Executive Summary

The Innova therapeutic platform consisting of various molecules targeting SFRP2 is being developed to treat various cancers and fibrosis. In addition, a diagnostic biomarker is being developed to assess SFRP2 levels in the blood for early cancer detection and monitoring for efficacy and recurrence.

"The cancer treatment platform, based on 30 years in the pharmaceutical industry where my primary focus was on development of cancer treatments, has the highest potential in my view to change the paradigm of treatment of patients with many types of solid and hematological cancers, resulting in long term survival. Given the extensive global patent protection (including composition of matter) through 2042 and beyond, the commercial value of this platform is high, both as monotherapy and in combination."

Dr. Robert Ryan, CEO

Summary

Innova Therapeutics is a Charleston, South Carolina based biotechnology company developing a monoclonal antibody (mAb) platform targeting a protein that is highly expressed in multiple solid cancers and shown to correlate with patient outcome. The lead humanized mAb has been selected and is designated as IVT-8086. Innova's platform technology is initially focused on targeting cancers including pediatric osteosarcoma, sarcomas, breast cancer, multiple myeloma and pancreatic cancer, however given that this pathway is common across solid and hematological malignancies there are options to treat other cancers. The opportunity for this anticancer therapy as a monotherapy and in combination with other chemotherapy agents will expand across other solid tumors.

The focus on pediatric osteosarcoma as one of the initial targets will allow a fast-regulatory approval. **Osteosarcoma is a rare disease which was granted both orphan designation and rare pediatric disease designation from the FDA**, which will expedite the regulatory approval timeline including the opportunity to obtain a Rare Pediatric Disease priority review voucher. Because Priority Review Vouchers (PRVs) may be sold, a secondary market for the vouchers has emerged, with revenue ranging between $80M and $350M (most recent voucher sales in $100-158M range).

SFRP2 has been further validated as an important molecular target across human cancers, where expression levels have been shown to correlate with patient outcome. A diagnostic is also in development which will be assessed as a potential marker for early cancer detection, as well as a prognostic marker for assessing therapeutic benefit of treatments and assessment of potential reoccurrence of cancer. **The program patent portfolio, including composition of matter, consists of 46+ patents ensuring <u>global</u> protection through 2042 and beyond.**

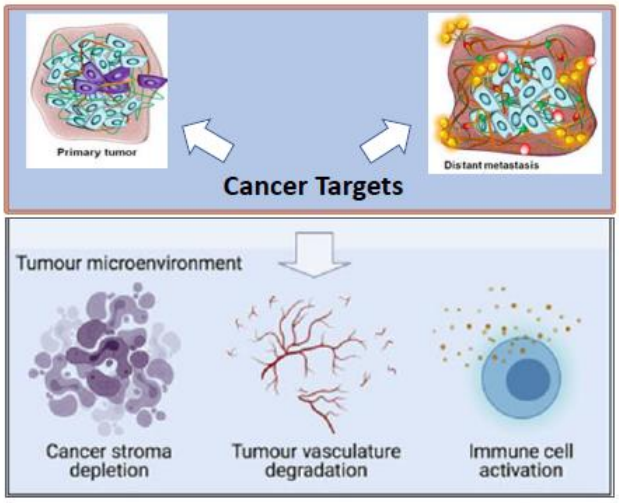
Company Description and Experienced Management Team

Innova Therapeutics was founded on the research conducted by Co-founders Nancy Klauber-DeMore, MD, FACS, Professor of Surgery and BMW Endowed Chair Cancer Research, Medical University of South Carolina (MUSC) and Cam Patterson, MD, MBA who is currently the Chancellor, University of Arkansas for Medical Sciences.

Innova is comprised of a highly experienced management/development team with a successful track record of building new companies, developing effective therapeutics and successful partnering/exits. All members have more than 20 years of global drug development experience covering all functional areas, including extensive cancer therapy development. The team is led by one of the co-founders and CEO, Robert Ryan, Ph.D., who is a

successful serial biotech entrepreneur. Key functional expertise including clinical, regulatory, preclinical, and manufacturing, and business development are provided by the team within Innova Therapeutics.

Innova has Developed a Novel Anti-Cancer Platform and Diagnostic



Most cancer therapies target <u>only one</u> of the four targets identified in this figure (tumor or one of 3 components of the tumor microenvironment).

Secreted frizzled-related protein-2 (SFRP2) is a novel anticancer therapeutic target that is highly expressed across most solid cancers (including primary and metastatic disease). SFRP2 is a signaling protein that is secreted by tumor cells, endothelial cells, and activated T-cells. SFRP2 selectively modulates the non-canonical Wnt/Calcium (Ca2+)-signaling cascade in different cancers, which plays a role in a series of cellular processes including angiogenesis, cell survival, cell migration and metastasis, and production of T-cell exhaustion. SFRP2 binds to the frizzled 5 precursor (FZD5) receptor and activates the calcineurin/nuclear factor (NFATc3) pathway.

