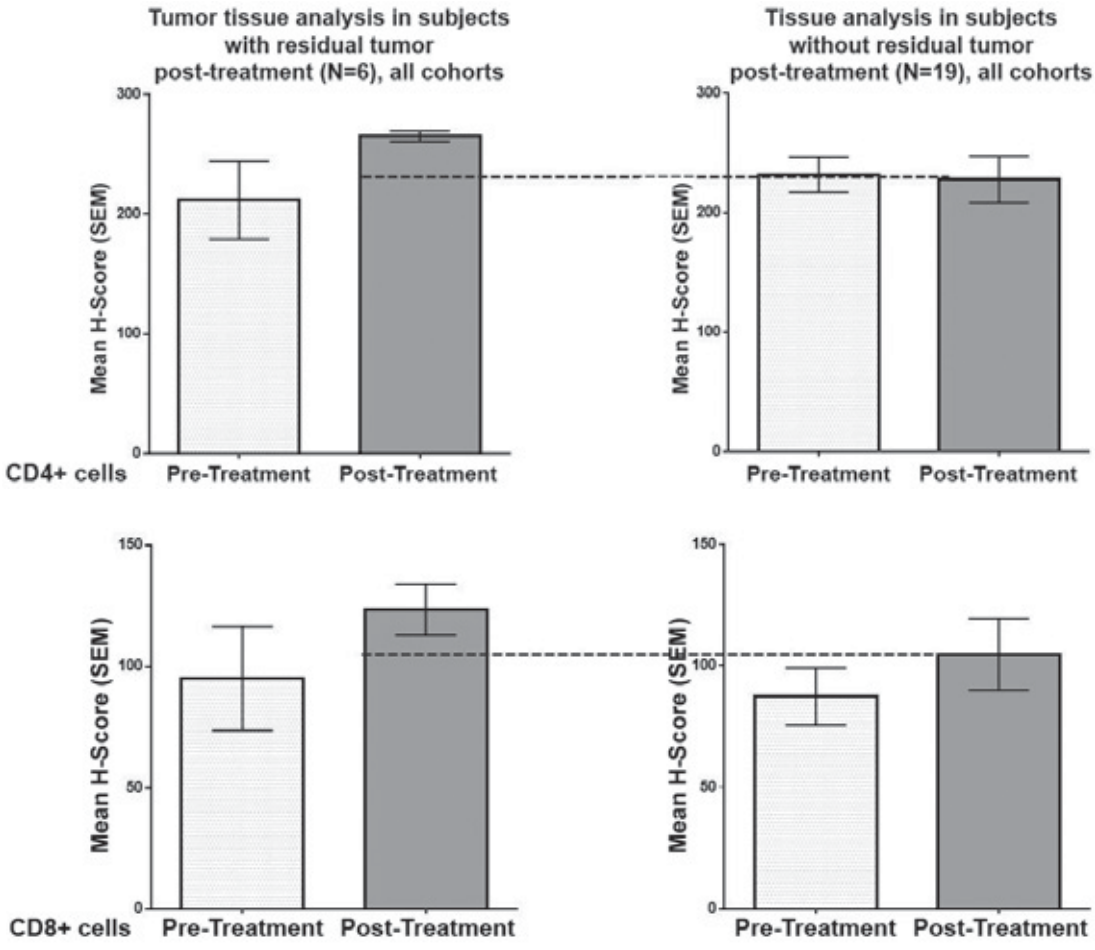
Potential for Combination Therapy with Immune Checkpoint Inhibitors

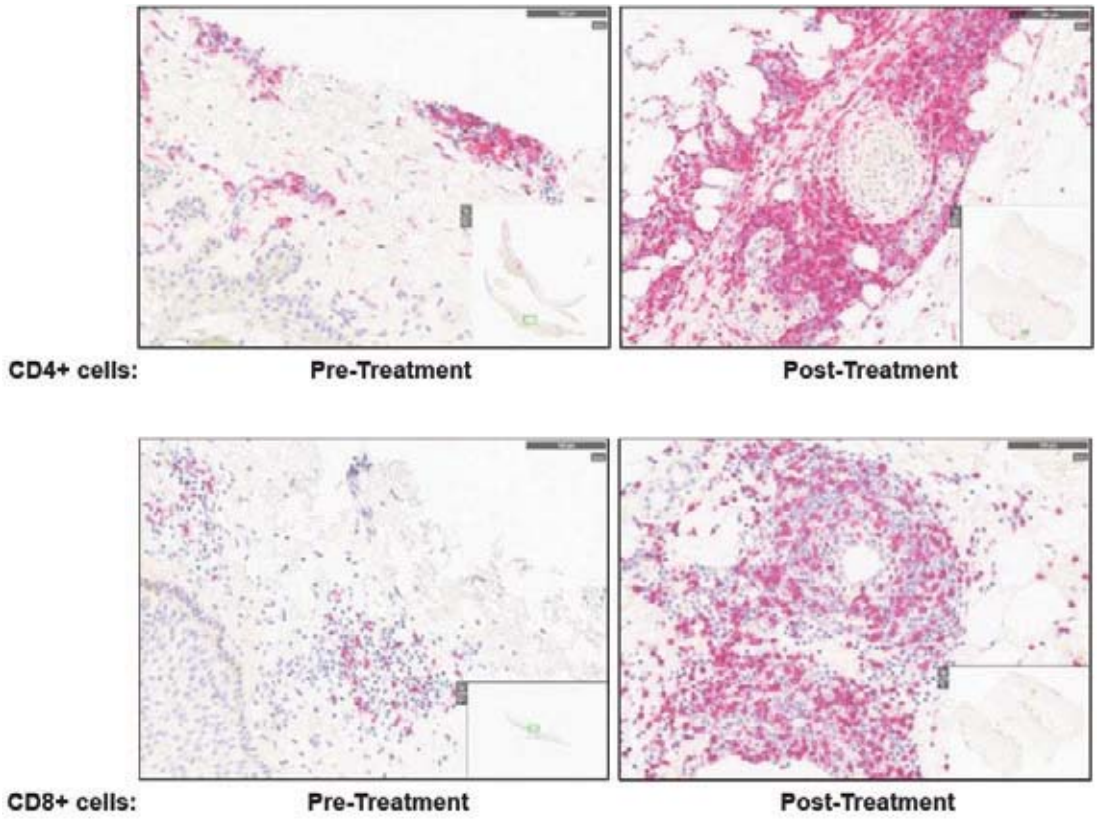
STP705 has significant potential to leverage the market for immune checkpoint inhibitors in cancer therapeutics through combination therapy. Immune checkpoint proteins function in normal tissue to prevent excessive immune response that could destroy healthy tissue, but

when elevated in the tumor microenvironment prevent T-cells from attacking cancer cells. Immune checkpoint inhibitor drugs have been approved to treat patients with a variety of cancer types. TGF-ß1 has also been validated in the literature as having an inhibitory effect on T-cell activity in tumors, making it a promising candidate for combination therapy with immune checkpoint inhibitor drugs as a means to strengthen T-cell response to tumor cells.

Administration of STP705 alone in tumors enhances killing of tumor cells by the immune system. T-cell infiltration of tumors is shown after administration of STP705 in our Phase IIa clinical trial for the treatment of isSCC. Histological analysis of CD4+ and CD8+ immune cell infiltration of tissues of patients with and without residual tumor after treatment with STP705 showed that patients with residual tumor post-treatment reported increased CD4+ and CD8+ immune cell infiltration compared to pre-treatment tissue or tissues without tumor.

Increased T-Cell Infiltration of the Tumor Microenvironment





Source: Company data

Increased T-cell infiltration activity by STP705 treatment strongly suggests that combination therapy with both STP705 and immune checkpoint inhibitors is likely to benefit from synergistic effects. The combined administration of different therapies that improve T-cell response via complementary pathways may improve T-cell response more than one therapy alone. In addition, the increased T-cell infiltration suggests that STP705 may cause tumors that are not initially responsive to immune checkpoint inhibitors to become sensitive, thus boosting the efficacy of immune checkpoint inhibitor therapies.

Summary of Clinical Trial Results

We are currently evaluating STP705 in a series of clinical trials in order to explore its potential to address several indications, in an attempt to address or underserved medical needs in several therapeutic areas. As of the Latest Practicable Date, we had evaluated the safety and efficacy profile of STP705 in the completed Phase I/II clinical trial for isSCC and are conducting five ongoing trials covering various indications.

The combined Phase I/II clinical trial for isSCC fulfilled the safety profile of conventional Phase I clinical trials, and thus on the basis of the completion of the combined Phase I/II clinical trial for isSCC, and the fact that FDA reviewed our clinical data and did not raise any objections to our plans to proceed with our Phase IIb clinical trial for isSCC, which

was initiated in May 2021, we have fulfilled the Phase I safety purpose, and the isSCC indication of STP705 fulfills the requirement of Core Product, under paragraph 3.3(b) of Guidance Letter 92-18.

Overview – Phase I/II Clinical Trial of STP705 for isSCC

We conducted a Phase I/II clinical trial for STP705 for the treatment of isSCC between March 2019 to October 2020 resulting in encouraging results in safety and efficacy, indicating promising commercial and therapeutic potential to address the sizable and growing market for NMSC therapeutics.

Trial Design

This Phase I/II clinical trial was designed to evaluate the safety, tolerability, and efficacy of various doses of STP705 administered as an intralesional injection in subjects with cutaneous squamous cell carcinoma in situ skin cancer (isSCC). In order to determine the optimal dose for treating isSCC in patients, this study was an open label, dose escalation trial using 10 μg, 20 μg, 30 μg, 60 μg, and 120 μg doses of STP705 for direct intralesional injection, given once a week for up to 6 weeks. The dose escalation was based on lack of adverse events in previous dosing cohorts. The primary endpoint for this study was the proportion of participants with histological clearance of treated isSCC lesion at the End of Treatment (EOT), where histological clearance was defined as the absence of detectable evidence of isSCC tumor cell nests as determined by blinded central pathology review. The secondary endpoints included (i) time to histological clearance of treated isSCC lesion over the 6-week treatment period and (ii) proportion of participants with complete clinical clearance of treated isSCC lesion based on investigator assessment at the End of Treatment (EOT). Histological clearance is a measure of Complete Response, which is defined by FDA as no detectable evidence of tumor. Complete Response is widely used as an endpoint for clinical trials for localized skin cancer rather than Objective Response Rate. Generally, FDA defines Objective Response Rate as the proportion of patients with tumor size reduction, or, more simply, as the sum of Complete Response and partial response. Partial response is not an acceptable endpoint for localized, low risk NMSC because it means cancer cells remain and thus is insufficient as a treatment option. Instead, the clinically acceptable outcome, is Complete Response, or clearance of the lesion. Complete clearance of low risk, localized NMSC is in line with market practice, rather than partial response, which is part of Objective Response Rate. Use of Complete Response by measurement of histological clearance was discussed with KOLs during preparation of the clinical trial protocol, and we determined to use this metric in the clinical trial protocol that was accepted by FDA.

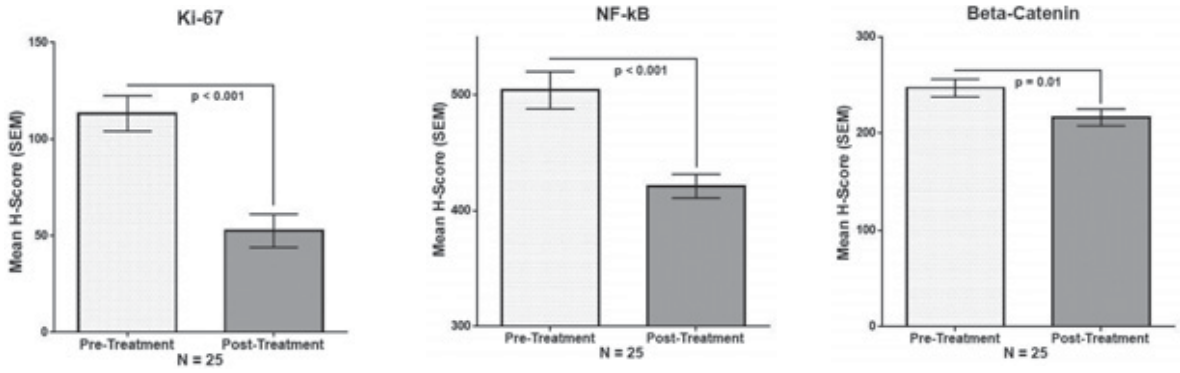
Trial Status

This trial was completed in October 2020 and we finalized the analysis in December 2020.

Efficacy Data

Efficacy results show that STP705 is effective in treating isSCC lesions. The majority of subjects in each dose group and the majority of subjects overall in this study (76%, 19/25) achieved histological clearance of lesion by EOT, which was the primary efficacy endpoint of this study. The recommended Phase IIb dosing levels achieved a 90% (9/10) histological clearance rate, demonstrated excellent safety profile with no drug related AE's or SAE's and demonstrated improvement in Local Skin Scores which suggests and improved cosmetic appearance from pre and post treatment. Histological analysis of treated lesions showed significant suppression of multiple cancer related markers. As shown in the figures below, Ki-67, NF-κB, and ß-Catenin all exhibited reduced expression.

Downregulation of Multiple Cancer Related Biomarkers



Source: Company data

Safety Data

Safety results from this study demonstrate that STP705 is a safe treatment option for isSCC patients. Incidence of treatment emergent adverse events (TEAEs) was low, with any TEAEs reported in only five (5) subjects (20%, 5/25). Only one (1) subject reported a moderate TEAE, with the remainder of reported TEAEs being mild. No TEAEs led to death, treatment discontinuation, or treatment interruption. No TEAEs were related to study treatment. No serious adverse events (SAEs) were reported. In addition, the injection itself was well-tolerated, with a majority of subjects experiencing no or low-grade local skin responses (LSRs). No clinically notable shifts in LSR occurred between pre- and post-dose at any visit, except for case of erythema in the 30 µg dose group that changed from Grade 3 at pre-dose T1 to Grade 4 at post-dose T1. At pre-dose T1, the average sum of skin response results were 3.6, 3.2, 3.6, 4.2, and 2.8 for the 10 µg, 20 µg, 30 µg, 60 µg, and 120 µg dose groups, respectively. By EOT, a decrease in the average sum of skin response results was observed in the 10 µg, 20 µg, 30 µg, and 60 µg dose groups. Safety parameters did not occur in a dose-dependent pattern, demonstrating that higher doses pose no more safety risk to subjects than lower doses of STP705.

Overview - Phase II Clinical Trial of STP705 for Basal Cell Carcinoma

We are conducting a Phase II clinical trial for the treatment of BCC, performing the dose administration for our first patient in January 2021. We obtained initial clinical trial data in September 2021.

Trial Design

This Phase II clinical trial is an open label, dose escalation study designed to evaluate the safety, tolerability and efficacy of various doses of STP705 administered as localized injection in patients with BCC. Initially, the clinical trial was designed to evaluate a total of 15 subjects (5 per cohort) assigned to receive treatment by intradermal injection of 30 µg, 60 µg, and 90 µg doses of STP705. A fourth cohort will be added to the study that will receive 120 µg doses of STP705. All subject will receive direct intralesional injection once a week for up to 6 weeks. The primary endpoint for the study is the proportion of participants with histological clearance of treated BCC lesion at the EOT, where histological clearance will be defined as the absence of detectable evidence of BCC tumor cell nests as determined by central pathology review. The secondary endpoints include determination of the safe and effective recommended dose of STP705 for the treatment of BCC and analysis of biomarkers common to the BCC formation pathway, including TGF-ß1 and COX-2.

Trial Status

This clinical trial is ongoing.

Efficacy Data

Initial efficacy results indicate dose responsive histological clearance of treated BCC lesions, as shown in the table below. We are currently awaiting completion of dosing in 4 subjects in the cohort receiving 90 µg doses and the entire cohort receiving 120 µg doses.

Dose Responsive Histological Clearance of BCC lesions

	Cohort A: 30 µg (N=5)	**Cohort B: 60 µg (N=5)**
Histological Clearance	1/5 20%	3/5 60%
Average Skin Response Scores		
Pre-treatment	3.2	2.8
Post-treatment	2.4	2.6

Source: Company data

Safety Data

Initial results from this clinical trial show no significant cutaneous skin reactions and no treatment related AEs or SAEs reported. The Skin Response Scores showed no local reaction and there were no dose limited toxicities noted to date.

Overview - Phase I/II Clinical Trial of STP705 for HTS

We initiated a Phase I/II clinical trial in the U.S. for the treatment of HTS in January 2017. The clinical data from the initial cohort of patients indicated that there were several injection site reactions, which is an expected AE in many local injection site protocols. As a result of these findings, we conferred with an independent data safety monitoring board (DSMB), an independent committee of expert clinicians that we convened out of an abundance of caution after observing that the first cohort of clinical trial subjects experienced adverse skin events. DSMBs are independent committees that are neither affiliated with any regulatory authority nor with the sponsor of a clinical trial. DSMBs are not a requirement for all clinical trials under FDA and any recommendations by a DSMB are not binding. The DSMB after reviewing the data, recommended that the trial proceed with a reduced dosage and decreased injection frequency. At the time, we made the strategic decision to divert funding to build out other programs with the intent of moving forward with the HTS program later when more funding was available. Our decision was based on the limited resources we had at that time, the inability to progress all programs simultaneously and the potential promise in our NMSC programs. We are filing the revised protocol for HTS in the U.S. in the second half of 2021, which will have reduced dosage and decreased injection frequency in line with the DSMB recommendations. These modifications are intended to confer the advantage of reduced injection site reactions experienced by patients. We expect to file an IND in China for a Phase II clinical trial for the treatment of HTS in the second half of 2022. While we initially commenced our HTS clinical trial program in the U.S. in 2017 because FDA permitted us to conduct a combined Phase I/II clinical trial rather than a Phase I clinical trial (as was then required by NMPA), we are electing to re-initiate our clinical trial program in HTS in China due to the larger pool of potential clinical trial subjects in China compared to the U.S.

Trial Design

This Phase I/II clinical trial was designed to evaluate the safety and efficacy of various doses of STP705 administered as intradermal injection in subjects with linear HTS. Initially, twenty-four subjects were planned to be enrolled in the study (8 per cohort) assigned to receive treatment by intradermal injection of 20, 30 or 40 μg/cm^2/day. Each subject was planned to receive both active (STP705) and control (placebo) treatment twice per week for a total of four weeks. The total length of linear HTS was divided equally for treatment with STP705 and placebo. STP705 and placebo were injected intradermal every 1 cm length on the HTS. The primary endpoint for the study is the differences among the three dosage groups in the appearance of the scar from baseline evaluated with the use of validated scar assessment tools. The secondary endpoints include changes in appearance of the scar from baseline evaluated with the use of validated scar assessment tools.

Trial Status

The first cohort of eight subjects were enrolled and given injections (20 μg/cm^2/day) twice per week for four weeks. The clinical data from the initial cohort of patients indicated that there were several injection site reactions, which is an expected AE in many local injection site protocols. An independent data safety monitoring board recommended to us in June 2017 to initiate a modified clinical trial protocol increasing the interval between injections and/or reducing the dose of STP705 to mitigate injection site reactions. As a result of these findings, the initial clinical protocol did not proceed further pending future resource allocation for re-initiation.

Safety Data

There were no death, SAEs or dose limiting toxicities reported in this clinical trial. All subject experience AEs, the majority of which were associated with injection site reactions (pain, tenderness, swelling, induration and hemorrhage, etc). The injection site reactions were typically mild or moderate in severity and did not require further action. There were no clinically significant findings reported in physical examination or electrocardiogram results.

Clinical Development Plan

We have initiated Phase IIb clinical trials for STP705 for isSCC in the U.S. in May 2021. We filed our IND in China for a Phase IIb clinical trial for isSCC that would be part of a global multicenter clinical trials. We have initiated Phase II clinical trials for BCC in December 2020 and Phase I/II clinical trials for keloid scar recurrence post-keloidectomy in April 2021 in the U.S. We initiated Phase I/II clinical trials for HTS in the U.S. and expect to file an IND for a Phase II clinical trial in China in the second half of 2022. We intend to initiate the clinical trials in China led by a Chinese principal investigator because the demand for treatment of HTS is stronger in China than the U.S. We plan to submit the new clinical trial protocol to FDA in the second half of 2021 and the clinical trial in China will be a global study site. We have also initiated Phase I clinical trials for STP705 in the U.S. in March 2021 for CCA, HCC or liver metastases in patients with advanced/ metastatic or surgically unresectable solid tumors who are refractory to standard therapy and expect to file an IND in China as part of global multicenter clinical trials.

Our Phase IIb clinical trials for STP705 for isSCC will further evaluate the two most efficacious dosing regimens identified in our Phase IIa clinical trial in a randomized, double-blind, placebo-controlled study in up to 100 adult patients with isSCC. The primary endpoint for the trial is proportion of participants with histological clearance of treated isSCC lesion at the end of treatment. Histological clearance will be defined as the absence of detectable evidence of isSCC tumor cell nests as determined by central pathology review. We performed dose administration for our first patient in the U.S. in June 2021. We anticipate an interim data readout in the first half of 2022.

After completion of the Phase IIb trial for STP705 for isSCC, subject to continued efficacy and safety results as seen in our previous isSCC study, we anticipate participating in a meeting with FDA where we will receive FDA guidance for our further clinical development plan, including but not limited to such things as FDA's expectations for efficacy endpoints required for an NDA application and subsequent approval, as well as the number and size of Phase III trials required for NDA registration for the use of STP705 for the treatment of isSCC.

Our Phase I/II clinical trial for STP705 for keloid scar prevention will evaluate the safety and efficacy of various doses of STP705 when injected intradermally into a keloid excision site to prevent the recurrence of keloids in adult patients in a randomized, double-blind, multiple-arm, controlled study in 50 patients. The primary endpoint of this trial is to measure the rate of recurrence in patients who have undergone keloidectomy surgery alone (receiving placebo) versus surgery and administration of STP705 at three months, six months, and 12 months post-surgical excision. We performed dose administration for our first patient in the U.S. in May 2021. We expect to report initial clinical data in the first half of 2022.

Our Phase II clinical trial for STP705 for BCC will evaluate the safety and efficacy of intralesional injection in adult patients with cutaneous BCC confirmed with biopsy samples in an open-label, dose escalation study of at least 15 patients. Participants will receive injections of STP705 once a week for up to six weeks. The primary endpoint for the study is to evaluate patients for complete histological clearance of the tumor cells within the treated BCC lesion with secondary endpoints, evaluating subjects for investigational product treatment related adverse events, as well as serious adverse events, and cutaneous skin reactions. We performed dose administration for our first patient in the U.S. in January 2021.

Our Phase I clinical trial for STP705 in liver cancer will evaluate the safety, tolerability, pharmacokinetics, and anti-tumor activity of intratumoral administration of STP705 in a "basket study" of patients suffering from CCA, HCC or liver metastases from other cancers for patients with advanced/metastatic or surgically unresectable solid tumors who are refractory to standard therapy. The subjects in this study have previously failed multiple rounds of standard of care therapy including novel oncology drugs and traditional chemotherapies and thus represent a very resistant class of tumor. The study is an open-label, dose escalation study of up to 50 patients. In order to determine the maximum tolerated dose (MTD), up to 30 patients (6 per cohort) will be enrolled in the dose escalation phase of the trial, during which cohorts will be assigned to receive doses of 20 μg, 40 μg, 80 μg, 160 μg, and 320 μg doses of STP705 administered via intra-tumoral injection on days 1, 8 and 15 of a 28 day cycle. Once the MTD is achieved, up to 20 more subjects will be enrolled to confirm safety and explore anti-tumor activities. The primary endpoints are (i) to determine the MTD of STP705 when administered via intra-tumor injection and (ii) to establish the dose of STP705 recommended for future Phase II clinical trials when administered via intra-tumor injection. The secondary endpoints include determination of the pharmacokinetics (PK) of STP705, evaluation of tumor infiltrating lymphocytes at the site of STP705 administration, and observation of preliminary antitumor activity of STP705 at the site of administration and at other sites of disease.

We performed dose administration for our first patient in our liver cancer trial in June 2021. If subjects exhibit stable or improvement in tumor they will be treated with subsequent treatment cycles. If subjects exhibit advancing disease, they will be discontinued from study. We have completed cycle 4 for the first subject in our 20 μg cohort, and this subject exhibits stable disease in the treated tumor and will continue to cycle 5. We have completed cycle 3 for the first subject in our 40 μg cohort; this subject has exhibited stable disease in the treated tumor, but has developed a new lesion outside the liver and thus will be discontinued from the study. These subjects suffer from HCC and metastatic colon cancer, respectively. There have been no treatment related AEs or SAEs. We expect to complete the dose escalation phase in the first half of 2022.