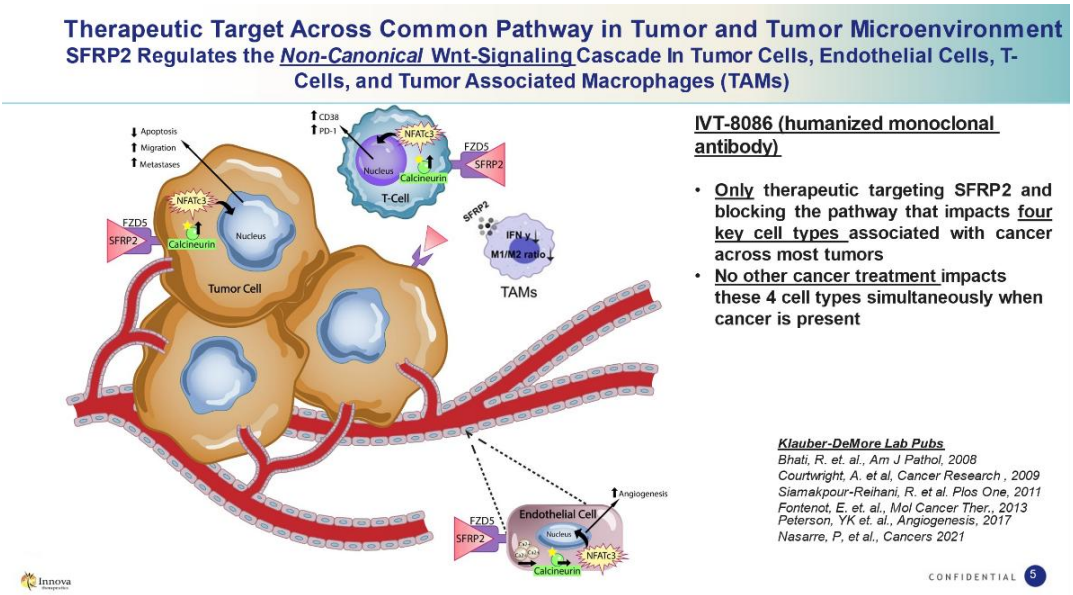
IVT-8086 inhibits SFRP2 in cancer and has multi-faceted activities in multiple cell types associated with cancer as shown in Figure 1, including:

- **Tumor cells -** reduced tumor growth (primary and metastatic disease), including increased apoptosis.
- **Tumor endothelial cells -** reduced angiogenesis resulting in reduced migration and metastasis**.**
- **Activated T-Cells -** rescues T Cell that become dysfunctional including T Cell exhaustion, impacting expression of PD-1 and CD-38.
- **Impacts tumor associated macrophages (TAMs)** by shifting balance to increase M1 “attack” TAMs and IFN-Ɣ
- **Cancer-associated fibroblasts (CAFs)** are one of the most prominent cell populations in the tumor microenvironment (TME). Cancer-associated fibroblasts (CAFs) have multiple tumor-promoting functions in drug resistance, regulation of the niche of cancer stem cells and formation of the immunosuppressive network. A recent publication, dated October 2024, analyzed multicenter bulk sequencing and comprehensive single-cell data from 702,446 cells, and identified an aggressive subpopulation of SFRP2 expressing CAFs (designated as SFRP2_CAFs) consistently present in primary and metastatic lesions in patients with advanced head and neck squamous cell carcinoma (HNSCC) impacting the stroma and was associated with poor survival outcome in these patients. Similar findings were found in patients with high grade appendiceal cancers and was also associated with patients with poor survival outcome. SFRP2 is a paracrine factor that has been shown in our laboratory to induce epithelial mesenchymal transformation in

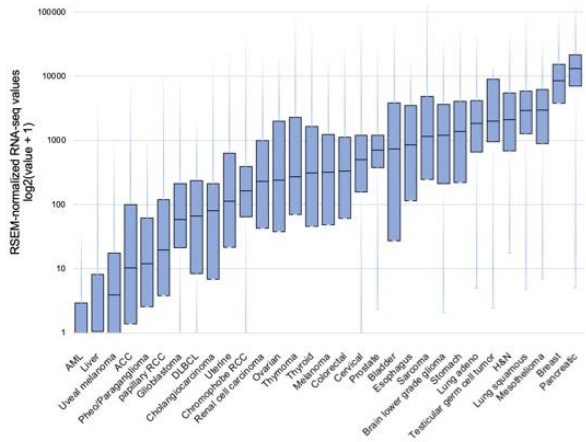
fibroblasts, and we have demonstrated a strong correlation between SFRP2 expression and the degree of stromal expansion in pancreatic ductal adenocarcinoma (PDAC). **Targeting SFRP2_CAFs across cancers with the IVT-8086 antibody presents an additional promising therapeutic approach for effectively treating patients that targets the invasive, metastatic, and immunosuppressive capabilities of SFRP2_CAFs.**

Figure 1: Schematic of Impact of SFRP2 on Common Pathway Across 4 Key Tumor Microenvironment Cell Types

- **There is <u>no therapeutic</u> that impacts these 4 cell types simultaneously through a common pathway <u>across both solid and hematological malignancies.</u>**