We are developing combination therapies with STP705 and immune checkpoint therapeutics for liver cancer where the proposed therapy would involve separate administration of STP705 and the immune checkpoint inhibitor pharmaceutical product. We are currently exploring the efficacy of combination therapy with STP705 and anti-PD-L1 targeted therapies in preclinical studies. We are collaborating with Innovent to conduct preclinical studies in the U.S. directed to combination therapy using STP705 and sintilimab, a novel anti-PD-1 monoclonal antibody approved by the NMPA for use in treatment of advanced cancers, such as NSCLC. We are also collaborating with Shanghai Junshi to conduct preclinical studies in the U.S. directed to combination therapy using STP705 and Shanghai Junshi's novel anti-PD-1 monoclonal antibody approved by the NMPA for use in treatment in advanced melanoma, squamous cell carcinoma and other indications. The clinical trials for STP705 and each immune checkpoint inhibitor product may require separate IND applications. We anticipate that whether any combination therapy using STP705 is regulated separately from STP705 will be determined on a case by case basis by U.S. FDA.

The table below sets forth the details of our clinical development plan for STP705.

Indication	Clinical Trial Identifier (FDA)	Clinical Stage	Location and Competent Authorities
Cutaneous squamous cell carcinoma *in situ*	NCT04844983	II (US/CN)	US/FDA China/NMPA*
Basal cell carcinoma	NCT04669808	II (US)	US/FDA
Keloid scar recurrence post-keloidectomy	NCT04844840	II (US)	US/FDA
Hypertrophic scarring	NCT02956317	II (US/CN)	US/FDA China/NMPA**
Cholangiocarcinoma, hepatocellular carcinoma or liver metastases	NCT04676633	I (US/CN)	US/FDA China/NMPA**

* IND not yet approved
** IND not yet filed

Licenses, Rights and Obligations

We have the global rights to develop and commercialize STP705.

Material Communication with Competent Authorities

As of the Latest Practicable Date, we were not aware of any legal claims or proceedings that may have an adverse effect on our development for STP705. As of the Latest Practicable Date, we had received no objections to our clinical development plans with respect to the regulatory review or approval process of STP705 and no material adverse change had occurred with respect to the regulatory review or approval process of STP705.

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 STP705 SUCCESSFULLY.

CLINICAL DRUG CANDIDATE

STP707

STP707 is a systemic formulation of STP705. STP707 is a dual TGF-ß1/COX-2 inhibitor that has been designed for systemic administration by employing our PNP in a formulation modified from that used for STP705. We are developing STP707 for the treatment of solid tumors including but not limited to liver and lung cancers as well as for liver and lung fibrosis. We initiated Phase I clinical trials for solid tumors in November 2021. As described under "– Our Drug Candidates – STP705 – Mechanism of Action", dual knockdown of TGF-ß1/COX-2 has significant anti-tumor and anti-fibrotic effects.

Competitive Advantages

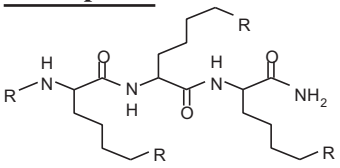
Based on our preclinical data, we believe that STP707 has potential competitive advantages as compared to the standard of care. STP707 is a systemic formulation of the same siRNA triggers contained in STP705 against TGF-ß1 and COX-2, and thus shares with STP705 most of the same competitive advantages, including the capability to achieve the synergistic effects of simultaneously silencing both genes, the potential lower cost of manufacture and the potential leveraging of the market for immune checkpoint inhibitors through combination therapy. Additionally, STP707 is formulated for systemic administration.

Formulated for Systemic Administration

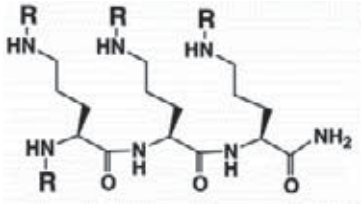
Both STP705 and STP707 are formulated using our PNP delivery platform; however, the polypeptide used in STP707 (histidine-lysine-histidine polypeptide; HKP+H) is distinguished from the polypeptide (HKP; histidine-lysine polypeptide) used in STP705 by an additional histidine. Both polypeptides comprise a lysine core with four branches that contain multiple repeats of histidines and lysines, differentiated by the additional histidine in the systemic formulation for STP707, as shown in the table below. In addition, the ratio of siRNA to peptide differs between the formulations. The additional histidine residue in the STP707

formulation results in an increased rate of endosomal release and thus more rapid release of the siRNA oligonucleotides into the cytoplasm of the target cells, which is preferred for systemic administration, rather than the more sustained release that is preferred for local administration.

HK Peptides



R=KHHHKHHHKHHHKHHHK,
H=histidine; K=lysine



R=KHHHKHHHKHHHKHHHK

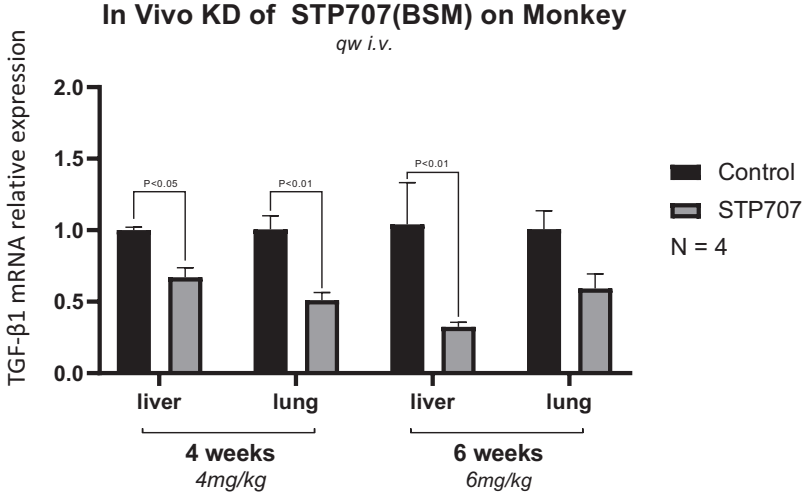
Applications

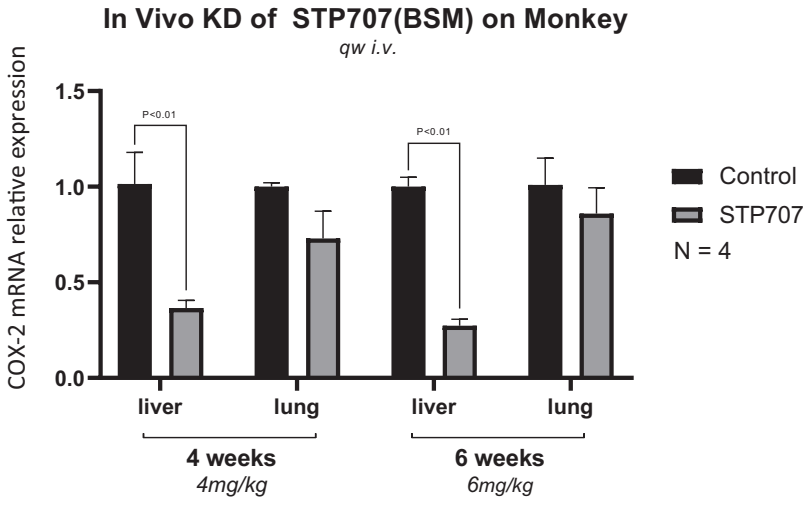
H3K4b, branched, is useful for local delivery of siRNA and is utilized in STP705

H3K(+H)4b, branched, is useful for systemic delivery of siRNA and mRNA and is utilized in STP707

Our preclinical studies demonstrated that intravenous administration of STP707 results in uptake in the multiple cell types of the liver, as well as spleen, lung and kidney tissues. Our GLP study in non-human primates demonstrated that intravenous administration of STP707 achieved TGF-ß1 and COX-2 knockdown in both liver and lung, as shown in the figure below, providing evidence of a strong potential to achieve therapeutic effect in lung tissue.

Silencing of TGF-ß1 and COX-2 in both Liver and Lung after Administration of STP707 in Non-human Primates





Source: Company data

In addition, unlike GalNAc mediated siRNA platforms which are limited to targeting of liver hepatocytes, our preclinical studies using labeled siRNAs in a liver fibrosis mouse model showed that after intravenous administration of labeled-siRNA using our PNP delivery platform, Kupffer cells and liver sinusoidal endothelial cells as well as hepatocytes exhibited high percentages of uptake of the PNP-siRNA.

We believe that the systemic formulation for STP707 will make STP707 broadly useful for treating a broad range of oncology and fibrosis indications via the reduction of the profibrotic and proinflammatory cytokines TGF-ß1 and COX-2.

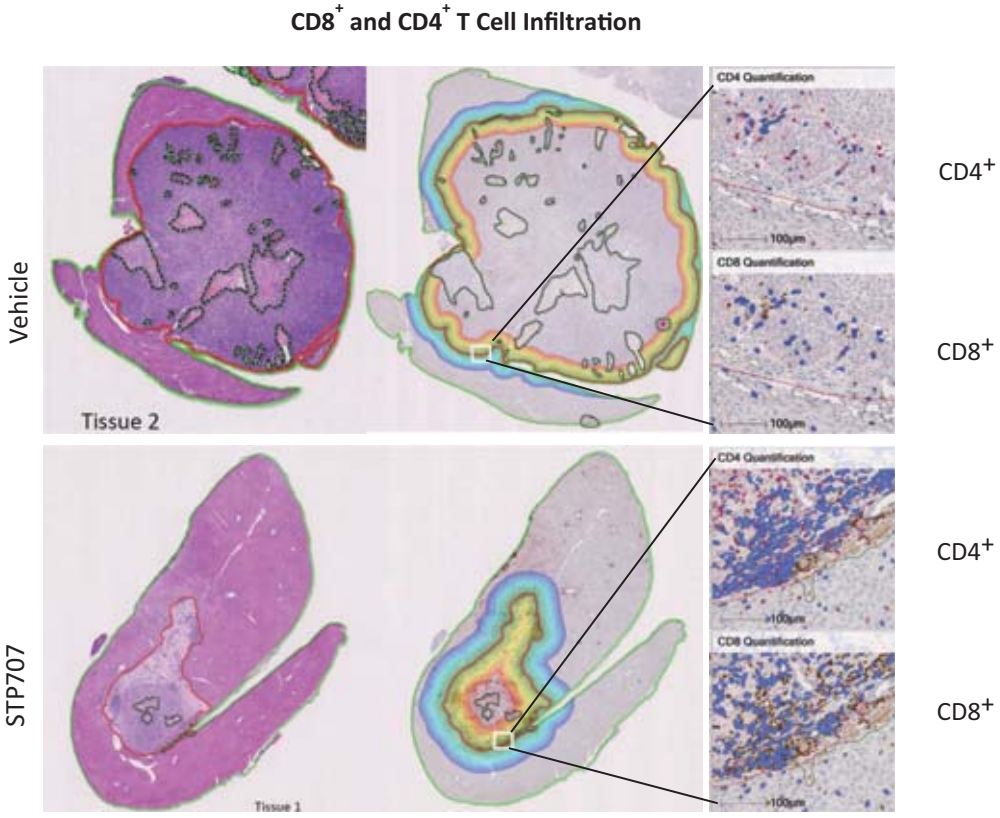
Favorable Safety Profile

We recently completed a GLP preclinical non-human primate study evaluating safety of STP707 which demonstrated a favorable safety profile in all treatment groups. The long term toxicity study involved 4-week repeated intravenous dosing in cynomolgus monkeys: 0.5 mg/kg/week (N=10), 1.5mg/kg/week (N=10), 5.0 mg/kg/week (N=10), and vehicle control group (N=10). We also completed a GLP safety pharmacology study administering a single does of 0.25 mg/kg (N=8), 0.75 mg/kg (N=8), 2.5 mg/kg (N=8) and vehicle control group (N+8). No clinically significant drug-related adverse toxicology findings were identified in the treatment groups, including no significant abnormalities in pathology, microscopic histology examinations, clinical observations, electrocardiogram, hematology, coagulation, clinical chemistry and T-lymphocyte subsets. The safety pharmacology study found no impairments of cardiovascular and respiratory functions in monkeys receiving an injected dose of STP707 of approximately 30 times the proposed Human Equivalent Starting dose for human clinical trial doses. We also completed a 4-week, repeated dose study of 5 mg/kg/week, with administration twice per week and, as of the Latest Practicable Date, are in the process of preparing the study report of a 13-week, repeated dose study of 5 mg/kg/week, with administration twice per week.

Potential for Combination Therapy with Immune Checkpoint Inhibitors

As describe above under "– Our Drug Candidates – STP705 – Competitive Advantage – Potential for Combination Therapy with Immune Checkpoint Inhibitors", STP705 has significant potential to leverage the market for immune checkpoint inhibitor drugs, which enhance T-cell responsiveness in tumors, through combination therapy based on results showing that silencing of TGF-ß1 and COX-2 promoted T-cell infiltration of tumors treated with STP705. STP707, which also targets TGF-ß1 and COX-2, is also a promising candidate for combination therapy with immune checkpoint inhibitor drugs. In an orthotopic HCC mouse model, in which STP707 was administered (1 mg/kg for 3 doses), histological analysis of the liver showed that administration of STP707 dramatically reduced tumor volume and that the penetration of T-cells (CD4+ and CD8+) around the tumor interface with normal tissue was much greater compared to the control comprising non-silencing siRNA in the same PNP delivery platform vehicle, as shown in the figure below. These results suggest that administration of STP707 improved T-cell penetration in and around the tumor microenvironment through the silencing of TGF-ß1 and COX-2, further supporting the potential for combination therapy to both block interaction with PD1 and maintain the action of T-cells for anti-tumor activity.

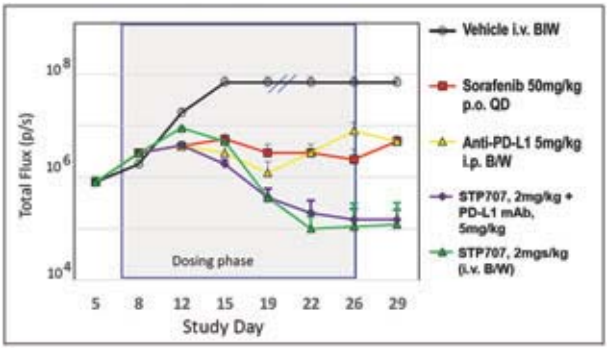
Improved T-Cell Infiltration of the Tumor Microenvironment after Administration of STP707



Source: Company data

We evaluated combination therapy with STP707 and anti-PD-L1 monoclonal antibody in a preclinical study using the orthotopic HCC mouse model in which STP707 was administered intravenously either alone (2 mg/kg) or in combination with anti-PD-L1 monoclonal antibody (5 mg/kg). The figure below shows a tumor growth curve measuring tumor associated bioluminescence and demonstrates that the combination of STP707 and anti-PD-L1 antibody was effective in eradicating tumors with no regrowth after 28 days.

Tumor Growth Curve

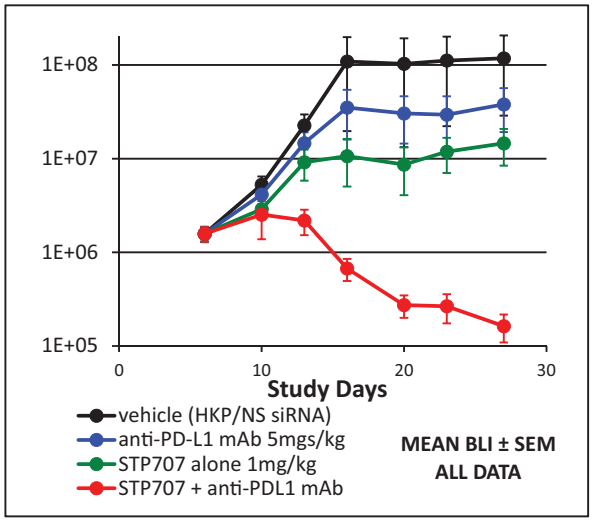


	p-value as completed control			
	Sorafenib	**Anti-PD-L1**	**STP707 + Anti-PD-L1**	**STP707 (2mgs/Kg)**
Day 15	0.0254	0.0228	0.022	0.0262
Day 19	0.022	0.016	0.0076	0.0076
Day 22	0.022	0.022	0.0082	0.007
Day 26	0.021	0.035	0.008	0.0073
Day 29	0.03	0.03	0.0073	0.0071

Source: Company data

In further studies in the same mouse model, administration of STP707 at a lower dose (1 mg/kg) in combination with the anti-PD-L1 monoclonal antibody showed more potent activity and synergistic activity than either STP707 or the anti-PD-L1 monoclonal antibody alone, as shown in the figure below. These data together provide support for the strong potential for combination therapy based on synergistic activity and enhancement of the efficacy of immune checkpoint inhibitors.

Tumor Growth Curve



Source: Company data

p-value of STP707 + anti-PD-L1 relative to Control	**Control (vehicle treated)**
Day 12	0.035
Day 15	0.02
Day 19	0.006
Day 22	0.006
Day 26	0.003

Clinical Development Plan

We initiated a Phase I clinical trial in a basket trial for solid tumors in November 2021 in the U.S. The basket study will allow us to study more than one tumor type and, apart from aiding in evaluation of safety and dosing, we will be able to gather valuable efficacy data in various tumor types that will better guide our future clinical development. We plan to submit an IND to NMPA for a Phase I clinical trial in China for HCC as part of a global study. For our submission in China we will develop a protocol for China sites that is limited to HCC. HCC is prevalent in China and of great interest to investigators in China, although the data will be valuable for integration with our U.S. clinical trial data as development proceeds. The protocol will be for a Phase I clinical trial in patients in China, rather than healthy volunteers, with recruitment conducted in parallel to our U.S. study. We also filed an IND for PSC, a rare form of liver fibrosis, in November 2021 in the U.S., and plan to file an IND for PSC in China at a later date. Depending on the response we see in our dose escalation Phase I clinical trial as well as efficacy data obtained in preclinical studies in various tumor models, we could potentially follow the Phase I clinical trial with Phase II clinical trials of STP707 for liver cancer, non-small cell lung cancer, metastatic cutaneous squamous cell carcinoma, and potentially other solid tumors in the second half of 2022 in the U.S. We also expect to initiate clinical trials for combination therapy with STP707 and other oncology therapeutics in promising indications.

Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP707.

PRECLINICAL DRUG CANDIDATES

We are developing a number of IND-enabling and preclinical research and development product candidates in our rich pipeline. As of the Latest Practicable Date, we were evaluating seven of our innovative product candidates in IND-enabling preclinical studies and are evaluating more than seven of our product candidates in earlier stage studies.

Our preclinical drug candidates that we are developing for oncology indications include:

STP355

STP355 comprises siRNA simultaneously targeting TGF-ß1 and VEGFR2, a target gene well-validated for its involvement in tumor angiogenesis and metastasis, formulated using our PNP delivery platform for systemic administration. We are developing STP355 for the treatment of multiple cancer types, including breast cancer, melanoma and colorectal cancer. We plan to file an IND for STP355 in the U.S. in the first half of 2022.

Mechanism of Action

Angiogenesis is a normal physiological process that is primarily, although not exclusively, regulated by the Vascular Endothelial-derived Growth Factor (VEGF) family. The main target cell type for VEGF proteins is the endothelial cell where VEGF functions through binding with its receptors on the cell membrane. After binding to VEGFR2, VEGF triggers a series of signal transducing pathways stimulating endothelial cell proliferation, migration and new blood vessel formation.

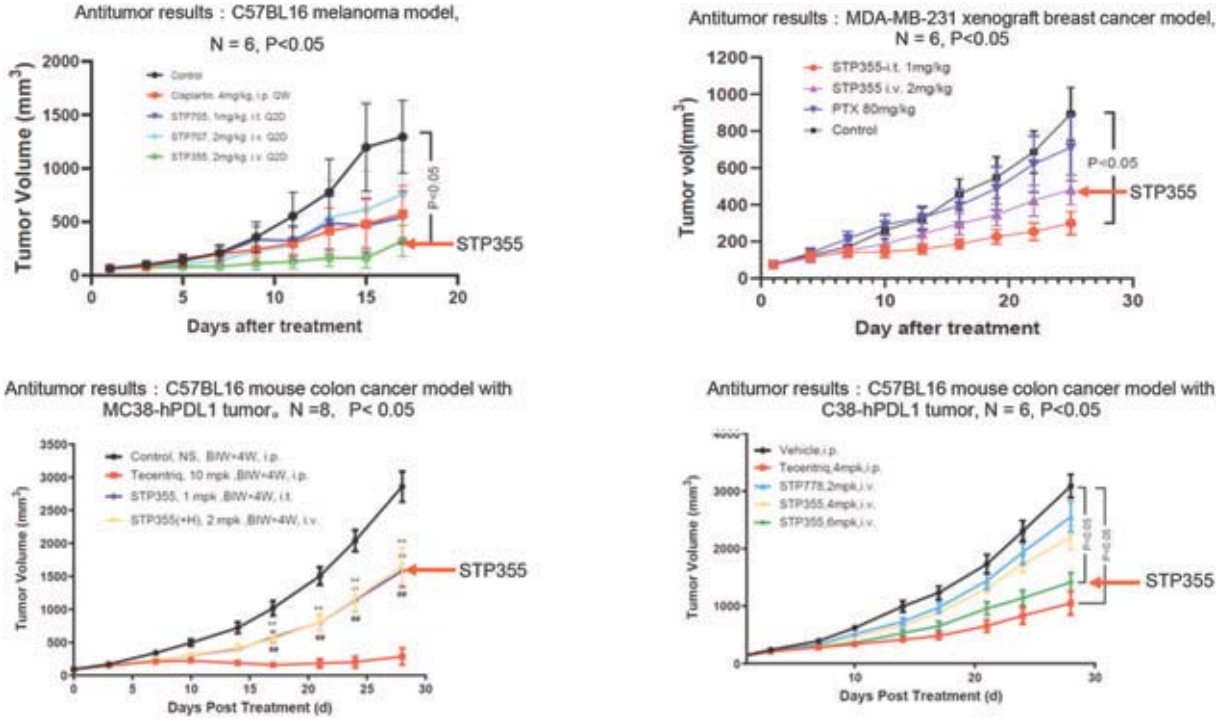
VEGF overexpression is found in most cancers. When overexpressed, VEGF causes aberrant neo-angiogenesis (i.e., growth of new blood vessels) within both the tumor and surrounding tissues to meet the nutrition demand for uncontrolled proliferation of tumors. Studies of VEGF functionality have led to therapeutic strategies targeting the VEGF/VEGFR signaling pathway, including the monoclonal antibody Avastin (Bevacizumab), which has been widely applied in many different cancer therapies. Preclinical studies have consistently shown additive or synergistic benefits from combinations of VEGF inhibitors with cytotoxic agents. A potential combinational partner target is TGF-ß1, described in " – Our Drug Candidates – STP705 – Mechanism of Action".

Competitive Advantages

We believe that STP355 has potential competitive advantages as compared to the standard of care. We expect that targeting of both TGF-ß1 and VEGFR2 in a single therapeutic will provide a more potent anti-tumor effect than inhibition of the VEGF/VEGFR2 pathway alone due to both combinatorial effects of targeting multiple points in interconnecting pathways, as well as hampering the upregulation of compensatory pathways. In addition, we expect that incorporating siRNA against both TGF-ß1 and VEGFR2 in the same drug product presents advantages over contemporaneous administration of two separate modalities targeting TGF-ß1 and the VEGF/VEGFR2 pathway because it ensures that both are simultaneously targeted in the same cells.

Our preclinical results in multiple mouse tumor models demonstrate the potential for STP355 as an antitumor agent for multiple cancer types.

STP355 Preclinical Results in Multiple Mouse (Xenograft) Tumor Models



Source: Company data

Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP355.

STP369

STP369 comprises siRNAs targeting BCL-xL and MCL-1, which are both validated tumorigenesis-associated genes, and formulated with our PNP delivery platform for intravenous or intra-tumoral injection administration. We are developing STP369 for the treatment of head and neck cancer and bladder cancer. We are also exploring use of STP369 in combination therapy with platinum-based chemotherapy (cisplatin) due to its widespread use in treating patients to evaluate the potential for STP369 to improve the efficacy of cisplatin or replace its use. We anticipate filing an IND in the U.S. in the second half of 2022.

Mechanism of Action

Certain proteins in the BCL-2 family, which include BCL-2, BCL-xL, BCL-w, BFL-1/A1 and MCL-1, function to counteract the pro-apoptotic effects of other proteins in the BCL-2

family such as BAX and BAK. Following various stress signals, pro-apoptotic family members either neutralize the anti-apoptotic proteins or directly activate effector proteins BAX and BAK, which will eventually lead to apoptosis in normal cells. Cancer cells can evade apoptosis triggered by drug treatment by overexpressing the BCL-2 antiapoptotic proteins like BCL-xL and MCL-1. BCL-xL and MCL-1 have been validated in the public literature as promising targets for cancer therapeutics using small molecule inhibitors, as combining small molecule inhibitors against the two targets has shown therapeutic benefit in a number of cancer types, including cervical cancer, lung squamous cell carcinomas and head and neck cancer and combining anti- BCL-xL and anti-MCL-1 siRNAs for anti-tumor activity with respect to ovarian tumors and pancreatic tumors.

Competitive Advantages

Based on our preclinical data, we believe that STP369 has two potential advantages compared to standard of care: (1) strong potential efficacy in antitumor effects and (2) significant combination potential with validated chemotherapy drugs, such as cisplatin. Our preclinical studies have demonstrated that simultaneous silencing of BCL-xL and MCL-1 by STP369 inhibits tumor growth in other cancer types, including bladder cancer and head and neck cancer xenograft studies. We also assessed the anti-tumor activity of STP369 in combination with cisplatin, a first line cancer therapeutic for both bladder cancer and head and neck cancer, compared to cisplatin alone. In this study, STP369 in combination with cisplatin displayed dramatic improvement in the response of cancer cells to cisplatin.

Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP369.

STP779

STP779 comprises siRNA targeting TGF-ß1 and SULF-2, another validated tumorigenesis-associated gene, formulated with our PNP delivery platform for systemic administration. We are developing STP779 for the treatment of liver cancer, lung cancer and pancreatic cancer. We maintain the global rights to develop and commercialize STP779.

STP302

STP302 comprises miR-150 miRNA formulated with our PNP delivery platform for intravenous or intra-tumoral injection administration. We are developing STP302 for treatment of colorectal carcinoma alone and in a combination therapy with gemcitabine. We maintain the global rights to develop and commercialize STP302.

STP902

STP902 comprises siRNA targeting RAF-1, a validated tumorigenesis-associated gene, formulated with our PNP delivery platform for intravenous and intra-tumoral injection

administration. We are developing STP902 for the treatment of breast cancer. We maintain the global rights to develop and commercialize STP902.

Our preclinical candidates that we are developing for medical aesthetics include:

STP705

As described under "– Our Drug Candidates – STP705", STP705 is a dual TGF-ß1/COX-2 inhibitor that has been formulated using our PNP delivery platform for local administration. In addition to our more advanced development programs for oncology and fibrosis indications, we are also developing STP705 as a localized treatment for fat sculpting.

Mechanism of Action

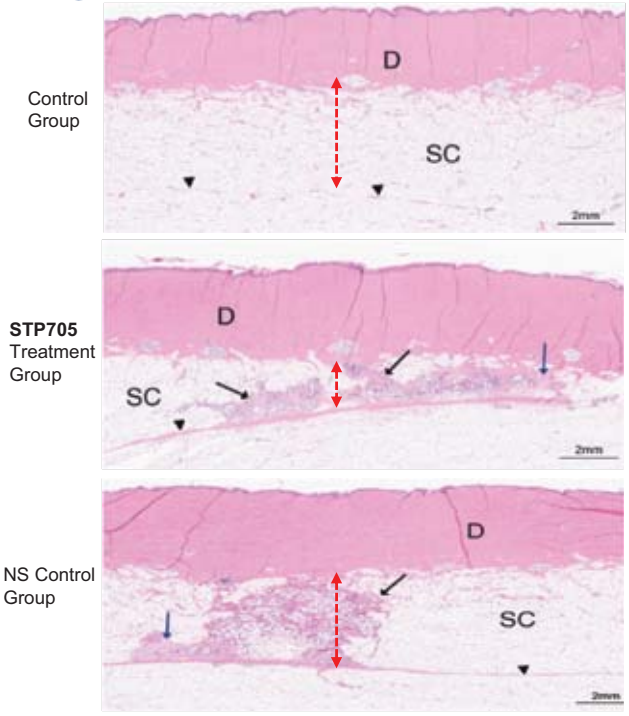
Based on our clinical studies for STP705, we noted that one of the biological effects of local administration of STP705 is localized fat reduction.

Competitive Advantages

We believe that STP705 has potential advantages compared to the available medical aesthetic treatments for fat sculpting. Our preclinical results in a Yucatan minipig model demonstrate reduction in subcutaneous adipose tissue. The figure below (A) shows reduction in subcutaneous fat in a Yucatan minipig model compared to predose biopsy 56 days after subcutaneous administration of STP705. Non-targeting siRNA (NS) in the same PNP delivery platform formulation was used as a control. At day 56, findings associated with the administration of either test article were granulomatous inflammation with fat necrosis in the subcutis and fibrosis/fibroplasia in the subcutis. Other findings, including dermal inflammatory cell infiltration and serocellular crusts on the epidermal surface, were sporadically present and represent the variability in typical background cellular infiltrates in the skin of pigs. The figure below (B) shows quantified measurements of the subcuticular adipose layers of different groups. The STP705-treated group showed significant reduction of the subcuticular adipose. Decreased subcuticular thickness (up to the superficial fascia) was reduced in test article-treated samples compared to untreated or pre-dosing samples. This reduced subcuticular thickness corresponded with the presence of inflammation and fibroplasia in this zone. STP705 was also compared to treatment with Kybella (deoxycholic acid), an FDA-approved drug indicated to improve the appearance and profile of moderate to severe fullness associated with submental fat, also called double chin. Using single dose of STP705 at day 0 with either (120µg) or (200µg), resulted in better subcuticular thickness at day 56 compared with double doses of Kybella at day 0 and day 30.

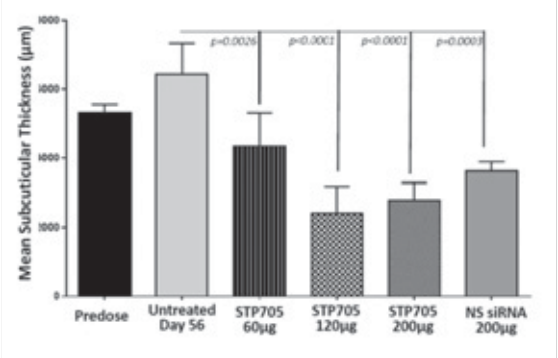
STP705 Preclinical Results Demonstrate Efficacy in Fat Sculpting

A Yucatan Minipig Model Histology Analysis

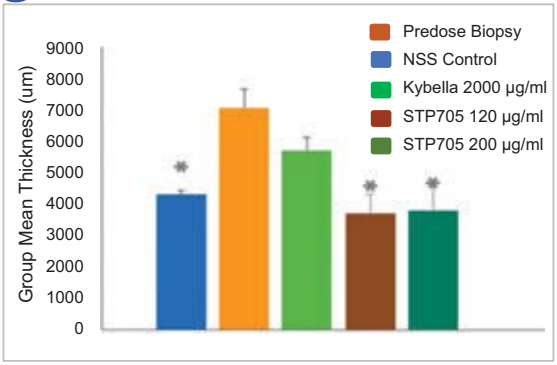


Note: D: Dermis, SC: Subcuticular Adipose

B First Fat Reduction POC Study Results (d56)



C STP705 and Kybella Comparison at Day 56



Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP705.

Our preclinical drug candidates that we are developing for antiviral indications include:

STP702

STP702 comprises siRNA simultaneously targeting the M1 and PA influenza viral gene sequences formulated with our PNP delivery platform. We are developing STP702 for treatment of influenza. We anticipate filing an IND in the U.S. in the second half of 2022.

Mechanism of Action

Influenza A virus transmission causes respiratory infections that can be debilitating and may lead to death. Newly emerging strains, such as H5N1 and H7N9, have exhibited higher mortality rates, while vaccine development response has been very slow. The rapid emergence of a novel strain that may not respond well to existing therapeutics could result in a significant death toll before the development and distribution of a vaccine or other prophylactic or therapeutic. Therapeutic strategies that may prevent and/or reduce the emergence of resistant variants and may increase the breadth of efficacy across multiple strains include: (1) targeting regions of essential viral genes that are highly conserved, and/or (2) targeting two or more viral genes simultaneously. While single siRNAs against specific influenza genes have been shown to inhibit the virus, we believe that combining siRNAs against two of the most conserved segments of the influenza genome will increase coverage across multiple influenza strains. Using a bioinformatics approach using viral genes from the Flu Database, siRNA sequences designed against M1, NP and PA gene segments in select pairwise combinations were predicted to provide coverage against >95% of influenza strains demonstrated to infect humans, including the majority of strains of H1N1, H3N2, H5N1 and H7N9.

Competitive Advantages

In vitro testing of combinations of two siRNAs against these viral target genes identified synergism with increased potency of two siRNAs against multiple flu strains. Our preclinical results show that combining two siRNAs (targeting M1 and PA) provided a potent therapeutic able to significantly reduce viral titer in three strains of the virus (H1N1, H3N2 and H5N2). Nanoparticle-mediated delivery of this siRNA pair in vivo (10mg/kg) demonstrated antiviral activity equivalent to Tamiflu (25mg/kg). That STP702 was more potent than Tamiflu suggests that STP702 may have better efficacy and coverage than neuraminidase inhibitors that have proven to be ineffective against the latest avian flu strains (H5N1 and H7N9).

Nanoparticle delivery of siRNA combinations may provide a rapid therapeutic response against newly emergent strains of Influenza and targeting multiple segments within the virus improves coverage across strains and, also, improves efficacy within a strain by reducing the ability of the virus to escape therapeutic pressure.

Licenses, Rights and Obligations

We have out-licensed development and commercialization rights in mainland China, Hong Kong, Macau and Taiwan to Walvax, and retain development and commercialization rights in the rest of the world. See "– Collaboration and Licensing Arrangements – Licensing Arrangement with Walvax."

STP908

STP908 comprises siRNA targeting the SARS-CoV-2 ORF1Ab and N-protein genes formulated with our PNP delivery platform. We are developing STP908 for the treatment of COVID-19 and other diseases caused by SARS coronaviruses for intravenous and inhalation administration. STP908 is directed to providing prophylactic options for uninfected people as well as therapeutic options for patients to both prevent hospitalization or treat hospitalized patients. We have previously collaborated with researchers at the Boston University National Emerging Infectious Disease Laboratory on preclinical research relating to STP908. We anticipate filing an IND in the U.S. in the second half of 2022.

Mechanism of Action

Silencing the ORF1Ab and N-protein genes of SARS-CoV-2 inhibits the ability of the virus to replicate inside the host cell.

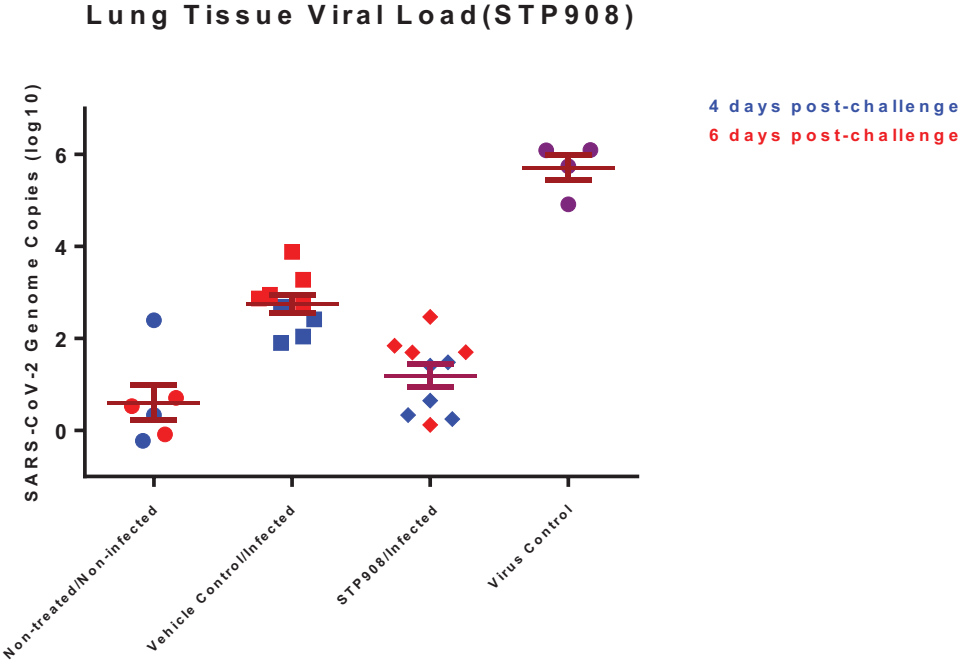
Competitive Advantages

We believe that STP908 has potential competitive advantages compared to the available therapeutics for COVID-19 or other SARS coronavirus infection. STP908 demonstrated excellent potency in an in vitro live virus infectivity assay. Each of the siRNAs for ORF1Ab and N-protein separately produced >75% inhibition of virus at concentrations of 41pM. When combined, the combination showed even greater potency. The siRNAs in STP908 are designed against conserved regions of SARS-CoV-2 and other viruses, including SARS and several specific bat strains.

The target indication will be patients infected with SARS-CoV-2 or SARS viruses. We intend to develop STP908 for both prophylactic and therapeutic uses. Intravenous administration avoids the need to inhale the product by sick patients who already have difficulty breathing; however, aerosol delivery will enable use as a prophylactic.

By targeting two different gene segments within the SARS-CoV-2 viral genome allows immense specificity against the virus and we expect it will inhibit the virus while minimizing the ability for the virus to escape therapeutic pressure through mutation because the virus would require not only simultaneous mutation at two different gene segments, but also mutations at the exact sequence being targeted by each siRNA. We designed the siRNAs using highly conserved regions of many viruses in the SARS family to target regions that we expect will not readily undergo mutation.

Our preclinical results in a mouse model show both prophylactic and therapeutic efficacy. We evaluated STP908 against a sublethal dose of the Italian strain of SARS-CoV-2 in a prophylactic model using mice expressing human ACE2 in their lungs, as ACE2 acts as a receptor for viral entry. Virus was administered intranasally at day 0. STP908 (2mgs/Kg) was administered intravenously at days -5 and -2 (prior to virus administration) and again at day 1 and day 3. At day 4 and day 6 of the treatment regimen mice were sacrificed, the lungs were removed and quantitative RT-PCR used to determine the viral load present at those time points. Animals treated with STP707 were used as a control to show the level of virus present in untreated animals. We observed in animals treated with STP908 a reduction in viral titer almost to baseline. We believe that these results suggest that STP908 is able to silence the viral genes and prevent the growth of the virus in the lungs.



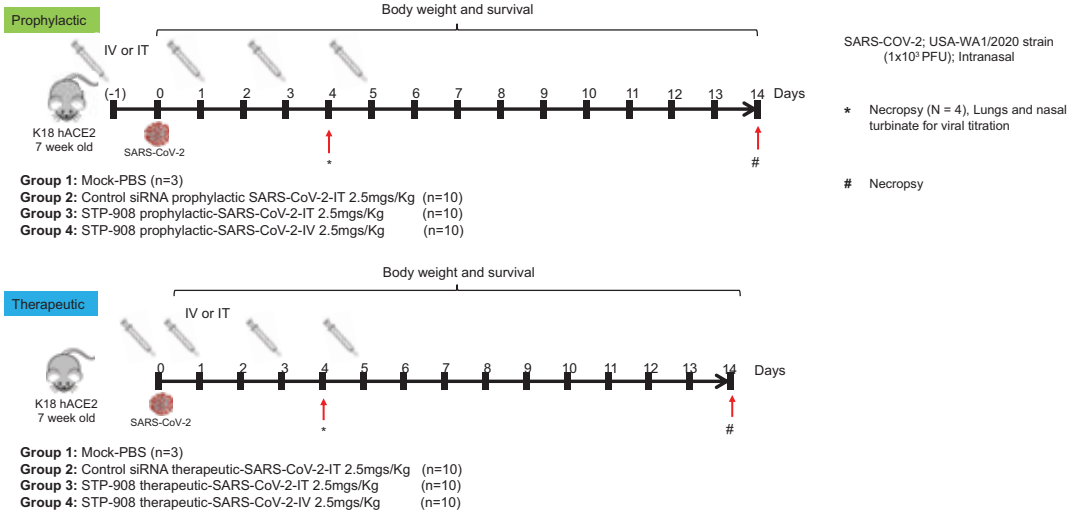
Source: Company data

We also conducted experiments using the Washington strain of SARS-CoV-2 administered intranasally at a lethal dose to mice expressing the human ACE2 in their lungs. We analyzed two regimens of STP908 administration (as illustrated in A in the figure below): first, a prophylactic regimen where STP908 was administered 1 day prior to virus administration (day -1) and then again at days 1, 3 and 5 and second, a therapeutic regimen where virus was administered at day 0 and the first injection of STP908 was given 1 hour after infection and again at days 1, 3 and 5. We also compared intratracheal and intravenous administration of STP908. Our results showed that all animals infected with virus exhibited significant weight loss over the first 5-7 days, and weight regain in treated animals was used to determine the efficacy of STP908. Control animals (not treated with STP908) were all dead by day 7-8 after administration. As shown in B in the figure below, in the prophylactic model STP908 reversed the weight loss back to 95% of uninfected controls by day 14. In the

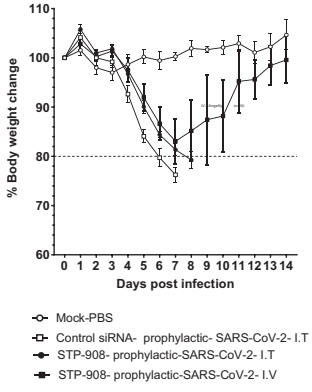
therapeutic model (shown in C in the figure below), STP908 reversed weight loss back to 100% of control (uninfected) animals by day 9. Both therapeutic and prophylactic regimens showed a rescue of 50% of the animals from death by day 14 (shown in D in the figure below). In our comparisons of intractracheal and intravenous administration, we observed that animals administered STP908 intratracheally (lung) at 2.5mgs/kg lost greater than 20% body weight within 6-7 days and were euthanized. In contrast, animals administered STP908 intravenously at 2.5mg/kg demonstrated a significant regain of body weight between days 7-9 with 50% of the animals rescued from death at day 14 when the experiment was concluded. We believe that our preclinical results demonstrate that both prophylactic and therapeutic administration protocols can be used with STP908 to treat SARS-COV2 infections.

Prophylactic and therapeutic efficacy of STP908 against SARS-CoV-2

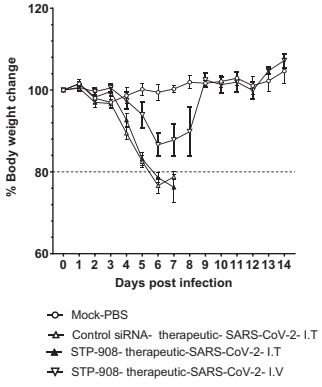
A. Prophylactic and therapeutic treatment regimens



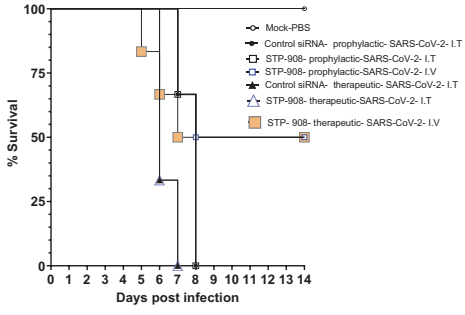
B. Morbidity data (prophylactic)



C. Morbidity data (therapeutic)



D. Mortality data (both)



Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP908.

RIM730

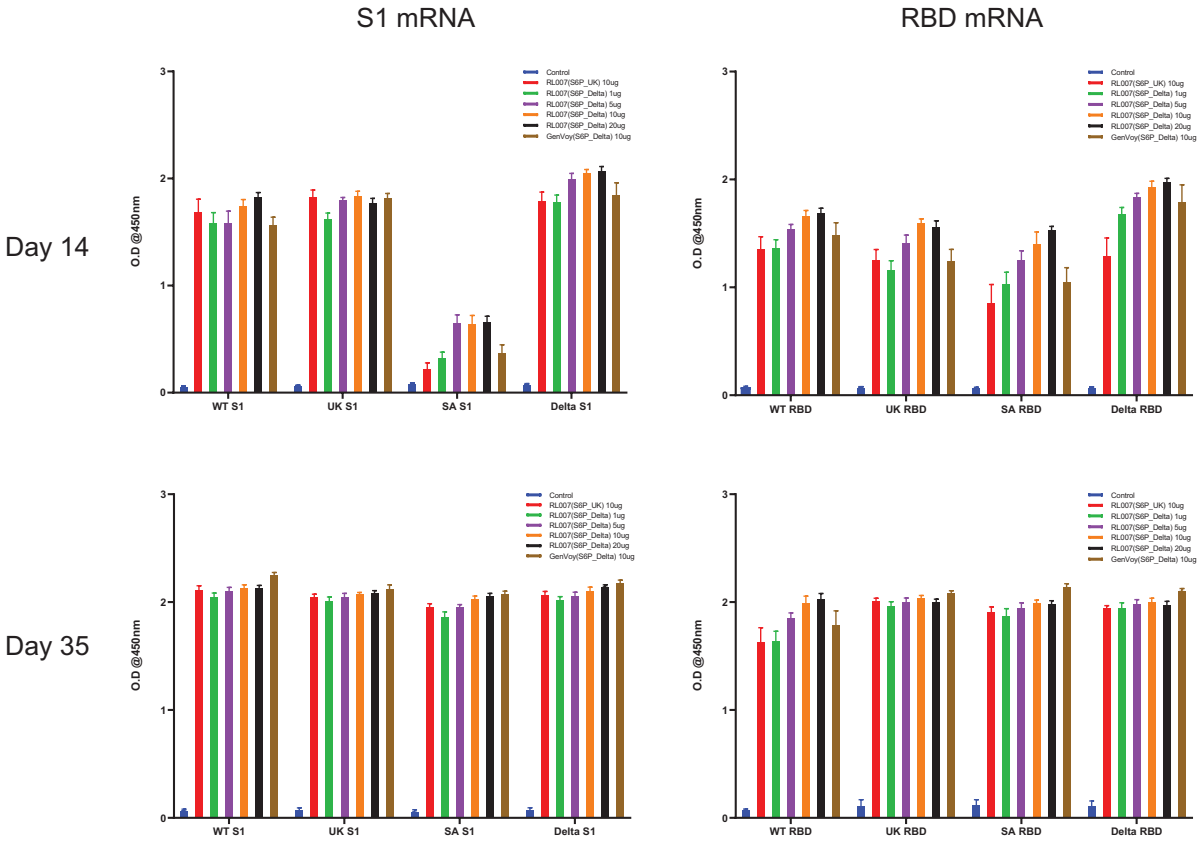
RIM730 comprises mRNA coding for SARS-CoV-2 full length spike protein from the Delta variant formulated with LNP delivery technology for intramuscular administration. We are developing RIM730 as a prophylactic vaccine for the prevention of COVID-19. We have submitted a pre-IND package to U.S. FDA on October 1, 2021. We maintain the global rights to develop and commercialize RIM730.

Our preclinical results in an in vivo mouse model show induction of a strong immune response by RIM730. Female Balb/c mice were immunized on Day 0 and Day 21 with the Alpha (UK) variant S mRNA (10ug) and the Delta variant S mRNA (1ug, 5ug, 10ug, 20ug), formulated with LNP mRNA delivery technology (RL007), and with the Delta variant S mRNA (10ug) formulated with commercially available GenVoy LNP (Precision Nanosystems). Blood was collected by submandibular bleeding using a lancet after 14 days of each injection (blood taken at Day 14 and Day 35).

The figure below (A - C) shows that 14 days after each dose (Day 14 and Day 35), elicited strong IgG titer against multiple SARS-CoV-2 viral variants, including full length spike protein (S1) and the receptor binding domain (RBD) of wild-type, Alpha, Beta (South Africa) and Delta variants. Furthermore, as shown in (C), the neutralization antibody titer against SARS-CoV-2 pseudovirus particles showed that RIM730 elicited strong neuralization IgG titer in all tested SARS-CoV-2 variants.

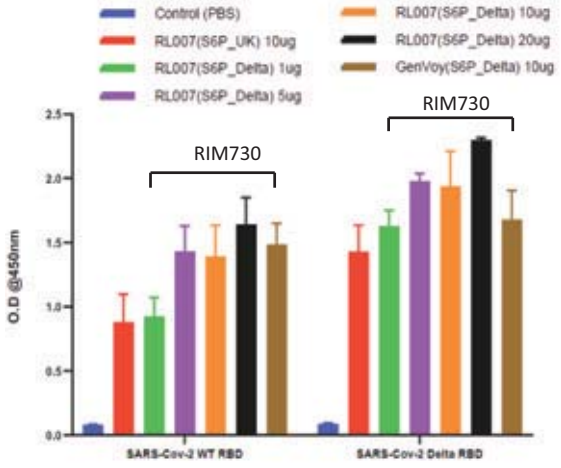
RIM730 is a Covid-19 mRNA Vaccine with Delta S Antigen:
Full length S protein mRNA formulated with RL007 LNP

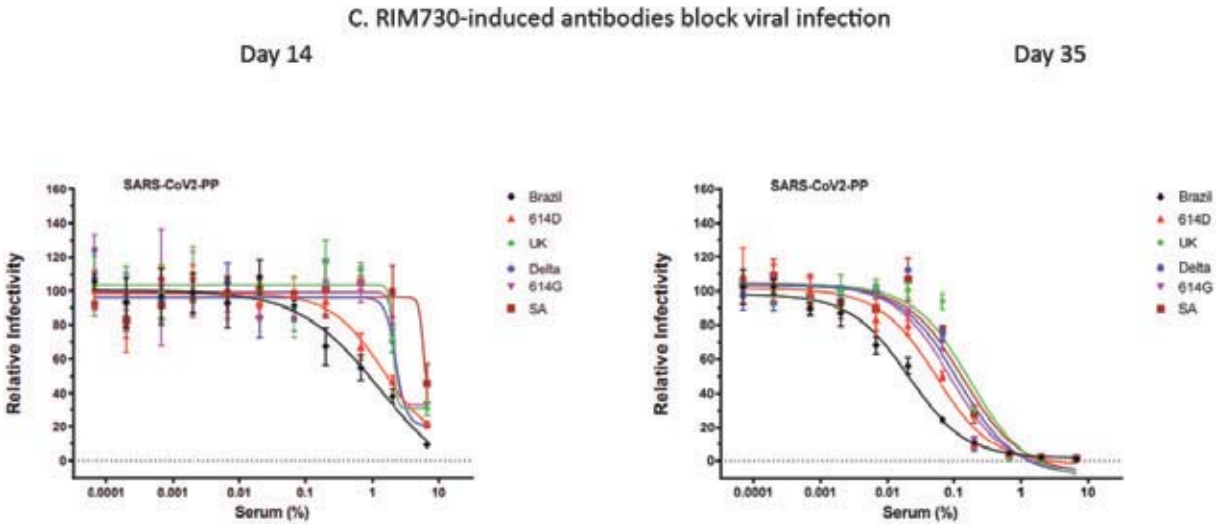
A. RIM730-induced antibodies present broad activity across variants



Source: Company data

B. RIM730-induced antibodies bind to RBD





WT = wildtype, S1 = full length spike protein, RBD = receptor binding protein of the spike protein, UK = UK or alpha variant, SA = South African or beta variant, Brazil = Brazil or gamma variant, Delta = delta variant, 614G = D614G missense mutation variant, 614D = Wuhan wildtype.
Source: Company data

STP909

STP909 comprises siRNA targeting human papillomavirus (HPV) sequences formulated with our PNP delivery platform for intravenous and topical administration. We are developing STP909 as a prophylactic vaccine for prevention of cervical cancer and other disease caused by HPV. We maintain the global rights to develop and commercialize STP909.

Our preclinical drug candidates that we are developing using our GalNAc delivery platforms include:

STP122G

STP122G comprises RNAi triggers targeting Factor XI and formulated with our GalAhead™ (GalNAc-based) delivery platform for subcutaneous administration. We are developing STP122G as an anticoagulant therapeutic. We anticipate filing an IND in the U.S. for STP122G in the first half of 2022.

Mechanism of Action

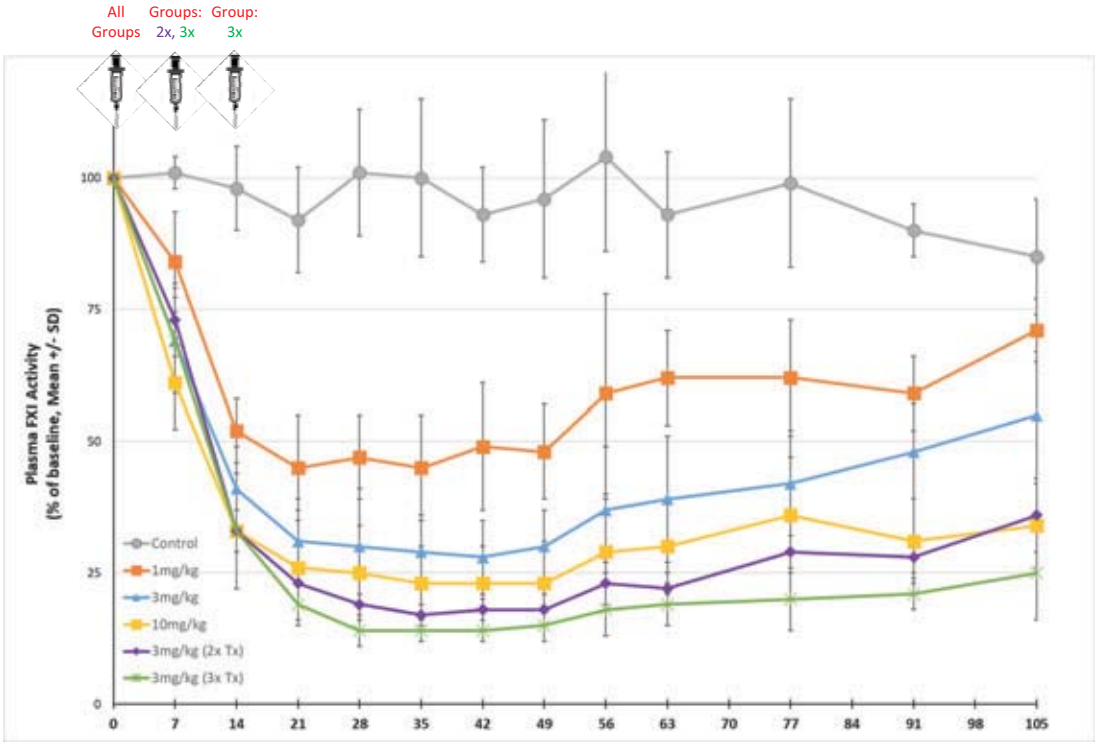
STP122G comprises RNAi triggers targeting Factor XI. Factor XI is a plasma glycoprotein that is primarily synthesized in the liver and is part of the coagulation cascade, playing a role in clot stabilization and expansion. Factor XI is an attractive target for anticoagulant therapy because while individuals deficient in Factor XI have reduced risk of thrombosis-related events, they exhibit little increase in bleeding, thus providing the potential to separate antithrombotic activity from bleeding risk.

Competitive Advantages

We believe that STP122G has potential competitive advantages over other anticoagulant therapies. Based on the low risk for increased bleeding in patients deficient in Factor XI due to genetic disorders, we believe that STP122G is likely to have a favorable safety profile. Further, we believe that STP122G may be useful broadly across different therapeutic settings where anti-coagulant therapies are needed.

Our preclinical results in an extended 13-week study in non-human primates demonstrate that STP122G has the potential for long-lasting therapeutic effects based on our results showing continuous knockdown of the target gene through week 13. Continuous knockdown effect is a potential advantage for the treatment of chronic diseases.

STP122G Preclinical Results Demonstrate Long-Lasting Knockdown Effect



Source: Company data

Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP122G.

STP133G

STP133G comprises RNAi triggers simultaneously targeting PCSK9 and ApoC3, formulated with our GalAhead™ delivery platform for subcutaneous administration. We are

developing STP133G as part of our cardiometabolic disease program. We anticipate filing an IND in the U.S. for STP133G in the second half of 2022.

Mechanism of Action

Proprotein convertase subtilisin/kexin type 9, or PCSK9, is expressed in the liver and is involved in the regulation of LDL-cholesterol. Apolipoprotein C-3, of ApoC3 is also expressed in the liver and is involved in the regulation of triglyceride metabolism.

Competitive Advantages

We believe that STP133G has competitive advantages over other drugs developed for cardiometabolic disease therapy because of its ability to achieve additive effects by targeting both LDL cholesterol and triglyceride regulating pathways.

Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP133G.

STP144G

STP144G comprises RNAi triggers targeting Complement Factor B, formulated with our GalAhead™ delivery platform for subcutaneous administration. We are developing STP144G for use in treating complement-mediated diseases. We maintain the global rights to develop and commercialize STP144G. We anticipate filing an IND in the U.S. for STP144G in the second half of 2022.

Mechanism of Action

Complement Factor B is expressed in the liver and circulates throughout the body. Complement Factor B is a key component of the innate immune system; its dysregulation may cause a number of diseases, including age-related macular degeneration, paroxysmal nocturnal hemoglobinuria, and C3 glomerulopathy.

Competitive Advantages

We believe that STP144G has potential competitive advantages over many commercialized drugs. STP144G may be administered far less frequently than small molecule therapeutics because of the longer half-life exhibited by RNAi therapeutics compared to small molecules. We believe that STP144G may be useful for treatment of complement-mediated diseases in many different therapeutic settings. See "– Our Research and Development Platforms – Our GalNAc RNAi Platform."

Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP144G.

STP135G

STP135G comprises siRNA targeting PCSK9, formulated with our PDoV-GalNAc RNAi delivery platform for subcutaneous administration. We are developing STP135G as part of our cardiometabolic disease program.

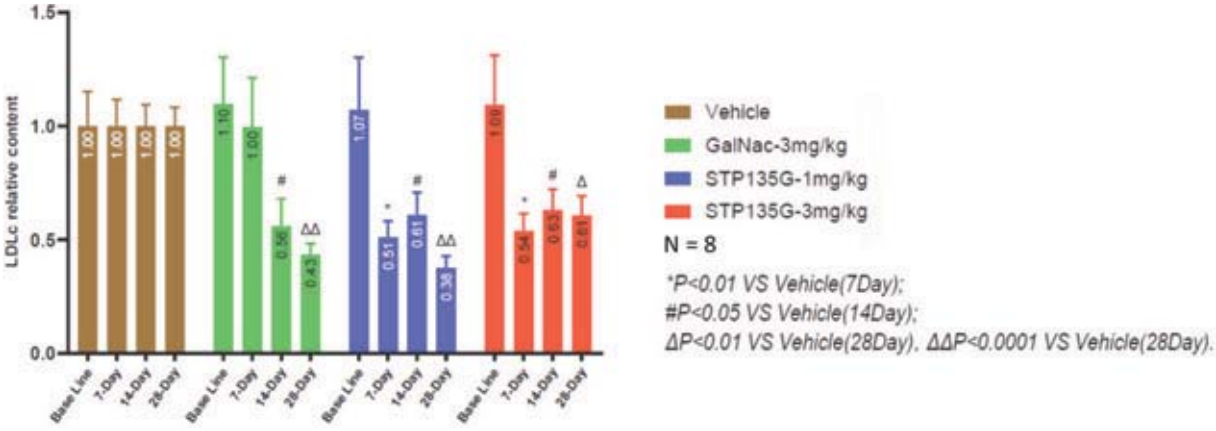
Mechanism of Action

Proprotein convertase subtilisin/kexin type 9, or PCSK9, is expressed in the liver and is involved in the regulation of LDL-cholesterol.

Competitive Advantages

We believe STP135G has potential competitive advantages for therapeutic efficacy. STP135G leverages our PDoV-GalNAc delivery platform, which has the benefits provided by the PDoV peptide to protonate in the acidic endosomal environment and improve the endosomal escape of the released siRNA. As described in "—Our Research and Development Platforms –GalNAc-Peptide Docking Vehicle (PDoV) Delivery Platform," two siRNAs may be coupled to the PDoV backbone thus introducing twice the amount of functional siRNA per molecule and halving the amount required per therapeutic dose. As shown in the figure below, we observe the benefits of promoted endosomal escape produced by the PDoV backbone and observe a much more rapid silencing effect (blue and red bars) than that observed with GalNac coupled directly to the siRNA (green bars). This means that the therapeutic effect will be observed much more rapidly than with standard GalNac conjugates that take up to 21 days to show maximal silencing. Maximal silencing effect was observed with the PDoV constructs after just 7 days compared with traditional GalNac (coupled to a single siRNA) used in this experiment of 28 days.

STP135G Preclinical Results Demonstrate Therapeutic Reduction of LDLc



A single dose of STP135G was administered by subcutaneous injection in a mouse LDLc model. Plasma LDLc was measured at days 7, 14 and 28.

Source: Company data

Licenses, Rights and Obligations

We maintain the global rights to develop and commercialize STP135G.

STP155G

STP155G comprises siRNA targeting hepatitis B viral sequences formulated with our PDoV-GalNAc RNAi delivery platform for subcutaneous administration. We are developing STP155G for the treatment of hepatitis B. We maintain the global rights to develop and commercialize STP155G.

RESEARCH AND DEVELOPMENT

We are committed to developing innovative biopharmaceutical drugs leveraging our novel delivery platforms in a wide variety of disease indications, including oncology, fibrotic diseases and conditions, viral diseases and cardiometabolic diseases. We are focused on developing new delivery platforms for RNA therapeutics to maintain and broaden the scope of our product pipeline, and to overcome the limitations of conventional RNA delivery tools. Once our targets have been selected based on clear scientific rationale, we apply a proprietary algorithm based on our understanding of the biochemical mechanisms involved in RNA interference to identify promising candidate RNAi trigger sequences against the selected target gene and employ high throughput processes to design, screen and rigorously test future pipeline products. We had research and development expenses of US$10.2 million and US$14.9 million in 2019 and 2020, respectively, and US$9.8 million and US$22.0 million in the nine months ended September 30, 2020 and 2021, respectively.

Our Research and Development Platforms

We have built our biopharmaceutical research development capabilities to enable our strategic focus on building delivery platforms for RNA therapeutics to enable the research, development and commercialization of innovative RNA-based therapies, including RNAi triggers and mRNA, across a broad range of therapeutic indications. Our platform encompasses research and development into RNA delivery technology, design and selection of RNAi triggers and mRNAs for product candidates, preclinical development, clinical development and manufacturing.

We identify targets implicated in driving disease and use our design algorithm to predict, and then rapidly test multiple RNAi triggers for their potency in inhibiting the expression of

the gene. We select the most potent sequences and then use these sequences to examine the effect of combining the RNAi trigger against a first target gene with a second RNAi trigger against a second target gene to identify those RNAi triggers that exhibit improved potency or efficacy when combined. The capability to provide simultaneous targeting is an important advantage when treating cancer since cancers often upregulate resistance pathways that prevent the action of a single agent. Those combinations of two RNAi triggers demonstrating improved efficacy and potency are then tested across multiple cell types (from the same and different tumor types) in in vitro assays to determine breadth of efficacy. Those that demonstrate potency in a large number of tumor cells are then progressed through in vivo testing to validate their ability to function in an appropriate setting.

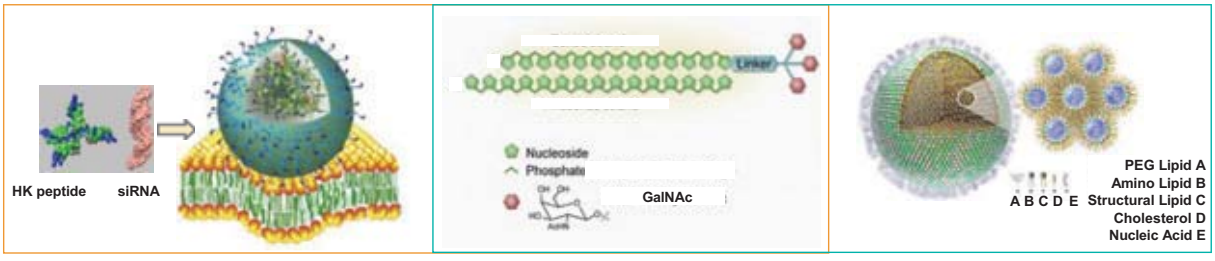
RNA interference (RNAi) is a natural cellular defense mechanism that is activated in response to the invasion of exogenous genes, such as viral DNA or RNA. RNAi therapeutics, taking advantage of this natural mechanism, are designed to use double-stranded RNA oligonucleotides, small interfering RNA (siRNA), or single-stranded RNA oligonucleotides such as microRNA (miRNA), to activate an intracellular enzyme complex, referred to as the RNA-Induced Silencing Complex, or RISC. The oligonucleotides are designed as a copy of a short region of the mRNA for a gene that has been targeted for silencing. Once delivered to the relevant tissues or cells, siRNA are loaded into RISC. Although single-stranded, miRNA oligonucleotides double-back on themselves forming a double-stranded region, and are first processed to yield a double-stranded RNA oligonucleotide that is then loaded into RISC. RISC then processes the double-stranded oligonucleotide to release one strand, usually the so-called "sense" strand that has the same sequence as the corresponding target gene mRNA. RISC uses the antisense strand as a guide to locate the mRNA with the complementary sequence that is targeted for silencing, ultimately leading to cleavage of the entire target mRNA. The consequence of the cleavage of the target mRNA is that the protein that would have been translated and produced from target mRNA is not translated and produced, thereby "silencing" the gene.

RNAi therapeutics employing siRNA or miRNA formulated into drugs have the potential to form a third major class of drugs, in addition to conventional small molecule and antibody drugs. Unlike small molecules or antibodies that must act by neutralizing the function of proteins implicated in disease through physical interaction with the protein, RNAi therapeutics prevent those proteins from being made in the first place. RNAi therapeutics are designed based on the genetic sequence of the target protein, and thus are capable of inhibiting disease-causing proteins once considered undruggable. The sequence-level targeting allows potential for protein isoform-specific knockdown. Drug discovery is also significantly faster using RNAi therapeutics, since developing a new product is based on design and synthesis of oligonucleotides rather than screening small molecules or generating antibodies against the protein.

One of the primary challenges in harnessing RNAi to create therapeutics is formulating the siRNA (or miRNA) to protect it from degradation when administered to the patient while

also permitting efficient uptake into the target cell and delivery into the cytoplasm where it needs to be available to act on the target mRNA. Naked RNA is prone to nuclease degradation, may activate the immune system and is too large and negatively charged to passively cross the cell membrane. Delivery platforms protect the RNA, may selectively deliver it to selectively targeted tissues or cell types, and may improve uptake into the cytoplasm. RNAi therapeutics currently marketed by our competitors use either lipid nanoparticles (LNP) or GalNAc for formulation of siRNAs. LNP technology can be used to deliver RNAs targeting multiple organs and tissues by way of intramuscular, intravenous or subcutaneous administration. Manufacturing LNP-based therapeutics is highly complex, requiring the use of multiple components and the finished dosage form has limited stability of about six months, requiring cold chain storage and transport. GalNAc RNAi technology chemically links the N-acetylgalactosamine (GalNAc) molecules to an RNAi oligonucleotide trigger and actively targets delivery to liver hepatocytes where the GalNAc moieties bind to the asialoglycoprotein receptors (ASGPR). GalNAc RNAi drugs can be administered subcutaneously or intravenously. Manufacturing GalNAc-based RNAi therapeutics is less complex than LNP-based therapeutics and the finished dosage form can be lyophilized for increased stability with no cold chain storage and transport is necessary. Our innovative and proprietary delivery platforms include polypeptide nanoparticle (PNP) technology and improved GalNAc RNAi technology platforms.

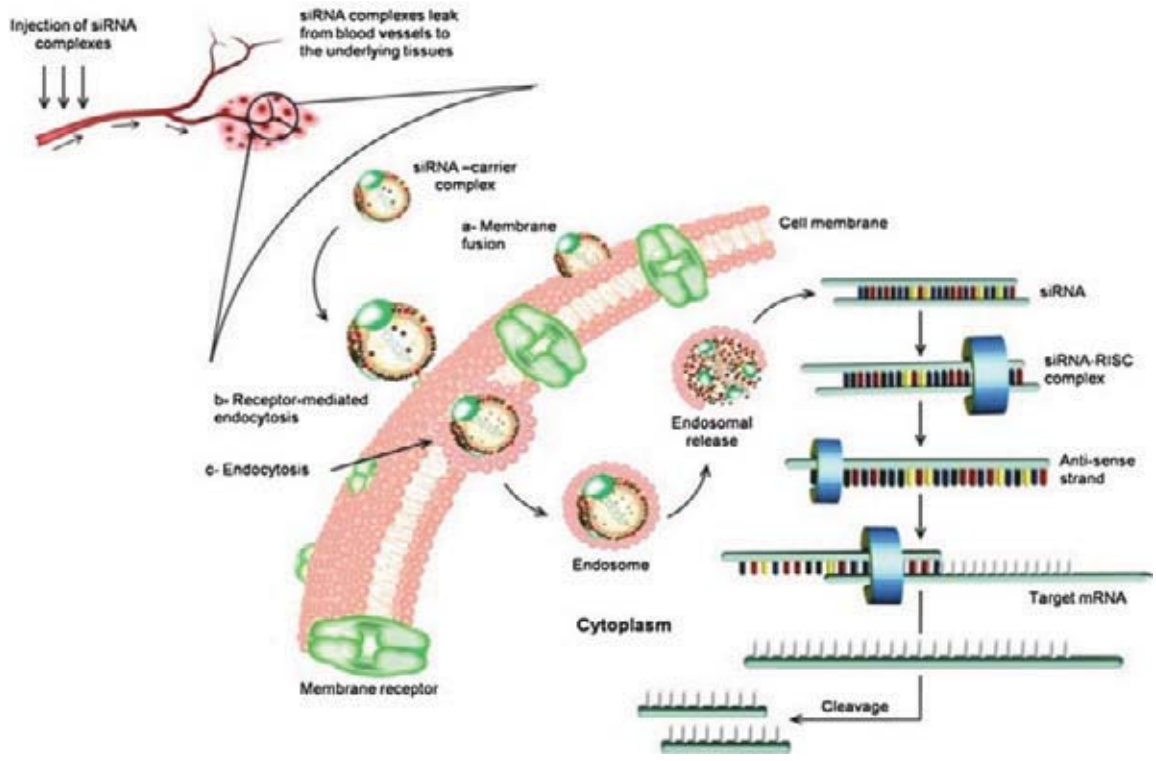
Comparison between RNAi delivery platforms



PNP Delivery Platform | GalNAc RNAi Technology | LNP RNAi Technology

Sources: Chou, S.-T. et al. Biomaterials, 2014: 35, 846-855; Arrowhead Pharmaceutical; Samaridou, E. et al. Adv. Drug Deliv. Rev. 2020: 154-155, 37-63.

Mechanism of Delivery for siRNA



Source: Draz, M. et al.. Theranostics, 2014:4(9), 872 – 892.

Our Polypeptide Nanoparticle (PNP) Delivery Platform

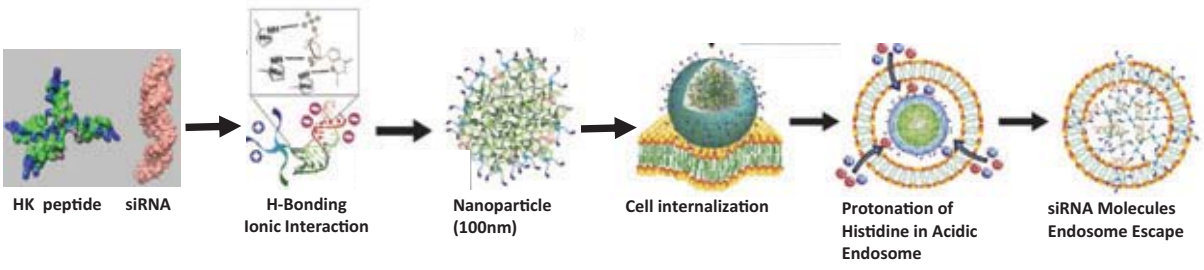
Our PNP delivery platform is based on a naturally biodegradable polypeptide molecule, a histidine-lysine (HK) polymer. The HK polymers vary in the pattern of repeating histidines and lysines and may be branched. When admixed at the appropriate ratio with RNA, the HK polymers self-assemble into nanoparticles that encapsulate the RNA. siRNA, miRNA and mRNA can all be used with our PNP delivery platform. Importantly, the nanoparticles capture and encapsulate multiple RNA molecules at once such that more than one distinct RNA oligonucleotide can be carried within the PNP. We leverage the capability of the PNP delivery platform to carry distinct RNA oligonucleotides in our development efforts that focus on identification of siRNAs (or miRNAs) that produce synergistic effects when simultaneously silencing two distinct target genes. We estimate there can be thousands of RNA molecules in a single 100 nm PNP. The lysine component of the HK peptide is important for binding the HK polymer with the negatively charged phosphates of the nucleic acids, while the histidines act not only to condense the nucleic acids to some extent, but also facilitate the release of the RNA into the cytoplasm once the PNP enters the cell. The PNP formulation is designed to ensure that the RNA cargo is neither degraded by nucleases nor filtered out by the kidney when administered systemically before it reaches its intended target tissue. The PNP can be

gradually taken up by target cells at the administration site when locally administered, or by the target cells in the blood circulation when administered systemically.

Endocytosis is the primary mechanism for movement of extracellular material across the cellular membrane. Once endocytosed, the material is engulfed within an endosome where is it sequestered within the cell. Under normal circumstances, endosomes eventually fuse with lysosomes, which create an acidic microenvironment for degradation of the material within the endosome. With the pKa of histidines reaching 6.3 or lower in the endosome, we speculate that electrostatic repulsion between the histidines upon protonation in the acidic endosomes plays the dominant role in disrupting and/or unpacking the PNP polyplexes. Unpacking of the polyplex could occur with further polyplex disruption into smaller and less dense smaller polyplexes, with monomeric HK siRNA units as part of the continuum. Upon unpacking of the polyplex, the protonated HK peptides would likely interact with negatively charged endosomal membranes, which would thus act similarly to detergents to aid in the escape of siRNA from the endosome. Once the RNA payload is released, the HK polymers disassemble into polypeptide chains and are readily broken down into natural amino acids by proteases in the cell.

There are two main mechanisms mediating PNP entry into cells by endocytosis. First, the PNP can enter the cell through non-clathrin mediated endocytosis. Second, the HK polypeptide is recognized by the Neuropilin 1 (NRP1) receptor on the cell surface, as demonstrated in experiments that show PNP entry into cells is blocked when the cellular NRP1 receptor is masked by an antibody.

PNP Delivery Platform Structure and Mechanism of Delivery



Source: Chou, S.-T. et al. Biomaterials, 2014: 35, 846-855.

Our PNP delivery platform is effective in delivering PNP-encapsulated RNA to a variety of tumor cell types when delivered through systemic administration, including breast cancer tumors (MDA-MB-231 cells), cholangiocarcinoma tumors (HuCCt cells), mouse primary liver cancer tumors (Hepa1-6 cells), as well as human primary hepatic stellate cells, human primary brain cells, mouse alveolar epidermal cells, lung cells and others. Topical administration of PNP formulated RNA therapeutics are also effective, as demonstrated by the positive results thus far of our STP705 product candidate in treating isSCC, BCC, keloids and HTS. Transfection efficiency is highest for hepatic stellate cells (better than lipofectamine) and tumor cells also take it up with relatively high efficiency. We believe that the PNP is

preferentially taken up by activated endothelial cells, such as tumor neovascular endothelial cells and fibrotic liver vascular endothelial cells, through upregulated NRP1 receptors or other receptors.

The safety profile for our PNP delivery platform is highly encouraging. We have conducted a large number of in vitro and in vivo studies in mammals over the course of several years confirming that the HK peptide is highly effective at delivering RNA with low toxicity. Our Phase IIa clinical trial for STP705 for treatment of isSCC demonstrated both safety and efficacy in humans. Our product candidate STP707 exhibited a favorable safety profile in a GLP toxicity study using non-human primates with intravenous administration of PNP-formulated siRNA. No drug-related toxicities were observed in any dose groups. No drug-related adverse events were found in the treatment groups. A safety pharmacology study found no impairments of cardiovascular and respiratory functions in monkeys receiving the injection of STP707. No dose limiting toxicity was observed in non-human primates at a dose representing roughly 30 times the human equivalent dose proposed for a clinical trial for treatment of solid tumors by intravenous administration, thus demonstrating that our PNP delivery platform is capable of developing drugs with wide therapeutic windows.

Our PNP delivery platform generates a highly stable RNA-based drug product and it is manufactured using a relatively low complexity, controllable and scalable process. The drug product is manufactured using two ingredients, synthesized oligonucleotides and synthesized peptides. We use a microfluidic platform that allows the peptide nanoparticles to encapsulate the RNA at a high packaging efficiency, with greater than 97% loading. Our microfluidic process can generate consistent PNP particle sizes within a narrow distributions, an important feature for nanoparticulate drugs administered intravenously. In a lyophilized powder state, the PNP-formulated drug product is stable for 36 months, and the aqueous solution for six months. No cold chain transportation or storage are necessary.

Our GalNAc RNAi Delivery Platforms

N-acetyl galactosamine, or GalNAc, is the ligand of choice for delivery of RNAi drugs to the hepatocytes within the liver, and the basis of conventional delivery platforms used by our competitors. GalNAc ligands bind to the asialoglycoprotein receptor, or ASGPR, which is preferentially expressed in hepatocytes in the liver. We have developed two novel proprietary siRNA delivery platforms that improve upon traditional GalNAc RNAi delivery platforms.

GalAhead™ Delivery Platform

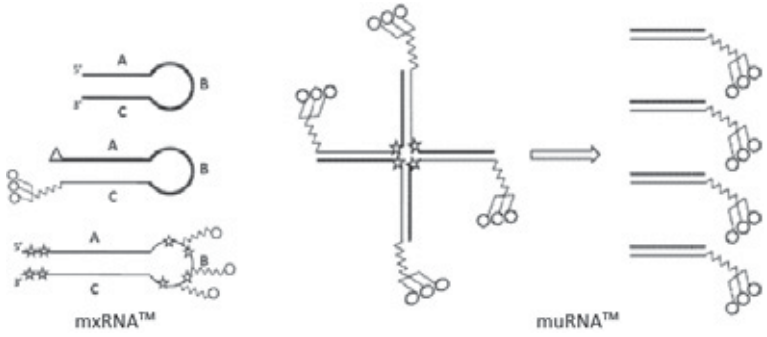
Our proprietary GalAhead™ delivery platform utilizes two technologies: the mxRNA™ (miniaturized RNAi triggers) that is designed to downregulate single genes, and the muRNA™ (multi-unit RNAi triggers) designed to downregulate multiple genes simultaneously.

The mxRNAs™ are composed of single-stranded oligonucleotides of approximately 32 nucleotides in length, which form small hairpin structures. GalNAc moieties can be covalently

attached at one or more positions on the oligonucleotide. We believe that mxRNAs™ are among the smallest RNAi triggers used. They also promise to be easier to manufacture than conventional GalNAc-siRNAs, since they require synthesis of only one oligonucleotide per RNAi trigger, rather than two oligonucleotides used in conventional GalNAc-siRNA drug products.

The muRNA™ molecules are comprised of multiple single-stranded oligonucleotides of approximately 32 nucleotides in length, with covalently attached GalNAc moieties. When mixed, the oligonucleotides self-assemble into multiplexed structures. Upon exposure to intra- and/or extra-cellular biological fluids the oligonucleotide particles controllably disassemble, producing multiple individual RNAi triggers, thus allowing knock-down of multiple targets simultaneously. Multitargeting with single drug molecules potentially opens wide therapeutic horizons.

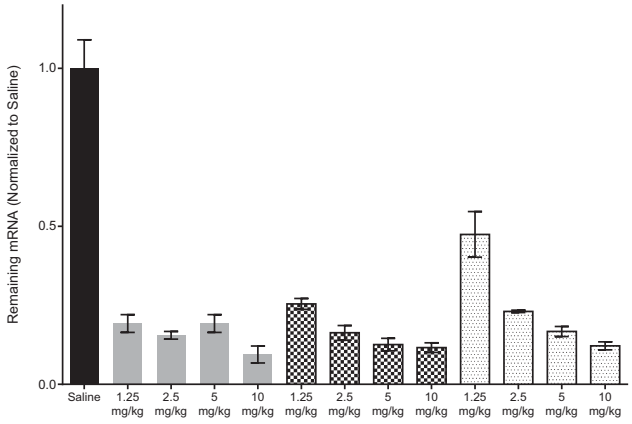
Schematic of GalAhead™ Delivery Platform



Source: Company

Both mxRNA™ and muRNA™ molecules demonstrate outstanding in vivo activities that match or exceed those of conventional GalNAc-siRNAs. In the figure below, in vivo activity in mice is shown using mxRNA™ where silencing of the target gene in the liver was observed in a dose responsive manner on analysis five days after administration. In the study, three molecules having the same targeting sequence, but using slightly different chemical modification patterns were administered to mice. Even at the lowest tested dose (1.25 mg/kg), constructs were capable of producing more than 80% knockdown of the target mRNA.

Knockdown of Gene Expression Using GalAhead™ Delivery Platform

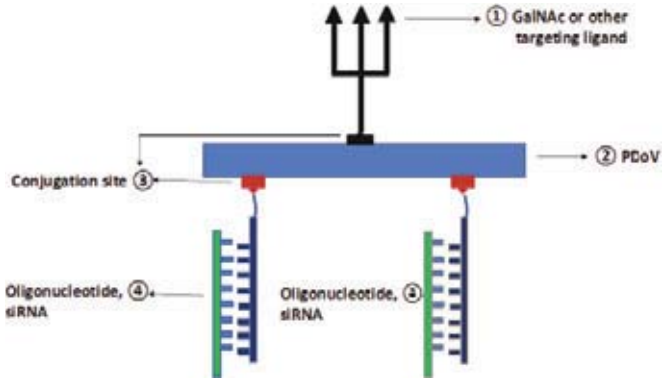


Source: Company data

GalNAc-Peptide Docking Vehicle (PDoV) Delivery Platform

We have also developed a Peptide Docking Vehicle (PDoV) delivery platform that consists of a histidine-lysine peptide sequence, similar to the peptide used in our PNP delivery platform, that is modified with GalNAc at one location and one to two siRNA sequences coupled via their sense strands to the backbone of the peptide at other locations. The figure below illustrates our GalNAc-PDoV platform.

Schematic of GalNAc-PDoV Delivery Platform



Source: Company

While the GalNAc ligand targets the vehicle to liver cells, we believe the PDoV moiety enhances the process of endosome escape of the siRNA once the vehicle is internalized into the cell and the endosome. As in our PNP delivery platform, the histidine moieties in the PDoV moiety have the ability to protonate in the acidic environment, which induces a proton mediated repulsion causing the release of the contents of the endosome into the cytoplasm

where the siRNAs can induce silencing. We expect our GalNAc-PDoV platform to result in improved efficiency of delivery to the intracellular target based on the enhanced endosomal escape created by the peptide moiety and thus anticipate that an increased concentration of siRNA will reach the cytoplasm to effect target gene silencing as compared to conventional GalNAc platforms. In addition, as with our other delivery platforms, our PDoV-GalNAc RNAi delivery platform is capable of leveraging the synergy of silencing two distinct targets by simultaneously delivering two siRNAs to the cell.

PLNP Delivery Platform and Other Delivery Platforms

We continue to invest in research and development of new delivery platform technology. RNAimmune is developing a novel PLNP delivery platform that modifies our PNP delivery platform to combine proprietary HK peptides with ionizable amino lipids for encapsulation of mRNA for novel mRNA vaccines and therapeutics. We believe the combination of the HK polypeptide and liposome components in the PLNP improve the efficiency of cellular delivery of the mRNA cargo through better endosomal escape once the PLNP enters the cell. In addition, manufacture of products using our PLNP delivery platform is simpler than products using LNP platforms, since there are fewer components and, unlike current LNP platforms, our PLNP delivery platform does not utilize polyethylene glycol (PEG), which is thought to cause severe adverse effects in some patients receiving LNP-based mRNA vaccines. Our PLNP delivery platform results in products that are stable at ambient temperatures and do not require cold chain storage and transportation. Our novel PLNP-mRNA platform has been validated in in vitro studies and preclinical in vivo mouse and non-human primate studies.

We are developing advanced conjugates of siRNA and drugs and peptide-drug conjugates where drugs are conjugated to the HK polymer in the PNP for enhanced combination therapies. Moreover, we are further enhancing our PNP delivery platform by researching and developing tumor cell targeted PNPs. We are also researching novel formulations for airway delivery for the treatment of respiratory viruses.

Our Research and Development Team

Our research and development function is led by Dr. Lu, our Founder, President and CEO, Dr. David Mark Evans, our Chief Scientific Officer, and Dr. Dmitry Samarsky, our Chief Technology Officer. Dr. Lu has more than 25 years of experience in nucleic acid drug development, and has led our research and development teams from our early discovery efforts through to our current clinical stage programs. Dr. David Mark Evans has worked in pharmaceutical drug discovery, primarily in oncology for over 25 years and has worked in the RNAi field since 2003. Dr. Dmitry Samarsky has been involved in scientific research in the RNAi field since 2001. Dr. David Mark Evans leads our teams focused on target gene discovery, siRNA therapeutic design, development, and in vitro and in vivo testing and toxicology. Dr. Dmitry Samarsky leads our team focused on our novel GalAhead™ (GalNAc-based RNAi delivery) platform technology and therapeutic programs. Dr. Zhifeng Long, our

Chief Development Officer, leads our teams focused on preclinical studies and Dr. Edward Yongxiang Wang, our Chief Production Officer, leads our teams focused on manufacturing and regulatory compliance.

We have research laboratory facilities in Suzhou, China and Gaithersburg, Maryland. Our facilities in Suzhou consists of approximately 1800 square meters of laboratory and office space. The laboratory space includes biological laboratories, a chemistry laboratory and a GLP testing laboratory. Our facilities in Gaithersburg consist of approximately 1280 square meters of leased laboratory and office space with each representing about half of the space. The laboratory space includes a main biology laboratory, a tissue culture laboratory, a chemistry laboratory shared laboratory space. Our Gaithersburg laboratory space also includes a cold room and a central space as well as utility and storage space.

Leveraging these in-house laboratories we have research capabilities and engage in research activities such as rapid design and testing of siRNAs against selected targets in vitro and then migration of these products to in vivo testing. We also work closely with CROs for large scale production of our therapeutic candidates, validation of efficacy of our products against an array of tumor types in vivo and toxicity testing in appropriate animal models. Our clinical development function is led by Dr. Michael V. Molyneaux, our Chief Medical Officer, and builds on Dr. Michael V. Molyneaux's expertise and familiarity with all aspects of preclinical, clinical operations, medical affairs and regulatory affairs in clinical stage biopharmaceutical companies. As of the Latest Practicable Date, our clinical operations and regulatory teams consist of 11 employees and consultants, including five based in the U.S. and six based in China. Our clinical operations team ensures timely execution of all clinical trial deliverables and also provides detailed oversight of our CROs and vendor selection and management. Our clinical operations team oversees the selection and management of clinical trial sites, and implementation of our clinical trials. Our regulatory team is responsible for development of clinical trial protocols and other key documentation as well as managing the global regulatory submission process. Our regulatory team works with various stakeholders to deliver high quality and timely regulatory submissions for our product candidates, which require filings to be made to and approved by the relevant authorities before clinical trials and commercialization can be initiated. We possess ample knowledge and experience with regard to regulatory filings in China and the U.S.

As of the Latest Practicable Date, our research and development team (including preclinical research, clinical and manufacturing but excluding RNAimmune) in China consists of 87 employees and consultants with eleven members holding doctorate degrees and 22 members holding masters degrees, and in the U.S. our team consists of 32 employees and consultants, with 18 members holding doctorate degrees and seven members holding masters degrees. The following table sets forth the membership of our research and development team, including both employees and consultants, across China and the U.S. during the Track Record Period according to functional areas:

	As of December 31,		As of September 30,
	2019	2020	2021
Preclinical research	37	33	66
Clinical	1	2	8
Manufacturing	8	15	27

Our change in headcounts for employees and consultants involved in preclinical and clinical activities between 2020 and 2021 reflects the expansion of our pipeline of product candidates and the growth of our clinical trials over that time period, as well as the funding increase as a result of the completed Series D financing in 2020. Our change in headcount for employees and consultants involved in manufacturing reflects the increase in product candidates at the IND-enabling stage of development as well as the increase in ongoing clinical trials and the build out of our Guangzhou facility. Our preclinical research staff are primarily responsible for in-house design, planning and conducting research experiments, as well as the management and oversight of the relevant CROs, CDMOs and research and medical institutions, with respect to the identification of novel siRNAs and RNAi triggers, development of our delivery platforms and our product candidates that utilize our delivery platforms. Our clinical research staff are primarily responsible for regulatory filings, and planning of clinical trials and protocols and the management and oversight of the relevant CROs and research and medical institutions. Our manufacturing staff are primarily responsible for optimizing manufacturing of nanoparticles for our PNP delivery platforms, quality control and quality assurance management, manufacturing process development for our delivery platforms and product candidates and the management and oversight of CDMOs and CMOs.

Our research and development cash operating costs during the Track Record Period, as allocated between our core product and other products, are set forth in the table below.

	Year ended December 31,		Nine months ended September 30,
	2019	**2020**	**2021**
	US$'000	*US$'000*	*US$'000*
Research and development costs for core product			
Preclinical test expenses	679	583	284
Chemistry, manufacturing and controls expenses	1,909	2,795	708
Clinical trials expenses	1,264	1,572	3,388
Materials consumed	509	611	701
Directors' emolument and staff costs	1,520	1,538	2,143
Consultancy fee	702	721	696
Others	536	412	250
Research and development costs for other products			
Preclinical test expenses	90	1,026	3,537
Chemistry, manufacturing and controls expenses	995	631	4,796
Clinical trials expenses	–	–	–
Materials consumed	271	371	2,301
Directors' emolument and staff costs	2,057	2,054	3,154
Consultancy fee	212	264	483
Others	582	328	1,348
Total	11,326	12,906	23,789

Our research and development costs reflect the steady advance of our research and development program and the expanding pipeline of product candidates. For our research and development costs for our core product, STP705:

- Preclinical test expenses reflect that activities for our core product STP705 decreased as the multiple programs gradually reach clinical phase during the Track Record Period.

- Chemistry, manufacturing and controls expenses for our core product increased from 2019 to 2020 to prepare drug material for the multiple clinical trials for STP705.

- Clinical trial expenses reflect that the Phase IIa clinical trial for isSCC commenced in 2019 and was completed in 2020, followed by the Phase IIb clinical trials which commenced in 2021. Expenses increased from 2020 onwards as we initiated multiple trials for keloid scarless healing, BCC, and liver cancer.

- Materials consumed expenses increased between 2019 and 2020 in line with the expansion of our research and development program and our chemistry, manufacturing and controls team.

- Directors' emolument and staff costs were incurred in 2021 to expand our research and development and clinical programs after we obtained our funding from our Series D Financing in 2020.

- Consultancy fees have increased between 2019 and 2020 in line with the expansion of our research and development program.

- The remaining operating costs include without limitation equipment rental, laboratory space rental and utilities allocated to our core product.

For our research and development costs for our other products:

- Preclinical test expenses reflect that development of our GalNAc delivery platform programs were initiated in 2019, expanding in 2020. The expenses incurred during the first nine months of 2021 were incurred after we obtained funding from our Series D financing in 2020.

- The chemistry, manufacturing and controls cash operating costs were higher in 2019 as compared to 2020 is a result of multiple advance payments made during the year for contracts performed in 2020. The expenses incurred during the first nine months of 2021 were primarily in support of conducting safety studies for our other products.

- No other products except for STP705 has entered into clinical phase yet.

- Directors' emolument and staff costs were incurred in 2021 to expand our research and development program after we obtained our funding from our Series D Financing in 2020.

- Materials consumed and consultancy fees have increased between 2019 and 2020 in line with the expansion of our research and development program.

- The remaining operating costs mainly include equipment rental, space rental and utilities, license fee and traveling expenses.

Engagement of Third Parties in Research and Development

We engage reputable CROs, CDMOs, CMOs and research and medical institutions to manage and support our clinical trial and preclinical studies. CROs provide us with an array of products and services necessary for preclinical experimentation and complex clinical trials. We select CROs by reviewing various factors, including their professional qualifications, research experience and industry reputation. We have selected CROs that have experience

serving large international pharmaceutical companies. In order to protect integrity and authenticity of the data from our trials and studies, we closely supervise our CROs to ensure that they perform their obligations in a manner that complies with our protocols and applicable laws.

Our CROs are responsible for providing services including in vivo testing of products to validate their efficacy in suitable models and to test our later stage products in toxicity testing in two species (typically mice and NHPs). We also engage CROs for submission of ethical documents, data management, and statistical analysis for clinical trials. We will make payments after fulfillment of certain milestones under the relevant agreements. Key terms of an agreement we typically enter into with our CROs are summarized as below:

- *Services*. The CRO provides us with services related to a preclinical or clinical research project as specified in the agreement or a work order.

- *Term*. The CRO is required to complete the preclinical or clinical research project within the prescribed time limit.

- *Payments*. We are required to make payments to the CRO in accordance with the payment schedule agreed by the parties.

- *Intellectual property rights*. We own all intellectual property rights arising from the preclinical or clinical research project.

Our CDMOs are responsible for manufacturing drug candidates for preclinical studies and provide manufacturing process development and optimization services.

Our CMOs are responsible for manufacturing drug candidates for preclinical studies and clinical trials.

Research and medical institutions include academic and other research institutions that conduct preclinical studies for us, as well as a medical institution that provides clinical trial facilities and related services.

We are the owner of the drug candidates and the sponsor of the relevant clinical development activities. We are in charge of the full lifecycle management of the drug candidate including research and development, manufacturing and future commercialization. We make key decisions regarding the overall development direction, clinical trial plans and procedures, and provide funding.

The involvement and roles of third party service providers in the development of novel molecule drug candidates are typically standardized and similar among different projects. The work scope of these third parties in the development of our drug candidates may have slight variation, subject to our overall management and instructions.

The following table sets forth the number of independent CROs, CDMOs, CMOs and research and medical institutions we have engaged during the Track Record Period:

	Year ended December 31,		Nine months ended September 30,
	2019	2020	2021
CRO	16	23	26
CDMO	9	7	5
CMO	5	8	8
Research and medical institutions	4	7	7

The following table sets forth the total fees incurred by us with respect to all CROs, CDMOs, CMOs and research and medical institutions for the Track Record Period:

	Year ended December 31,		Nine months ended September 30,
	2019	2020	2021
	US$'000	*US$'000*	*US$'000*
CRO	1,329	2,459	5,067
CDMO	1,393	3,972	3,991
CMO	679	978	1,373
Research and medical institutions	270	236	775

During the Track Record Period, our expenses attributable to CROs, CDMOs, CMOs and research and medical institutions have increased, reflecting the growth of our research and development capability, expansion of our preclinical product pipeline, initiation of clinical trials and the success of our proprietary delivery platforms in generating new product candidates for further development in the clinical stage.

The following table sets forth the identities and background of CROs, CDMOs and CMOs engaged by us wherein aggregate expenses incurred exceeded US$500,000 during the Track Record Period. We note that the amount of expenses incurred to research and medical institutions did not exceed US$500,000 in aggregate for any one institution during the Track Record Period.

	Name/Background	Expenses incurred by us during the Track Record Period
		(US$,000)
CRO	A Maryland based clinical research services company	2,126
	A Beijing based clinical research services company	1,862
	An Arizona based clinical research services company	1,293
	A Massachusetts based clinical research services company	865
CDMO	A Massachusetts based manufacturing and development services company	3,462
	A Guangzhou based oligonucleotide manufacturing and development services company	2,172
	A Switzerland based peptide manufacturing and development services company	1,154
	A US based oligonucleotide manufacturing and development services company	1,633
CMO	A UK based manufacturing services company	978
	A Canadian based manufacturing services company	700

To the knowledge of our Directors, other than the ordinary business relationship, none of our CROs, CDMOs and CMOs nor the research and medical institutions engaged by us (including their directors, shareholders and senior management), had any past or present relationships (including, without limitation, business, employment, family, trust, financing or otherwise) with our Group, our shareholders, Directors, senior management or any of their respective associates during the Track Record Period.

COLLABORATION AND LICENSING ARRANGEMENTS

Collaboration with Innovent

In January 2020, US Sirnaomics entered into a collaboration agreement (the "Innovent Agreement") with Innovent to develop a combination therapy consisting of STP705 and sintilimab, an anti-PD-1 monoclonal antibody, for use in advanced cancers, including NSCLC ("Combination Therapy") in the U.S. Commercialization of the Combination Therapy will be the subject of a separate definitive agreement to be negotiated between the parties. Innovent is a biopharmaceutical company that develops and commercializes medicines for the treatment of oncology, autoimmune, metabolic and other major diseases. US Sirnaomics approached Innovent for a potential collaboration after obtaining an understanding of the mechanism of

action for STP705 based on its own preclinical research and learning of sintilimab. Preclinical studies prior to the parties entering into the Innovent Agreement showed that US Sirnaomics' siRNA dual-targeted (TGF-ß1 and COX-2) product candidate, STP705, when combined with an anti-PD-L1 antibody demonstrated enhanced anti-tumor activities in the mouse xenograft tumor model of human cholangiocarcinoma and orthotopic mouse liver cancer model. Based on the anti-tumor activities exhibited by the combinations between US Sirnaomics' siRNA therapeutic candidates and the immune checkpoint inhibitory antibody, Innovent and US Sirnaomics entered into an agreement for evaluating the scientific rationales and potential clinical value of a combination therapy that utilizes both parties' products. Neither party has payment obligations under the Innovent Agreement. Since early 2020, US Sirnaomics has completed multiple preclinical combination studies with animal liver cancer models that illustrate potent antitumor activities. The parties are separately advancing clinical trials with their own products, which will necessarily be relied on for future clinical trials evaluating the combination therapy. As of the Latest Practicable Date, no clinical trials under the collaboration have been initiated.

Joint Development Committee: US Sirnaomics, together with Innovent, shall establish a joint development committee consisting of three representatives from each party. The committee shall review, discuss and adopt any proposed development plans, or amendments to any development plan. The development plan sets out the activities for the preclinical studies and clinical trials using sintilimab and STP705 to be performed that are necessary to obtain regulatory approval for the Combination Therapy. The committee shall oversee all material activities under the development plan, discuss and approve terminating any development plan and formulate, facilitate and approve regulatory strategy for each part to obtain regulatory approval of the Combination Therapy. US Sirnaomics has the final decision-making authority to approve the initiation of the initial development plan and the initiation of the subsequent development plan if the pre-agreed and defined success criteria for the outcome of the initial development plan have been met. If the criteria have not been met, then mutual agreement is required. If the joint development committee fails to reach a decision, disputes are referred to the chief executive officers of the respective parties, and if disputes are not resolved through good faith negotiation, either party may seek to resolve the dispute through arbitration.

Obligations of the Parties: US Sirnaomics is responsible for preparing the development plan and oversight of the activities under the development plan, subject to oversight by the joint development committee. US Sirnaomics and Innovent are each obligated to provide clinical supplies of STP705 or sintilimab at their own expense. US Sirnaomics shall use commercially reasonable efforts to conduct and lead the preclinical and clinical trials under the development plan and shall be responsible for preparing and submitting all correspondence, filings and other submissions of its collaboration molecule to a regulatory authority. If it is preferable for Innovent to conduct clinical trials for combination therapy, the parties will coordinate with each other to obtain regulatory approval to conduct clinical trials in that jurisdiction. Each party grants to the other party a right of reference for all data included in the regulatory submissions and regulatory approvals in the territory controlled by

such party for use to obtain regulatory approval on clinical trials for combination therapy. Each party has non-exclusive rights to develop sintilimab and STP705 with any other third parties with written notice to the other party in 60 days' prior notice.

Intellectual Property Ownership: US Sirnaomics and Innovent shall jointly own all intellectual property created, conceived or reduced to practice by either party solely or jointly in the performance of the development activities under the Innovent Agreement that relate to the method of use of the Combination Therapy or that consists of clinical data or results (the "Joint Technology"), except for any Joint Technology that is created, conceived or reduced to practice solely by US Sirnaomics through clinical trials with respect to the combination therapy, including the clinical data (the "Combination Clinical Trial Technology"), which shall be owned by US Sirnaomics. US Sirnaomics shall own all intellectual property created, conceived or reduced to practice by either party solely or jointly in the performance of the development activities under the Innovent Agreement that is not Joint Technology and relates solely to STP705. Innovent shall own all intellectual property created, conceived or reduced to practice by either party solely or jointly in the performance of the development activities under the Innovent Agreement that is not Joint Technology and relates solely to sintilimab.

Nature of the rights: Under the Innovent Agreement,

a) Innovent grants US Sirnaomics a non-exclusive, royalty-free, sublicensable license under intellectual property rights owned or controlled by Innovent that are necessary to use sintilimab in the conduct of the development activities under the Innovent Agreement solely to use sintilimab in the performance of the development activities to be conducted by US Sirnaomics in accordance with the relevant development plan.

b) US Sirnaomics grants Innovent a non-exclusive, royalty-free, sublicensable license under intellectual property rights owned or controlled by US Sirnaomics that are necessary to use STP705 in the conduct of the development activities under the Innovent Agreement solely to use STP705 in the performance of the development activities to be conducted by Innovent in accordance with the relevant development plan.

c) US Sirnaomics grants Innovent a non-exclusive, royalty-free, non-transferable, non-sublicensable (except to Innovent's affiliates and to Eli Lilly and Company ("Eli Lilly") to the extent Eli Lilly retain rights in sintilimab and such sublicense is in accordance with then-effective agreement between Innovent and Eli Lilly) perpetual and irrevocable license to use and access the Combination Clinical Trial Technology.

Sublicensing: Both parties have the right to sublicense solely to its affiliates and third parties who are performing development activities under the Innovent Agreement.

Term and Termination: The Innovent Agreement will remain effective until the earlier of the completion of the development activities under the development plan or when there is no development plan in progress and the joint development committee fails to adopt any new development plan within 60 days of the termination of the last development plan. Each party has termination rights for uncured breach of material obligations and bankruptcy of the other party.

Collaboration with Shanghai Junshi

In January 2020, US Sirnaomics entered into a collaboration agreement (the "Shanghai Junshi Agreement") with Shanghai Junshi to develop a combination therapy consisting of STP705 and Shanghai Junshi's anti-PD-1 monoclonal antibody, toripalimab (the "Shanghai Junshi Product") for use in advanced melanoma, squamous cell carcinoma and other agreed clinical applications ("Combination Therapy") in mainland China, Hong Kong, Macau, Taiwan and the United States. Commercialization of the Combination Therapy will be the subject of a separate definitive agreement to be negotiated between the parties. Shanghai Junshi is a biopharmaceutical company that develops and commercializes medicines for the treatment of oncology, and other major diseases and is mainly engaged in the research and development of therapeutic antibodies. US Sirnaomics approached Shanghai Junshi for a potential collaboration after obtaining an understanding of the mechanism of action for STP705 based on its own preclinical research and learning of the Shanghai Junshi Product. Preclinical studies prior to the parties entering into the Shanghai Junshi Agreement showed that US Sirnaomics' siRNA dual-targeted (TGF-ß1 and COX-2) product candidate, STP705, when combined with an anti-PD-L1 antibody demonstrated enhanced anti-tumor activities in the mouse xenograft tumor model of human cholangiocarcinoma and orthotopic mouse liver cancer model. Based on the anti-tumor activities exhibited by the combinations between US Sirnaomics' siRNA therapeutic candidates and the immune checkpoint inhibitory antibody, Shanghai Junshi and US Sirnaomics entered into an agreement for evaluating the scientific rationales and potential clinical value of a combination therapy that utilized both parties' products. Neither party has payment obligations under the Shanghai Junshi Agreement. Since early 2020, US Sirnaomics has completed multiple preclinical combination studies with animal liver cancer models that illustrate potent antitumor activities. The parties are separately advancing clinical trials with their own products, which will necessarily be relied on for future clinical trials evaluating the combination therapy. As of the Latest Practicable Date, no clinical trials under the collaboration have been planned or initiated.

Joint Development Committee: US Sirnaomics, together with Shanghai Junshi, shall establish a joint development committee consisting of three representatives from each party. The committee shall review, discuss and adopt any proposed development plans, or amendments to any development plan. The development plan sets out the activities for the preclinical studies and clinical trials using the Shanghai Junshi Product and STP705 to be performed that are necessary to obtain regulatory approval for the Combination Therapy. The committee shall oversee all material activities under the development plan, discuss and

approve terminating any development plan and formulate, facilitate and approve regulatory strategy for each party to obtain regulatory approval of the Combination Therapy. US Sirnaomics has the final decision making authority to approve the initiation of the initial development plan and the initiation of the subsequent development plan if the pre-agreed and defined success criteria for the outcome of the initial development plan have been met. If the criteria have not been met, then mutual agreement is required. If the joint development committee fails to reach a decision, disputes are referred to the chief executive officers of the respective parties, and if disputes are not resolved through good faith negotiation, either party may seek to resolve the dispute through arbitration.

Obligations of the Parties: US Sirnaomics is responsible for preparing the development plan and oversight of the activities under the development plan, subject to oversight by the joint development committee. US Sirnaomics and Shanghai Junshi are each obligated to provide clinical supplies of STP705 or the Shanghai Junshi Product at their own expense. US Sirnaomics shall use commercially reasonable efforts to conduct and lead the preclinical and clinical trials under the development plan and is responsible for all material communications with regulatory authorities. If it is preferable for Shanghai Junshi to conduct clinical trials for combination therapy, the parties will coordinate with each other to obtain regulatory approval to conduct clinical trials in that jurisdiction. Each party grants to the other party a right of reference for all data included in the regulatory submissions and regulatory approvals in the territory controlled by such party for use to obtain regulatory approval on clinical trials for combination therapy. Each party has non-exclusive rights to develop Shanghai Junshi Product and STP705, as applicable, with any other third parties with written notice to the other party in 60 days' prior notice.

Intellectual Property Ownership: US Sirnaomics and Shanghai Junshi shall jointly own all intellectual property created, conceived or reduced to practice by either party solely or jointly in the performance of the development activities under the Shanghai Junshi Agreement that relate to the method of use of the Combination Therapy or that consists of clinical data or results (the "Joint Technology"). US Sirnaomics shall own all intellectual property created, conceived or reduced to practice by either party solely or jointly in the performance of the development activities under the Shanghai Junshi Agreement that is not Joint Technology and relates solely to STP705. Shanghai Junshi shall own all intellectual property created, conceived or reduced to practice by either party solely or jointly in the performance of the development activities under the Shanghai Junshi Agreement that is not Joint Technology and relates solely to the Shanghai Junshi Product.

Nature of the rights: Under the Shanghai Junshi Agreement,

a) Shanghai Junshi grants US Sirnaomics a non-exclusive, royalty-free, sublicensable license under intellectual property rights owned or controlled by Shanghai Junshi that are necessary to use the Shanghai Junshi Product in the conduct of the

development activities under the Shanghai Junshi Agreement solely to use the Shanghai Junshi Product in the performance of the development activities to be conducted by US Sirnaomics in accordance with the relevant development plan.

b) US Sirnaomics grants Shanghai Junshi a non-exclusive, royalty-free, sublicensable license under intellectual property rights owned or controlled by US Sirnaomics that are necessary to use STP705 in the conduct of the development activities under the Shanghai Junshi Agreement solely to use STP705 in the performance of the development activities to be conducted by Shanghai Junshi in accordance with the relevant development plan.

Sublicensing: Both parties have the right to sublicense solely to its affiliates and third parties who are performing development activities under the Shanghai Junshi Agreement.

Term and Termination: The Shanghai Junshi Agreement will remain effective until the earlier of the completion of the development activities under the development plan or when there is no development plan in progress and the joint development committee fails to adopt any new development plan within 60 days of the termination of the last development plan. Each party has termination rights for uncured breach of material obligations and bankruptcy of the other party.

Licensing Arrangement with Walvax

In April 2021, Suzhou Sirnaomics, US Sirnaomics (Suzhou Sirnaomics and US Sirnaomics together, the "Sirnaomics Party") and Walvax entered into a co-development and license agreement (the "Walvax Agreement") to co-develop siRNA drugs targeting the influenza virus (the "Target Drug"). Walvax is a biopharmaceutical company specialized in research and development, manufacturing and distribution of vaccines and is an investor in our Series D Financing in 2020. During a program review meeting for the scientific teams from both parties, the management teams of both parties reached a consensus to collaborate on the influenza virus program, to combine the strength from the Sirnaomics Party's RNAi research and development expertise and Walvax's manufacturing and marketing capability, for a novel anti-influenza RNAi therapeutics product (STP702). Because of the Sirnaomics Party's expertise in RNAi therapeutics research and development and Walvax's capability in large scale pharmaceutical product manufacturing and in marketing antiviral vaccines/drugs in China, both parties agreed to have the Sirnaomics Party license out the greater China rights for STP702 for treatment of common influenza virus infection to Walvax, and Walvax has committed to pay an upfront payment plus milestone payment payments. The Sirnaomics Party is responsible for all preclinical research and development operations and Walvax will take over all clinical related responsibility at the appropriate time. As of the Latest Practicable Date, collaboration efforts for STP702 are ongoing. The Sirnaomics Party's scientific team is responsible for all preclinical related studies and IND-enabling study has been initiated, with large quantity of drug product and excipient in production. The vendors for a GLP

pharmacology/toxicity safety study have been identified and engaged for contract negotiation. As of the Latest Practicable Date, no clinical trials related to STP702 been planned or initiated.

Nature of rights: Under the Walvax Agreement, the Sirnaomics Party granted to Walvax the exclusive rights in the Target Drug in mainland China, Hong Kong, Macau and Taiwan (the "Territory"), including but not limited to clinical development, registration, manufacturing, and commercialization. The Sirnaomics Party retains nonexclusive rights to the relevant technologies developed in relevant fields of the Target Drugs and to apply those technologies in the Territory for research purposes only. The Sirnaomics Party retains the exclusive rights for the Target Drug outside the Territory.

Walvax has the first right to match any third-party offer to Sirnaomics to obtain manufacturing rights for the Target Drug outside the Territory if the Sirnaomics Party chooses to outsource drug manufacturing. Walvax also has the first right to match any third-party offer to the Sirnaomics Party to obtain sales and marketing rights for each Target Drug outside the Territory if the Sirnaomics Party chooses outsourcing product sales and marketing.

Sublicensing: Walvax may sublicense its rights to the Target Drug in the Territory to a third party after the IND filing. No further sublicensing by the sublicensee is permitted. The Sirnaomics Party shall have the first right to match the third party's offer to acquire the sublicense rights. The Sirnaomics Party may sublicense its rights to the Target Drug outside the Territory to a third party after the IND filing. Walvax shall have the first right to match the third party's offer to acquire the sublicense rights outside the Territory, including manufacturing and marketing rights.

Obligations of the Parties: The Sirnaomics Party is responsible for conducting all preclinical research and development studies that meet the clinical filing requirements in the Territory, which will be paid for by Walvax. Walvax will be responsible for all clinical filings, clinical trials and new drug applications for the Target Drug in the Territory at its own cost and expense. The parties may cooperate for filing international multicenter clinical trials, with clinical costs outside the Territory paid by the Sirnaomics Party. Walvax will allow the Sirnaomics Party to use all the preclinical research data for the Target Drug for joint clinical applications for international multicenter or separate clinical trial applications outside the Territory and the Sirnaomics Party will allow Walvax to use all the clinical research data for the Target Drug for the BLA filing in the Territory. The Sirnaomics Party will initiate the technology transfer to Walvax of production technology, formulation process and manufacturing technology for the Target Drug upon the completion of a Phase II clinical trial for the Target Drug.

The parties will agree in a separate agreement obligations and budget for Sirnaomics to assist in manufacture of the Target Drug for Phase I and Phase II clinical trials.

Project Management Committee: The Sirnaomics Party, together with Walvax, will establish a project management committee responsible for the project development plan formulation, project progress review, project management, communication and coordination.

Intellectual Property Ownership: The preclinical results related to the Target Drug and any intellectual property rights arising therefrom shall be jointly owned by the parties, regardless of whether independently or jointly developed by the parties, except Sirnaomics will own all the preclinical results developed alone and related intellectual property filed before signing the agreement. After the project is transferred to Walvax, Walvax will own all intellectual property rights arising from the commercialization of the Target Drug, including without limitation product technology and formulation process, and Walvax shall have the right to apply for patents.

Payments: Walvax shall pay to the Sirnaomics Party: (i) a one-time upfront payment of RMB 5 million, (ii) milestone payments upon achieving certain development and regulatory milestones, including filing, acceptance and/or approval of regulatory and marketing applications and completion of clinical trials, in the aggregate amount of RMB 136.5 million, and (iii) royalty payments of middle single-digit percentage of gross sales of the Target Drug. Royalty payments shall be made to Suzhou Sirnaomics and shall be paid for ten years after the commercial launch of the Target Drug in the Territory or until the expiration of the related licensed patents in the Territory covering the Target Drug, whichever is later. The Sirnaomics Party has no payment obligations in favor of Walvax under the Walvax Agreement.

Term and Termination: The agreement shall remain valid until terminated. Either party may terminate the Walvax Agreement on uncured material breach by the other party, bankruptcy of the other party or misrepresentation or violation of a warranty made by either party. If the parties mutually agree to terminate a project or the entire agreement if the preclinical study results are unsatisfactory or the clinical trial results do not meet expectations despite the joint efforts, then Sirnaomics agrees to return to Walvax all unused research and development funds related to the relevant project or the entire agreement.

Licensing Arrangement with the University of Maryland

In December 2020, US Sirnaomics and the University of Maryland (the "University") entered into a patent license agreement (the "University of Maryland Agreement") to license to US Sirnaomics certain patent rights related to a provisional patent application for improved delivery of mRNA with polymers (the "Patent Rights").

Nature of rights: Under the University of Maryland Agreement, the University granted to US Sirnaomics an exclusive, worldwide, sublicensable license during the term to make, use, sell, offer to sell and import any product, service or process covered by one or more claims of the Patent Rights (the "Licensed Product") and practice the patent rights.

The University retains royalty-free rights to practice the Patent Rights for non-commercial purposes and to license such rights to other governmental, academic and non-profit organizations for non-commercial purposes.

Intellectual Property Ownership: Improvements to the Patent Rights are owned according to inventorship. US Sirnaomics holds an option to obtain an exclusive license to any improvement owned solely by the University or the University's rights under any jointly owned improvement, subject to any rights held by third parties in those improvements. US Sirnaomics grants the University a non-exclusive, non-transferable, irrevocable, non-sublicensable and royalty-free license to practice improvements developed solely by US Sirnaomics solely for non-commercial purposes.

Sublicensing: US Sirnaomics may grant sublicenses to third parties subject to payment to the University of certain fees on any sublicensing income.

Diligence Obligations: US Sirnaomics is obligated to achieve certain diligence milestones set forth in a commercialization plan, including completion of preclinical safety and efficacy studies in animal disease model within one year of the effective date, GMP production and animal testing of the first Licensed Product within two and half years, filing an IND (or foreign equivalent) for the first Licensed Product within three and half years, dosing of first patient in a Phase I clinical trial of the first Licensed Product within five years, dosing of first patient in a Phase II clinical trial of the first Licensed Product within seven years, filing an NDA (or foreign equivalent) for the first Licensed Product within eight and a half years, first commercial sale of the first Licensed Product within ten years.

Payments: US Sirnaomics shall pay to the University: (i) a one-time upfront payment of US$20,000, (ii) a milestone payment of US$30,000 following the first patent issuing in any country, (iii) milestone payments upon achieving certain development, regulatory and commercial milestones for the first Licensed Product to reach such milestones in the aggregate amount of up to US$1.65 million, and (iv) royalty payments in low single-digit percentage of net revenues, provided that US Sirnaomics is obligated to pay minimum annual royalties. US Sirnaomics shall also pay to the University royalties payments on sublicense income. US Sirnaomics paid the one-time upfront payment in February 2021, but has not yet achieved any of the milestones triggering further payments. We anticipate that development of our RNAimmune product candidates may trigger further payments to the University.

Term and Termination: The term is effective until earlier termination or expiration. The term of the University of Maryland Agreement expires on a Licensed Product by Licensed Product and country by country basis until the later of (i) expiration of the last to expire of the Patent Rights covering such Licensed Product in such country, (ii) the expiration of any marketing or regulatory exclusivity or (iii) ten years after first commercial sale of the Licensed Product in that country. The term of the University of Maryland Agreement expires 15 years after the effective date with respect to any country in which (a) there were never any

patent rights, (b) there was never any marketing or regulatory exclusivity or (c) there was never a first commercial sale of a Licensed Product. The University may terminate the University of Maryland Agreement on US Sirnaomics' uncured material breach or Sirnaomics' bankruptcy or insolvency. US Sirnaomics may terminate the University of Maryland Agreement as to one or more countries for convenience.

Licensing Arrangement with Mixson

In 2015 and 2019, US Sirnaomics and A. James Mixson ("Mixson") entered into a patent license agreements (the "Mixson Agreement") granting US Sirnaomics a license to certain patent rights relating to polymers used in the PNP formulations of US Sirnaomics (the "Patent Rights"). The Mixson Agreement replaced earlier agreements from 2007 and 2009 between the parties on the same subject matter. Dr. Mixson is a professor at the University of Maryland School of Medicine and serves on the scientific advisory board for US Sirnaomics as an independent third party. US Sirnaomics initially became acquainted with Dr. Mixson through his academic publications and reputation in the field of academic drug discovery and development. US Sirnaomics determined to license the intellectual property developed by Dr. Mixson based on the potential of the histidine-lysine delivery technology developed by Dr. Mixson to provide advantages over the then-current state of the art. Dr. Mixson's current advisory role includes strengthening our understanding of theoretical and practical matters related to histidine lysine copolymers for siRNA and mRNA delivery to the cell and supervising our collaborative research program with the University of Maryland. To the knowledge of our Directors, other than the foregoing business relationships, Dr. Mixson has had no past or present relationship (including, without limitation, business, employment, family, trust, financing or otherwise) with our Group, our shareholders, Directors, senior management or any of their respective associates during the Track Record Period.

Nature of Rights: In 2015 Mixson granted to US Sirnaomics an exclusive, worldwide, sublicensable license to practice the Patent Rights in the Licensed Field including to make, have made, use, sell, offer for sale, import and otherwise exploit any product covered by the Patent Rights (the "Licensed Product"), where the Licensed Field is all therapeutic and non-therapeutic applications for the treatment, prevention, prophylaxis or diagnosis of ocular diseases, skin wound healing and scar, respiratory diseases, CNS diseases, tumor and cancer, organ fibrosis, metabolic diseases and organ transplantation, except for therapeutic and non-therapeutic applications of the following: (1) gene therapy, (2) antimicrobial and anti-infectious uses with histidine-lysine (HK) polymer alone or in combination with non-nucleic acids (such as amphotericin), and (3) use of HK polymer for delivery of non-nucleic acids in the tumor and cancer field. In 2019, Mixson and US Sirnaomics expanded the Licensed Field to include the fields defined in clauses (1) and (3) above.

During the first ten years of the term, Mixson may grant to a third party an exclusive license under the Patent Rights in other fields, provided that if Mixson does not enter into an agreement with a third party, US Sirnaomics shall have a right of first refusal for a licensing opportunity for such other fields.

Mixson retains a non-exclusive, non-transferable right under the Patent Rights for Mixson's own academic and educational purposes. During the first ten years of the term, Mixson has the right to practice the Patent Rights in the Licensed Field and such right includes without limitation the right to make and sell kits for animal models for laboratory and commercial purposes indicated for use in the Other Fields.

Intellectual Property Ownership: While Mixson owns the Patent Rights, the Mixson Agreement is silent regarding ownership of improvements to the Patent Rights, and does not prevent US Sirnaomics from developing improvements. Under U.S. patent laws, absent contractual provisions to the contrary, ownership of improvements vests in the inventor. Accordingly, having discussed with the legal advisors with regard to intellectual property, the Company is of the view that as between Mixson and US Sirnaomics, US Sirnaomics owns all rights in any intellectual property, including patents, invented by US Sirnaomics, whether or not such intellectual property qualifies as an improvement on patents owned by Mixson.

Payments: US Sirnaomics shall pay to Mixson: (i) an upfront fee of US$125,000, (ii) milestone payments upon achieving certain development, regulatory and commercial milestones in the aggregate amount of US$400,000 for each Licensed Product, (iii) royalty payments of less than one percent of net sales and (iv) certain non-statutory fully-vested options of common stock. US Sirnaomics paid the one-time upfront payment in May 2019, but has not yet achieved any of the milestones triggering further payments. We expect to make a payment of US$50,000 to Mixson during the second half of 2021 or first quarter of 2022 based on the achievement of a product development milestone.

Term and Termination: The term of the Mixson Agreement extends until the expiration of the last valid claim of the Patent Rights. Either party has the right to terminate the Mixson Agreement for the other party's uncured material breach. US Sirnaomics has the right to terminate the Mixson Agreement for convenience.

Collaboration Agreement with Guangzhou Xiangxue

In October 2010, Suzhou Sirnaomics and US Sirnaomics entered into a collaboration agreement with Guangzhou Xiangxue regarding the joint development of a small interfering RNA drug (STP705) for the treatment of Hypertrophic Scar (HTS) with a market right for greater China territory, including mainland China, Hong Kong, Macau and Taiwan. Under the collaboration agreement, Guangzhou Xiangxue was committed to an investment of RMB15.0 million into the project, while Suzhou Sirnaomics agreed to provide the relevant intellectual property and research and development team support equivalent to an aggregated value of RMB7.0 million. Consequently, Guangzhou Xiangxue and Suzhou Sirnaomics owned 68.18% and 31.82% interests in the collaboration respectively.

In November 2013, after investing RMB12.0 million into the collaboration, Guangzhou Xiangxue decided to provide further funding in the form of advances of RMB4.8 million (equivalently to approximately US$0.7 million) in proportion to our respective interests in the

collaboration. Suzhou Sirnaomics and US Sirnaomics therefore entered into a supplemental agreement with Guangzhou Xiangxue, using these advances to fund the project. In October 2014, Guangzhou Xiangxue and Suzhou Sirnaomics jointly filed an IND application to China Food and Drug Administration (CFDA) using STP705 to treat HTS. In April 2017, Guangzhou Xiangxue and Suzhou Sirnaomics obtained an approval from CFDA to conduct a Phase I clinical trial for the treatment of HTS using STP705 in China.

In the meantime, US Sirnaomics independently filed an IND application with US FDA in October 2016 for a clinical trial using STP705 to treat HTS, and received IND approval for a Phase IIa clinical trial in November 2016. Since then, US Sirnaomics pushed this Phase IIa clinical trial forward and expanded it into the skin cancer application. Since US FDA approval for the IND for STP705 to treat HTS was received earlier and allowed STP705 to directly enter into the Phase IIa clinical trial, we decided to permit the IND for the Phase I clinical trial approved by CFDA to lapse in April 2020.

In order to strategically seek full control over the project rights for STP705 in China and reach a full closure of the collaboration efforts between Suzhou Sirnaomics and Guangzhou Xiangxue, in October 2020, we entered into a termination agreement with Guangzhou Xiangxue, where Guangzhou Xiangxue agreed to surrender all its relevant project rights regarding STP705 for the treatment of HTS in mainland China, Hong Kong, Macau and Taiwan. Pursuant to the termination agreement, we agreed to pay Guangzhou Xiangxue a total amount of RMB57.8 million (equivalent to approximately US$8.5 million) and as a result we now have 100% of the rights and interests for STP705 for the treatment HTS in mainland China, Hong Kong, Macau and Taiwan under the agreement. The RMB57.8 million covered our settlement for advances of RMB4.8 million from Guangzhou Xiangxue in 2013 under the supplemental agreement. The parties' respective obligations regarding development did not survive termination of the collaboration agreement and supplemental agreement with Guangzhou Xiangxue.

Of the consideration of RMB57.8 million, Suzhou Sirnaomics agreed to (1) pay RMB12.0 million in cash to Guangzhou Xiangxue, and (2) issue a convertible loan in the amount of RMB45.8 million in 2020 which was later converted into Series D Preferred Shares.

In our view, the prior collaborations between Suzhou Sirnaomics and Guangzhou Xiangxue have provided strong support for Sirnaomics' growth in its early days. The termination of this collaboration is a strategic move allowing Sirnaomics to obtain full control over the research and development programs and related rights for STP705. We believe such termination has no material adverse impact on our business operations, financial performance, intellectual property position, or future growth. Also, according to our communications with Guangzhou Xiangxue, they agreed that this approach is the best to maximize the benefits of both parties and collaborated with us to complete related transactions with their best efforts.

INTELLECTUAL PROPERTY RIGHTS

Intellectual property rights, including patents and trade secrets are critical to our business and in biotechnology in general. Our success depends in part on our ability to obtain and maintain proprietary intellectual property protection for our drug candidates, discoveries, product development technologies, inventions, improvements and know-how, whether developed internally or acquired or licensed from third parties. Our success also depends in part on our ability to defend and enforce our patents including any patent that we have or may issue from our patent applications, preserve the confidentiality of our trade secrets and other confidential or proprietary information, and operate without infringing, misappropriating or otherwise violating intellectual property rights of other parties.

We rely on a combination of patent, and other intellectual property protection laws in China and the U.S., including trade secrets and fair trade practice, as well as confidentiality procedures and contractual provisions to protect our intellectual property with respect to our drug candidates and technology. Despite our precautions, third parties may infringe our intellectual property rights. Unauthorized use of our intellectual property by third parties and the expenses that we may incur in protecting our intellectual property rights from such unauthorized use may adversely affect our business and results of operations. See "Risk Factors – Risks Relating To Our Intellectual Property Rights – We may also initiate lawsuits to protect or enforce our patents and other intellectual property, which could be expensive, time-consuming and unsuccessful."

The area of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting any of our platforms, product candidates, discovery programs and processes. Furthermore, the terms of individual patents depends upon the legal term of the patents in the countries in which they are obtained and extend for varying periods depending on the date of filing of the patent application or the date of patent issuance. In most countries in which we file, the invention patent term is 20 years from the earliest non-provisional filing date. The life of a patent, and the protection it affords, is therefore limited and once the patent life of our issued patents has expired, we may face competition, including from other competing technologies. In China, the expiration of an invention patent is 20 years from its filing date, the expiration of a utility model patent is ten years from its filing date and the expiration of an industrial design patent is 15 years from its filing date. The Amendment to the PRC Patent Law introduces patent extensions to patents of new drugs that launched in the PRC, which may enable the patent owner to submit applications for a patent term extension. The precise length of any such extension is uncertain though the extended length has a maximum of five years. For more information regarding the risks related to our intellectual property, see "Risk Factors – Risks Relating To Our Intellectual Property Rights."

Based on the freedom to operate (FTO) analysis of our core product (STP705), we are not aware of any issued patents that may affect our rights to conduct research and development or commercialize our core product in China or the U.S. FTO analysis is a patent investigation, based on a search of patent databases, that is commonly used to determine whether any existing patents cover a company's product, and whether that product would infringe any existing patents. However, we cannot provide any assurance that all relevant third party patents were identified or that conflicting patents will not be issued in the future. For more information, see "Risk Factors – Risks Relating To Our Intellectual Property Rights."

From the early establishment of our company, we in-licensed patents pursuant to an exclusive, worldwide license under patent rights from Dr. A. James Mixson, a professor at the University of Maryland School of Medicine who also currently serves on our scientific advisory board as an independent third party. Of the three patents that were granted during the term of the agreement, all were granted in the U.S. and two out of the three of of those patents are now expired. The subject matter of these patent served as a jumping off point for our further development of our PNP delivery platform. Both expired patents broadly covered: (i) branched transport polymers containing a high proportion of histidine residues, (ii) pharmaceutical compositions containing the polymers and a pharmaceutical agent such as a nucleic acid, and (iii) methods of in vivo therapy by injection of the pharmaceutical compositions. The claims of the expired patents also covered the specific polymers used our products in clinical development. These expired patents had limited claims using the specific polymers for nucleic acid delivery generally. The claims of the third patent (scheduled to expire in 2026) recite methods of transfecting cells (i.e., delivering nucleic acids into the cell or infecting the cell with nucleic acids) with compositions containing siRNA and specific HKP molecules. Patents cannot be extended after expiration. Our products that are currently under development do not contain the specific HKP molecules recited in the claims although we may elect to use such HKP molecules in future products. To strengthen the protection of our PNP technology platform, we have filed multiple patent applications using modifications of peptide polymers with targeting ligands, chemodrugs, other amino acids and improved formulation methods. We also filed a number of patent applications (and have been issued patents) specifically for siRNA therapeutics in defined therapeutic areas, e.g. anti-cancer, anti-fibrosis and anti-viral, and others. Despite the fact that the now expired patents covered compositions that formed the basis of our PNP delivery platform, given that the patents are now in the public domain and that we have filed our own patent applications that aim to protect new developments and advancements built on top of and improving the original technology covered by the expired patents, these expired patents are therefore not material to our PNP delivery platform now enhanced by virtue of our research and development efforts. None of our patent applications conflicts or will conflict with any of our collaboration and licensing arrangements, including our licensing arrangement with Dr. Mixson.

Our PNP delivery platform used for STP705, STP707 and our other product candidates is an enhanced delivery platform built on top of the technology in-licensed from Dr. Mixson. Our research and development efforts built on the in-licensed technology to develop it into an

effective pharmaceutical delivery platform. In essence, the key improvements that have been made to the in-licensed technology were to take technology that is useful as a laboratory tool and develop it into a pharmaceutical delivery platform that can be combined with siRNAs to be safely administered to humans to achieve a therapeutic effect as a pharmaceutical product. We established high purity manufacturing processes and developed pharmaceutical-level formulation technology, including through the use of microfluidic technology. We developed specific formulations for local administration, including topical, intradermal and intratumoral delivery, and systemic administration including intravenous, subcutaneous and airway delivery. We have devoted our research and development efforts to developing improved pharmaceutical compositions containing the polymers described in the now-expired patents, and improved methods for making those compositions. More specifically, our efforts have resulted in, inter alia, the development of methods for formulating siRNAs into nanoparticles of a desired size distribution and zeta potential, which affects the pharmaceutical properties of the compositions. These methods include (i) optimizing the HKP:siRNA ratios used during nanoparticle formulation; (ii) determining the additional excipients required to prepare the compositions; and (iii) how to mix the various components of the compositions to produce pharmaceutically useful PNP compositions having the desired particle size, size distribution and zeta potential. In addition, we have developed methods of preparing PNP compositions that avoid aggregation of the nanoparticles, which prevents the significant toxicity that can result from nanoparticle aggregation. Our developments covering the PNP delivery platform itself (without regard to any particular product or product family) are covered by three pending patent applications that were filed in 2021 and are exclusively owned by us. We believe that each of these improvements represents a significant advance over the technology described in the Mixson patents.

In addition to our patents and patent applications, we also rely on confidential and proprietary know-how and trade secret protection for proprietary aspects of the manufacturing and pharmaceutical formulation technology and we are also in the process of filing further patent applications on aspects that we deem strategically appropriate for patent protection. Our filings include applications that cover improved manufacturing methods and improved pharmaceutical formulations that relate to our PNP delivery platform. The in-licensed patents that cover certain pharmaceutical compositions of our PNP delivery platform expired in 2021 (and the third in-licensed patent will expire in 2026) and therefore have entered the public domain. Anyone in the public (including us) may use the inventions claimed in the patents without Dr. Mixson's consent. According to the CIC Report, as of the Latest Practicable Date, no other biopharmaceutical companies are engaged in the research and development of RNA therapeutics using technologies that were formerly protected by the two expired patents. Given that we had the benefit of an exclusive license under the two now-expired patents, no third parties could conduct any activities under those patents without our authorization. As of the Latest Practicable Date, we have not authorized any third parties to conduct any activities under those patents. We no longer rely on the expired patents for the further research and development of our PNP delivery platform, but instead rely on our pending patent applications that we have filed in respect of our new advances and developments to our PNP delivery

platform. We expect that the expiration of those patents will have no material adverse impact on the Group's business operations, finance performance and prospects going forward because we continue to have the right to make and use the technology covered by the now expired patents (and will continue to after the 2026 expiration of the third in-licensed patent) and our business and products, including our core product, rely on a combination of our own patents and patent applications and other intellectual property protection laws, including trade secrets and fair trade practice. We believe that the combination of patent protection directed to each of our product candidates individually as well as our patent protection, trade secret and proprietary know-how in our PNP delivery platform will provide sufficient protection to prevent competitors from developing and commercializing copies of our product candidates in the future.

We have a comprehensive portfolio of patents to protect our drug candidates and technologies. As of the Latest Practicable Date, we owned (i) nine issued patents in China, (ii) nine issued patents in the U.S., (iii) two issued patents in Europe (validated in 11 and eight countries, respectively), and (iv) 119 pending patent applications, including 19 Chinese patent applications, 43 U.S. patent applications (including 32 U.S. provisional patent applications), eight patent applications under the Patent Cooperation Treaty, six patent applications in Europe and 43 patent applications in other jurisdictions. Our patents and patent applications span methods of delivering RNAi triggers and mRNA to cells, compositions of matter and devices used in our RNAi and mRNA delivery platforms, siRNA or RNAi trigger compositions, manufacturing processes, usage and indications. Our owned issued patents and any patents issuing from our pending patent applications are scheduled to expire on various dates from 2024 through 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees. Further details on certain segments of our patent portfolio are included below.

PNP Delivery Platform

We exclusively license an issued patent from Dr. James Mixson and own three pending patent applications that cover our PNP delivery platform. As of the Latest Practicable Date, our licensed patent portfolio included one issued patent in the U.S. directed to compositions and methods of use and we own three pending U.S. provisional patent applications directed to methods of manufacturing pharmaceutical compositions. More particularly, the patent and patent applications are directed to pharmaceutical agent delivery compositions comprising histidine-lysine polymers, methods of making and delivering the compositions; methods of delivering siRNA to cells using a histidine-lysine polymer carrier. The expected expiration for the issued patent is 2026 and for any patents that may issue from the currently pending patent applications is 2042.

GalAhead™ Delivery Platform

With regard to our GalAhead™ delivery platform that includes the GalNAc ligand, as of the Latest Practicable Date, we owned 26 patent applications, including two pending patent applications in China, two pending patent applications in the U.S. and 22 pending patent applications in other jurisdictions directed to compositions, methods of use and processes to make the compositions. The expected expiration for any patents that may issue from the currently pending patent applications is 2039, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

PDoV-GalNAc RNAi Delivery Platform

With regard to our PDoV-GalNAc RNAi delivery platform that includes the GalNAc ligand, as of the Latest Practicable Date, we owned two pending patent applications, including one pending patent application in the U.S. and one patent application under the Patent Cooperation Treaty directed to compositions and methods of use. The expected expiration for any patents that may issue from the currently pending patent applications is 2040, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP705/707

With regard to our STP705/707 product candidates, as of the Latest Practicable Date, we owned two issued patents in the U.S., and 20 pending patent applications, including three Chinese patent applications, seven U.S. patent applications (including five U.S. provisional patent applications), one European patent application and nine patent applications in other jurisdictions. Our patents and patent applications covering STP705/707 are directed to the drug product compositions and their methods of use. More particularly, our patents and patent applications are directed to the RNA sequences that comprise the drug substance (two patent families*), pharmaceutical formulations containing those RNA sequences (seven patent families), methods of using the combination of RNA sequences targeting the combination of TGFß1 and COX2 genes for the treatment of wound healing (e.g., HTS, keloid scarless healing (two patent families)) and cancer treatments (e.g., skin cancers such as isSCC) (two patent families). All of the foregoing cover what we view as the key characteristics of STP705 and STP707 separate from the PNP Delivery Platform. The expected expiration for the issued patents and any patents that may issue from the pending patent applications range from 2029 to 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP355

With regard to our STP355 product candidate, as of the Latest Practicable Date, we owned one Chinese patent application and one U.S. provisional patent application. Our patent

* Several of the patents and patent applications include subject matter that overlaps more than one of the categories.

applications covering STP355 are directed to the drug composition, drug product composition and methods of use. The expected expirations for any patents that may issue from the pending patent application range from 2041 to 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fee.

STP369

With regard to our STP369 product candidates, as of the Latest Practicable Date, we owned one pending U.S. provisional patent application. Our patent applications covering STP369 are directed to the drug composition, drug product composition and methods of use. The expected expiration any patents that may issue from the pending patent application is 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP779

With regard to our STP779 product candidate, as of the Latest Practicable Date, we owned one pending U.S. provisional patent application. Our patent application covering STP779 is directed to the drug composition, drug product composition and methods of use. The expected expiration any patents that may issue from the pending patent application is 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP302

With regard to our STP302 product candidate, as of the Latest Practicable Date, we owned one issued patent in Europe (validated in eight countries), and two pending patent applications, including one pending patent application in China and one pending patent application in the U.S. Our issued patents and pending patent applications covering STP302 are directed to the drug product composition and methods of use. The expected expiration for the issued patents and any patents that may issue from the pending patent applications range from 2035 to 2036, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP902

With regard to our STP902 product candidate, as of the Latest Practicable Date, we owned one issued U.S. patent. Our patent covering STP902 is directed to the drug composition and drug product composition. The expected expiration for this patent is 2030 without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP702

With regard to our STP702 product candidate, as of the Latest Practicable Date, we owned one issued patent in the U.S. and one pending Chinese patent application. Our patents covering STP702 are directed to the drug product compositions and their methods of use. The expected expiration for the issued patents and pending patent application range from 2033 to 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP908

With regard to our STP908 product candidate, as of the Latest Practicable Date, we owned three pending patent applications, including two pending patent application in the U.S. (including one U.S. provisional patent application) and one patent application under the Patent Cooperation Treaty. Our patent applications covering STP908 are directed to the drug composition, drug product composition and methods of use. The expected expiration for any patents that may issue from the currently pending patent applications is 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

RIM730

With regard to our RIM730 product candidate, as of the Latest Practicable Date, we owned three pending U.S. patent applications (including two U.S. provisional patent applications), and one patent application under the Patent Cooperation Treaty. Our patent applications covering RIM730 are directed to the drug composition, drug product composition and methods of use. The expected expiration any patents that may issue from the pending patent applications is 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP909

With regard to our STP909 product candidate, as of the Latest Practicable Date, we owned one issued patent in the U.S. and one pending patent application in China. Our issued patent and pending patent application covering STP909 are directed to the drug product composition and methods of use. The expected expiration the issued patent and any patents that may issue from the pending patent application range from 2031 to 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP122G

With regard to our STP122G product candidate, as of the Latest Practicable Date, we owned two pending U.S. provisional patent applications. Our patent applications covering STP122G is directed to the drug composition, drug product composition and methods of use. The expected expiration for any patents that may issue from the pending patent applications is 2042 without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP133G

With regard to our STP133G product candidate, as of the Latest Practicable Date, we owned three pending U.S. provisional patent applications. Our patent applications covering STP133G are directed to the drug composition, drug product composition and methods of use. The expected expiration for any patents that may issue from the pending patent applications is 2042 without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP135G

With regard to our STP135G product candidate, as of the Latest Practicable Date, we owned two pending patent applications including one pending patent application in China and one U.S. provisional patent application. Our patent applications covering STP135G are directed to the drug product composition and methods of use. The expected expiration any patents that may issue from the pending patent applications range from 2041 to 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP144G

With regard to our STP144G product candidate, as of the Latest Practicable Date, we owned one pending U.S. provisional patent application. Our patent application covering STP144G is directed to drug product composition and methods of use. The expected expiration of any patents that may issue from the pending patent application is 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

STP155G

With regard to our STP155G product candidate, as of the Latest Practicable Date, we owned two pending patent applications including one pending patent application in China and one U.S. provisional patent application. Our patent applications covering STP155G are directed to the drug product composition and methods of use. The expected expiration any patents that may issue from the pending patent applications range from 2041 to 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

The following table summarizes the details of the material granted patents and filed patent applications owned by us or licensed to us on our clinical stage product candidates and certain preclinical product candidates (Unless otherwise indicated, all patents and patent applications are invention patents or applications therefor):

Subject Area	Title	Country	Status	Expiration Date[1]	Applicant
PNP delivery platform	Highly Branched HK Peptides As Effective Carriers of siRNA	U.S.	Issued	2026	A. James Mixson
PNP delivery platform	Improved Methods For Preparing Nanoparticle Compositions Containing Histidine-Lysine Copolymers	U.S.[2]	Pending	2042	US Sirnaomics
PNP delivery platform	Nanoparticle Pharmaceutical Compositions With Reduced Nanoparticle Size And Improved Polydispersity Index	U.S.[2]	Pending	2042	US Sirnaomics
PNP delivery platform	Improved Nanoparticle Formulations Formed From Histidine-Lysine Copolymers	U.S.[2]	Pending	2042	US Sirnaomics
GalAhead delivery platform	Multi-Targeting Nucleic Acid Constructs Composed Of Multiple Oligonucleotides That Modulate Gene Expression Through Complimentary Interactions With Targets	CN, U.S., AU, BR, CA, EP, IL, IN, JP, KR, NZ, RU, ZA	Pending	2039	US Sirnaomics
GalAhead delivery platform	Miniaturized Hairpin RNAi Triggers (mxRNA) and Methods of Uses Thereof	CN, U.S., AU, BR, CA, EP, IL, IN, JP, KR, NZ, RU	Pending	2039	US Sirnaomics
PDoV-GalNAc delivery platform	Peptide Docking Vehicle for Targeted Nucleic Acid Delivery	U.S., PCT	Pending	2040	US Sirnaomics
STP705	Multi-Targeted RNAi Therapeutics for Scarless Wound Healing of Skin	U.S.	Issued	2029	US Sirnaomics

Subject Area	Title	Country	Status	Expiration Date[1]	Applicant
STP705, STP707	Combinations of TGFß and COX-2 Inhibitors and Methods for Their Therapeutic Application	U.S.	Issued	2031	US Sirnaomics
STP705, STP707	Pharmaceutical Compositions and Methods of Use for Activation of Human Fibroblast and Myofibroblast Apoptosis	U.S., CN	Pending	2037	US Sirnaomics & Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine
STP707	Silencing TGFBeta 1 and Cox2 Using siRNAs Delivered in Combination with Immune Checkpoint Inhibitors to Treat Cancer	U.S., CN, EP, ZA	Pending	2039	US Sirnaomics
STP705	The Composition of Matter and Methods for Treatment of Skin Cancers by RNAi Therapeutics	U.S.[2]	Pending	2042	US Sirnaomics
STP705, STP707	An siRNA Drug Composition and Formulation for Treatment of Skin Cancers	CN	Pending	2041	US Sirnaomics; Suzhou Sirnaomics; Guangzhou Sirnaomics
STP705	siRNA-Copolymer Compositions and Methods of Use for the Treatment of Liver Cancer	U.S.[2]	Pending	2042	US Sirnaomics
STP707	Methods for Prophylactic and Therapeutic Treatment of 2019-nCoV using siRNAs against TGFB1 and Cox2	U.S.[2]	Pending	2042	US Sirnaomics
STP705	Methods for inducing adipose tissue remodeling using RNAi Therapeutics	U.S.[2]	Pending	2042	US Sirnaomics
STP705	Methods for inducing adipose tissue remodeling using RNAi Therapeutics	U.S.[2]	Pending	2042	US Sirnaomics

Subject Area	Title	Country	Status	Expiration Date[1]	Applicant
STP355	Composition and use of siRNAs against VEGFR2 and TGF-beta1 in combination theraphy for cancer	U.S.[2]	Pending	2042	US Sirnaomics
STP 355	Small interfering ribonucleic acid-containing pharmaceutical composition for the treatment of multiple tumors	CN	Pending	2041	Suzhou Sirnaomics
STP369	Methods of cancer treatment by delivery of siRNAs against BCLxL and MCL1 using a polypeptide nanoparticle	U.S.[2]	Pending	2042	US Sirnaomics
STP779	Combinations of siRNAs with siRNAs against SULF2 or GPC3 for use in treating cancer	U.S.[2]	Pending	2042	US Sirnaomics
STP302	A Pharmaceutical Composition and its Therapeutic Application Thereof	CN	Pending	2035	Suzhou Sirnaomics
STP302	Pharmaceutical Composition and Applications Thereof	U.S. BE, DK, DE, FR, CH, ES, IT, GB	Pending Issued	2036	US Sirnaomics
STP902	Compositions and Methods Using siRNA Molecules and siRNA Cocktails for the Treatment of Breast Cancer	U.S.	Issued	2030	US Sirnaomics
STP702	Compositions and Methods for "Resistance-Proof" siRNA Therapeutics for Influenza	U.S.	Issued	2033	US Sirnaomics

Subject Area	Title	Country	Status	Expiration Date[1]	Applicant
STP702	siRNA Drug, Pharmaceutical Composition, siRNA-small Molecule Drug Conjugates and its Application	CN	Pending	2041	Suzhou Sirnaomics; Guangzhou Sirnaomics
STP908	Composition And Methods Of RNAi Prophylactics And Therapeutics For Treatment Of Severe Acute Respiratory Infection Caused By 2019 Novel Coronavirus (2019-nCoV)	U.S., PCT	Pending	2041	US Sirnaomics
STP908	Methods for prophylactic and therapeutic treatment of 2019-nCoV using siRNAs against ORF1AB and N-protein	U.S.[2]	Pending	2042	US Sirnaomics
RIM730	Composition And Methods Of mRNA Vaccines Against Novel Coronavirus Infection	U.S., PCT	Pending	2041	RNAimmune
RIM730	Composition and Methods of mRNA Vaccines Against Novel Coronavirus Infection	U.S.[2]	Pending	2041	RNAimmune
RIM730	Composition and Methods of mRNA Vaccines Against Novel Coronavirus Infection	U.S.[2]	Pending	2042	RNAimmune
STP909	siRNA Compositions and Methods for Treatment of HPV and Other Infections	U.S.	Issued	2031	US Sirnaomics
STP909	A nucleic acid polypeptide nanomedicine for the treatment and prevention of HPV infection	CN	Pending	2041	US Sirnaomics; Suzhou Sirnaomics; Guangzhou Sirnaomics

Subject Area	Title	Country	Status	Expiration Date[1]	Applicant
STP122G	Products and Compositions	U.S.[2]	Pending	2042	US Sirnaomics
STP122G	Products and Compositions	U.S.[2]	Pending	2042	US Sirnaomics
STP133G	Products and Compositions	U.S.[2]	Pending	2042	US Sirnaomics
STP133G	Products and Compositions	U.S.[2]	Pending	2042	US Sirnaomics
STP133G	Products and Compositions	U.S.[2]	Pending	2042	US Sirnaomics
STP144G	Products and Compositions	U.S.[2]	Pending	2042	US Sirnaomics
STP135G	Compositions and methods for inhibiting expression of PCSK9	U.S.[2]	Pending	2042	US Sirnaomics
STP135G	Compositions and methods for inhibiting expression of PCSK9	CN	Pending	2041	US Sirnaomics; Suzhou Sirnaomics
STP155G	Targeted Nucleic Acid Therapy For Hepatitis B	U.S.[2]	Pending	2042	US Sirnaomics
STP155G	A drug composition and formulation targeting HBV	CN	Pending	2041	US Sirnaomics; Guangzhou Sirnaomics

1 Patent expiration date is estimated based on current filing status, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other government fees.

2 Provisional patent application.

As of the Latest Practicable Date, our Directors confirm that we were not involved in any proceedings in respect of, and we had not received notice of any claims of infringements of, any third-party intellectual property that are threatened or pending.

PROCUREMENT

We procure raw materials, as well as technical services, equipment and infrastructure construction services needed for the operation of our business from qualified suppliers. The main raw materials that we procure for manufacturing and our clinical trials include oligonucleotides and polypeptides. As of the Latest Practicable Date, our product candidates for clinical trials were supplied by third-party CMOs.

In addition, we procure equipment for the development and manufacturing of our product candidates from reputable manufacturers and suppliers. We also procure technical services,

such as CRO services and consulting services that support our clinical trials and preclinical studies. See "– Research and Development – Engagement of Third Parties in Research and Development."

We engage experienced and qualified third parties such as CROs, CDMOs and consultants to support our research and clinical trials. We supervise these third-party service providers closely to ensure their compliance with our quality control procedures and applicable laws and the integrity of the data resulting from our trials and studies. See "– Suppliers."

MANUFACTURING AND QUALITY CONTROL

Chemistry, Manufacturing and Control

Since our inception, we have established an internal CMC team which is currently led by Dr. Zhifeng Long, our Chief Development Officer. Our CMC capability includes the following functions: (i) delivery platform research and development and optimization; (ii) formulation development; (iii) analytical sciences – our analytical science team implements a science-driven, phase-appropriate and commercial oriented approach to the development and application of both classic and state-of-the-art analytical techniques and tools throughout the development life cycle of each of our product candidates, including but not limited to development and validation of analytical methods for drug substance and drug product, technical transfer of process and analytical methods, establishment of specifications, testing and releasing of each batch of drug product; and (iv) quality control and assurance – with well-documented and comprehensive quality system, the quality control and assurance team is responsible for testing and verifying the product quality with predefined standards to assure the quality of all the batches, manufactured at every stage of manufacturing/processing drug substance and drug products.

We currently work with qualified CMOs to manufacture product candidates for preclinical and clinical supply. We have established GMP-compliant manufacturing processes in the U.S. with CMOs accredited by the U.S. FDA, and these CMOs will contribute, in total, an annual capacity of at least two million vials per year to our manufacturing process. We have adopted procedures to ensure that the production qualifications, facilities and processes of our CMOs comply with the relevant regulatory requirements and our internal guidelines. We select our CMOs by reviewing a number of factors, including their qualifications, relevant expertise, production capacity and product quality. As of the Latest Practicable Date, we have not experienced any difficulties in engaging our CMOs. As we maintain good relationships with the CMOs we worked with and there exist adequate alternative sources for such CMOs, we do not foresee any difficulties in engaging qualified CMOs in the future. To monitor and evaluate service performed by our CMOs, we set a series of pre-defined specifications on in-process control and release tests, and review manufacturing related documents including batch records and quality control test results to ensure specifications are met.

Our Manufacturing Facilities

We recently completed building our pilot manufacturing facility in Guangzhou, which is expected to have an anticipated annual production capacity of 50,000 vials of lyophilized doses for injection, which we expect to be sufficient to support all clinical trials we have in our current planning. We have not yet commenced production during the Track Record Period, but anticipate commencing GMP production in the first quarter of 2022.

Our Guangzhou facility will be capable of GMP-compliant manufacturing of our pipeline products, including formulation, fill and finish, test and release and will be sufficient to support our clinical trials in China, and potentially to supply our clinical trials globally in the future. We are currently planning to build a commercial scale manufacturing facility in China which will provide products for future commercialization needs. Our manufacturing team in Guangzhou consists of 18 employees and consultants as of the Latest Practicable Date, including quality control and quality assurance functions to support GMP manufacturing. Our manufacturing facilities are equipped with systems and equipment from industry leading, highly reputable manufacturers and suppliers around the world.

We expect to have in-house capabilities to manufacture our drug candidates by the first half of 2022. We expect our manufacturing facilities in Guangzhou will have sufficient capacity to meet our clinical manufacturing needs in the foreseeable future.

To secure our product supply and meet potential increasing business demands, we may also adopt a hybrid manufacturing model in the future that primarily utilizes our in-house manufacturing capabilities while employing CMOs for the manufacturing of our drug candidates. We expect that the manufacturing capacity of our new facility as well as our cooperation with qualified CMOs can provide sufficient supply for our clinical trials and meet the commercial sales demands of our drug candidates.

COMMERCIALIZATION AND BUSINESS DEVELOPMENT

Commercialization

We believe the scale and effectiveness of our commercial operation will be crucial to our business. We intend to commercialize our drug candidates, if approved, by utilizing both direct sales force and strategic partnerships to achieve geographical and channel coverage.

We will conduct marketing activities in both China and the U.S. We expect to facilitate academic engagement and education around our products by establishing relationships with KOLs, hospitals, and renowned doctors through clinical trials, R&D collaboration, and academic conferences. We also intend to enter into strategic partnerships with biopharmaceutical companies with advantageous sales and marketing networks. We plan to build up our sales and marketing team by recruiting professionals with extensive industry

knowledge and biopharmaceutical marketing skills to engage in the academic promotion, marketing, commercialization and channel management of our pipeline products. While our product candidates represent a relatively new class of therapeutics, RNAi therapeutics, our sales and marketing team will consist of medical directors and medical science liaisons who would be responsible for medical education, medical conference management and investigator-initiated study support, which facilitates the advocacy of our product candidates as RNAi therapeutics. Team members shall also be responsible for exploring collaboration patterns and promoting collaboration with strategic partners, as well as the academic promotion of our products to hospitals and doctors, which helps expand our distribution channels to commercialize our products. Along with the clinical development of our pipeline products, we will schedule the recruitment, training and evaluation of our sales and marketing team in accordance with the clinical development progress of our pipeline products, aiming to ensure the timely commercialization of our pipeline products once we obtain relevant approvals.

We are also evaluating partnership options to maximize market potential of our products. We intend to seek partners by setting comprehensive selection criteria, primarily including commercialization teams with extensive biopharmaceutical industry backgrounds, superior track record in commercialization partnership, and recognition of our vision and commitment to our pipeline products. We aim to gain market coverage by leveraging our current and future business partners' expertise and business network.

Business Development

Our strategy and business development team explores global and local cooperation opportunities with other industry players. These opportunities may include co-development, in-licensing and out-licensing arrangements. We have a proven track record of collaborating with biopharmaceutical and biotechnology companies across the globe which underscores our industry recognition and paves the way for long-term collaborations. See "– Collaboration and Licensing Arrangements."

SUPPLIERS

Our suppliers are primarily reputable CROs, CMOs, CDMOs and research and medical institutions with whom we collaborate on preclinical and clinical trials in China and overseas, and from whom we procure raw materials and equipment to support the manufacturing of our drug products. We select our suppliers by taking into account a number of factors, including their qualifications, industry reputation, cost competitiveness and compliance with relevant laws and regulations. In 2019, 2020 and the nine months ended September 30, 2021, our purchases from our five largest suppliers in the aggregate accounted for 35.3%, 42.7% and 38.5% of our total purchases, respectively, while purchases from our largest supplier in each period accounted for 11.2%, 16.7% and 12.0% of our total purchases, respectively.

The following table sets forth certain information of our five largest suppliers for each period during the Track Record Period:

Supplier	Supplier type	Purchase amount (US$ in thousands)	Percentage of total purchase
Year ended December 31, 2019			
Supplier A	CRO	704	11.2%
Supplier B	CDMO	523	8.4%
Supplier C	CDMO	385	6.2%
Supplier D	Lab equipment and consumables supplier	318	5.1%
Supplier E	CMO	276	4.4%
Total		2,206	35.3%
Year ended December 31, 2020			
Supplier F	CDMO	1,907	16.7%
Supplier C	CDMO	1,160	10.2%
Supplier B	CDMO	621	5.4%
Supplier G	CRO	618	5.4%
Supplier H	Manufacturing equipment supplier	571	5.0%
Total		4,877	42.7%
Nine months ended September 30, 2021			
Supplier I	CDMO	2,028	12.0%
Supplier F	CDMO	1,539	9.1%
Supplier G	CRO	1,199	7.1%
Supplier A	CRO	901	5.3%
Supplier J	CRO	846	5.0%
Total		6,513	38.5%

All of our five largest suppliers during the Track Record Period were Independent Third Parties. None of our Directors, their respective associates or any shareholder who, to the knowledge of our Directors, owned more than 5% of our issued share capital, had any interest in any of our five largest suppliers during the Track Record Period.

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

CUSTOMERS

During the Track Record Period and up to the Latest Practicable Date, we had not generated any revenue from product sales and do not expect to generate any revenue from product sales before the commercialization of one or more of our drug candidates.

COMPETITION

The biopharmaceutical industry is characterized by rapid market growth, fierce competition and a strong emphasis on proprietary drugs. While we believe that our strong research and development capabilities enable us to establish a favorable position in the industry, we encounter competition from international and China-based biopharmaceutical companies and specialty pharmaceutical and biotechnology companies of various sizes, as well as academic institutions and research institutions. Any drug candidates that we successfully develop and commercialize will compete with existing drugs or any new drugs that may become available in the future. See "Industry Overview."

LAND AND PROPERTIES

Our headquarters office is located at 401 Professional Drive, Gaithersburg, Maryland, U.S. We lease properties in China and the U.S. As of the Latest Practicable Date, none of the properties held or leased by us had a carrying amount of 15% or more of our consolidated total assets. According to section 6(2) of the Companies Ordinance (Exemption of Companies and Prospectuses from Compliance with Provisions) Notice, this prospectus is exempt from the requirements of section 342(1)(b) of the Companies (Winding up and Miscellaneous Provisions) Ordinance to include all interests in land or buildings in a valuation report as described under paragraph 34(2) of the Third Schedule to the Companies (Winding up and Miscellaneous Provisions) Ordinance.

Owned Properties

As of the Latest Practicable Date, we did not own any property in China or in the U.S.

Leased Properties

As of the Latest Practicable Date, we leased 12 properties in China with an aggregate gross floor area of approximately 5,923.36 sq.m., which were primarily used for offices and research and development. Among them, we had obtained valid title certificates from relevant landlords of 12 leased properties with an aggregate gross floor area of approximately 5,923.36 sq.m., accounting for 100% of the aggregate gross floor area of our leased properties. In addition, as of the Latest Practicable Date, we leased four properties in the U.S. with an aggregate site area of approximately 69,884 rentable square feet, which was primarily used for office as well as laboratory facility purpose.

As of the Latest Practicable Date, we had not completed lease registration of some lease agreements with the relevant regulatory authorities. According to PRC law, the non-registration of lease agreements will not affect the validity of such lease agreements, but the relevant local housing administrative authorities can require us to complete registrations within a specified timeframe and we may be subject to a fine between RMB1,000 and RMB10,000 per lease for any delay in making these registrations. As of the Latest Practicable Date, we were not subject to any penalties arising from the non-registration of lease agreements. During the Track Record Period, we did not experience any dispute arising out of our leased properties.

INTERNAL CONTROL AND RISK MANAGEMENT

We have devoted ourselves to establishing and maintaining risk management and internal control systems consisting of policies, procedures and risk management methods that we consider to be appropriate for our business operations, and we are dedicated to continuously improving these systems. We have adopted and implemented comprehensive internal control and risk management policies in various aspects of our business operations such as financial reporting, information system, quality control and human resources management.

Financial Reporting Risk Management

We have in place a set of accounting policies in connection with our financial reporting risk management, such as financial reporting management policies and budget management policies. We have various procedures in place to implement accounting policies and our finance department reviews our management accounts based on such procedures.

Information System Risk Management

Sufficient maintenance, storage and protection of user data and other related information is critical to our success. We have implemented relevant internal procedures and controls to ensure that user data is protected and that leakage and loss of such data is avoided. During the Track Record Period and up to the Latest Practicable Date, we did not experience any material information leakage or loss of user data. We provide information security training to our employees and conduct ongoing trainings and discuss any issues or necessary updates from time to time.

Quality Control Risk Management

Our quality control system is an essential component of our risk management and internal control system. Our quality control measures cover all aspects of our manufacturing operations, including design and construction of manufacturing facilities, the installation and maintenance of manufacturing equipment, procurement of raw materials and packaging materials, quality checks of raw materials, work-in-progress and finished products, monitoring

adverse drug reactions and verification of documentation. The procedures and methodologies of our quality control system are based on GMP standards, and other applicable domestic and international standards.

Human Resources Risk Management

We formulate recruitment plan for the upcoming year based on our future business plan, and we constantly improve our recruitment process. We have formulated anti-bribery and corruption policy to ensure that our employees' skill sets and knowledge regarding anti-bribery and corruption policy remain up to date.

LEGAL PROCEEDINGS AND COMPLIANCE

Legal Proceedings

During the Track Record Period and up to the Latest Practicable Date, we were not a party to any actual or threatened legal or administrative proceedings which would have a material and adverse impact on our business, financial condition or results of operations, and we were not aware of any pending or threatened legal, arbitral or administrative proceedings against us or our Directors that could, individually or in the aggregate, have a material adverse effect on our business, financial condition and results of operations.

Compliance

Our Directors confirmed that, during the Track Record Period and up to the Latest Practicable Date, we had not been and were not involved in any non-compliance incidents that led to fines, enforcement actions or other penalties that could, individually or in the aggregate, have a material adverse effect on our business, financial condition or results of operations. Our PRC Legal Advisors confirmed that during the Track Record Period and up to the Latest Practicable Date, we had complied with applicable PRC laws and regulations in all material aspects.

Licenses and Permits

We have obtained all material licenses, permits, approvals and certificates that are material for our business operations and such licenses, permits, approvals and certificates are valid and subsisting.

The following table sets forth the major certificates, permits, licenses and other approvals held by us as of the Latest Practicable Date:

Certificates/License/ Permit	Holder	Authority	Date of Grant	Expiry Date
Registration certificate of pollutant discharge for fixed pollution sources	Suzhou Sirnaomics	Ministry of Ecology and Environment of the People's Republic of China	March 31, 2020	March 30, 2025
Registration certificate of pollutant discharge for fixed pollution sources	Guangzhou Sirnaomics	Ministry of Ecology and Environment of the People's Republic of China	June 9, 2020	June 8, 2025
High and New Technology Enterprises Certificate	Guangzhou Sirnaomics	Jointly by the Department of Science and Technology of Guangdong Province, the Department of Finance of Guangdong Province, Guangdong State Taxation Bureau	December 9, 2020	December 8, 2023
Montgomery County, MD Hazardous Materials Use Certificate Number 41296	Sirnaomics, Inc.	Montgomery County, Maryland Office of Emergency Management & Homeland Security	December 20, 2020	September 1, 2022[(1)]
Certificate of Treatment, Disposal and Destruction	Sirnaomics, Inc.	Environmental Enterprises Incorporated	December 18, 2020	N/A[(2)]

Notes:

(1) We were initially granted the certificate in December 2020, which expired in September 2021. We thereafter applied for a renewal of the certificate and received the renewed certificate in December 2021. The renewed permit period runs from September 2021 to September 2022. As advised by our U.S. Legal Advisor, the failure to have had the certificate for a limited period of time from September 2021 to December 2021 does not have a material adverse impact on our business.

(2) The Environmental Enterprises Incorporated ("EEI") conducts sampling inspections to ensure certificate holder's compliance with regard to waste treatment, disposal and destruction services. Our Certificate of Treatment Disposal and Destruction would remain valid unless we fail such inspection.

We intend to apply for renewal of the above key license prior to its expiry date. The successful renewal of our existing licenses, permits and certifications will be subject to our fulfillment of relevant requirements. Our Directors are not aware of any reason that would cause or lead to the non-renewal of the licenses, permits and certificates. As of the Latest

Practicable Date, there was no legal impediment for us to renew the licenses, permits and certificates as long as we comply with the relevant legal requirements.

EMPLOYEES

As of the Latest Practicable Date, we had 157 full-time employees.

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

	Number of Employees
Management	9
Research	76
Manufacturing	29
Clinical and Regulation	10
General and Administrative	33
Total	157

Our company leadership places great importance on the retention of key staff and talent. We endeavor to attract and retain our employees by offering stock options to employees and employee benefits including but not limited to medical plan, dental plan and other benefits, providing tuition assistance and training opportunities, offering flexible worksite schedules and recognizing employee commitment and achievement by offering bonus and cash incentive award on performance basis and promotions based on annual performance appraisal process. The research and development of novel therapeutic products utilizing new drug modalities such as RNAi therapeutics is a complex process that requires collaborative efforts at each step of the drug development and production process between professional and scientific personnel having a range of expertise and knowledge. Our company leadership recognizes that the key members of our company with unique skills and niche knowledge are important assets in the growth of our business.

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. The contracts also typically include undertakings regarding assignment of inventions and discoveries made during the course of employment.

We provide regular and specialized trainings tailored to the needs of our employees in different departments. We regularly organize training sessions conducted by senior employees or third-party consultants covering various aspects of our business operations including overall management, project execution and technical know-how.

As required by PRC laws and regulations, we participate in various employee social security plans for our employees that are administered by local governments, including housing provident fund, pension insurance, medical insurance, maternity insurance, work-related injury insurance and unemployment insurance.

We provide various incentives and benefits to our employees. Employees typically receive welfare benefits, including medical care, pension, occupational injury insurance and other miscellaneous benefits.

We believe that we maintain a good working relationship with our employees. During the Track Record Period, we did not have any strikes, protests or other material labor conflicts that may materially affect our business and image. As of the Latest Practicable Date, we had not established any labor union.

INSURANCE

We maintain insurance policies that we consider to be in line with market practice and adequate for our business. Our principal insurance policies cover our key persons and AEs in clinical trials. See "Risk Factors – Risks Relating to our Operations – We have limited insurance coverage, and any claims beyond our insurance coverage may result in our incurring substantial costs and a diversion of resources."

ENVIRONMENTAL MATTERS, SOCIAL RESPONSIBILITY AND WORKPLACE SAFETY

We are committed to operating our business in a manner that protects the environment and providing our employees with a healthy and safe workplace. We have implemented a set of policies on environment, employee welfare and corporate governance, which we believe are in line with industry standards and in compliance with the requirements of the Listing Rules.

In order to ensure that our operations are in compliance with the applicable laws and regulations, we have implemented group-wide environmental, health and safety policies and standard operating procedures, mainly comprising management systems and procedures relating to wastewater generation and treatment, management of process safety and hazardous substances, employee health and safety requirements, third-party safety management and emergency planning and response. We conduct environmental evaluation and take environmental protection measures relating to emissions of air and wastewater generation and treatment. In particular, to manage and mitigate climate-related risks, we strictly comply with the GMP qualification requirements and relevant pollutant emission standards during our production process. We implemented safety guidelines setting out information about potential safety hazards and procedures for operating in the laboratory and manufacturing facilities. We also store hazardous substances in special warehouse and contract with qualified third parties for the disposal of hazardous materials and wastes. As advised by our PRC Legal Advisers, during the Track Record Period and up to the Latest Practicable Date, we were in compliance with the relevant PRC environmental and occupational health and safety laws and regulations in all material aspects and we have not had any significant workplace accidents in the PRC.

In respect of social responsibilities, we have entered into employment agreements with our employees in accordance with the applicable PRC laws and regulations. We hire employees based on their qualifications and experiences and it is our corporate policy to offer equal opportunities to our employees regardless of gender, age, race, religion or any other social or personal characteristics. We strive to operate our facilities in a manner that protects the environment and the health and safety of our employees and communities.

In addition, we have implemented measures to identify and address potential risks relating to environment, health and work safety. These measures include continuous employee trainings to enhance our employees' awareness of environment, health and work safety issues and skills to comply with safety and operation guidelines, timely provision of protection equipment to our employees, periodic inspection of our operational facilities, special health examinations for employees who may have contact with hazards, medical examination for employees and establishment of procedures to appropriately handle work safety incidents. We have installed video surveillance systems inside our facilities to monitor the operation process.

Our safety committee is responsible for monitoring and enforcing the compliance of our operations with environment, health and safety laws and regulations. Upon identification of any EHS risks, our safety committee will make filings with local governmental authority if required under local laws and regulations, and take all applicable measures to reduce the impact of such risks or incidents.

AWARDS AND RECOGNITIONS

We have received recognition for our research and development achievements. The table below sets forth our selected awards and recognitions as of the Latest Practicable Date.

Year	Name of award or recognition	Awarding entity
2017	Small Giant Enterprise in Science and Technology of Guangzhou Province of 2016 2016年度廣州市科技創新小巨人企業	Guangzhou Science Technology and Innovation Commission廣州市科技創新委員會
2017	Third Prize of the Sixth National Innovation & Entrepreneurship Competition (Biopharmaceutical Growth Group) 第六届中國創新創業大賽生物醫藥行業成長組三等獎	National Innovation &Entrepreneurship Competition Committee中國創新創業大賽組委會
2017	National New and Advanced Technology Enterprise 國家高新技術企業	National Office of Leading Group for Administration of Hi-tech Enterprise Recognition全國高新技術企業認定管理工作領導小組辦公室
2020	National New and Advanced Technology Enterprise 國家高新技術企業	National Office of Leading Group for Administration of Hi-tech Enterprise Recognition全國高新技術企業認定管理工作領導小組辦公室