The Cancer Genome Atlas (TCGA): SFRP2 Expression in Human Tumors



SFRP2 is Overexpressed Across Many Human Tumors, both Solid and Hematological Malignancies

Executive Summary

The competitive advantage of IVT-8086 is that it simultaneously targets both the tumor and the tumor microenvironment, without targeting normal cells, exploiting a common pathway across most cancers. The lead humanized SFRP2 mAb has been selected, IVT-8086, and has been shown to antagonize SFRP2 by selectively blocking the non-canonical Wnt/Ca2+ pathway in tumor cells, activated T-cells, and tumor endothelial cells. IVT-8086 monotherapy treatment has demonstrated efficacy (**with no adverse safety effects**) in multiple animal models implanted with either human xenografts or genetically engineered mouse model (GEMM) cell lines. **In addition, combination therapy with IVT-8086 and PD-1 mAb has demonstrated synergistic efficacy with no noted safety concerns.**

Recent publication has demonstrated that in pancreatic ductal adenocarcinoma (PDAC), SFRP2 is regulated by KRAS, which is the most lethal mutation seen in pancreatic cancer. Blockage of this pathway should have beneficial survival outcomes to patients with this cancer. In patients with PDAC, the reduction in SFRP2 levels has been shown to be prognostic for survival.

SFRP2 has been further validated as an important molecular target across human cancers, where expression levels have been shown to correlate with patient outcome. **A diagnostic** is in development which will be assessed as a potential diagnostic for early cancer detection, as well as a prognostic marker for assessing therapeutic benefit of treatments and assessment of potential reoccurrence of cancer.

Competitive Landscape

Treatment options for many cancers are limited due to inadequate efficacy and/or significant toxicity. There is tremendous recent interest in the development of next generation bispecific and even trispecific antibodies, which have the ability to hit two or three targets impacting cancer growth and progression simultaneously. The global bispecific antibody market for cancer therapy is experiencing rapid growth, with a projected market size of $50 billion by 2030, expanding at a CAGR of 23.2%. This growth is fueled by increasing cancer prevalence, the advantages of bispecific antibodies over traditional therapies with the ability to target multiple cancer cell types with a single therapy. . The market's rapid expansion from US$ 12 Billion in 2024 to an expected US$ 50 Billion by 2030, reflects the increasing recognition of bispecific antibodies as key solutions for treating complex and life-threatening diseases. **Innova Therapeutics has developed a cancer therapy that can impact 4 or more cancer targets simultaneously across a common pathway across both solid and hematological malignancies, without the toxicity of targeting individual cancer targets as noted with bi- or tri- specific antibody.**

Another area of growth and development of cancer treatments are antibody-drug conjugates (ADC). Antibody-drug conjugates (ADCs) are a type of targeted cancer therapy that combines a monoclonal antibody with a cytotoxic (cell-killing) drug. The antibody acts as a delivery system, targeting specific proteins on cancer cells and guiding the drug directly to the tumor. This targeted approach aims to maximize cancer cell destruction while minimizing damage to healthy cells. However, a significant number of ADCs in clinical development have failed, often due to insufficient efficacy or safety concerns at tolerated doses. ADCs can have a narrow therapeutic index, meaning the effective dose is close to the toxic dose, making dose optimization crucial but challenging which can lead to dose reductions or discontinuation of treatment. **The clear advantage of IVT-8086 is the ability to target and block a pathway which is common in tumors and key tumor microenvironment cell types simultaneously, without off target toxicity.**

Recent Research and Market Reports have indicated that the opportunity for more effective and safe therapies in the treatment of cancer with monoclonal antibodies are needed both as monotherapy and in combination with Checkpoint inhibitors: PD-1 / PD-L1 Inhibitor Market: (current market size approx. $50B). **PD-1**

inhibitors are the most commonly used cancer therapeutics, and are approved for treating over 20 types of cancer. The global market for PD-1 and PD-L1 inhibitors is expected to reach $137 billion by 2031.

- **Primary and acquired resistance to PD-1 Inhibitors has been shown to be associated with CD-38 overexpression in T-Cells. The pathway that causes the over expression of CD-38 has been shown to be blocked by IVT-8086, resulting in downregulation of CD-38.**
- **Combination therapy of IVT-8086 with PD-1 inhibitors will dramatically benefit patients across multiple cancers by increased efficacy.**
- **There is a tremendous commercial opportunity for usage of IVT-8086 in combination with PD-1 inhibitors.**

The global monoclonal antibodies market is currently valued at $180.5 billion, with by 2030 this market is estimated to reach >$520 billion. The Immuno-Oncology Market, By Type [mAb (Naked, Conjugate), Cancer Vaccines, Immune Checkpoint Inhibitors (PD-1, PD-L1, CTLA-4)], and by Application (Lung, Melanoma, Leukemia, Lymphoma) is currently in excess of US$ 100 Billion.

Last, one of the several initial targeted cancers with our therapy, which is a rare cancer is metastatic osteosarcoma (OS), which is a deadly cancer in which patients often have treatment-resistant disease resulting in survival rates of only 15 to 30%. In the last 20 years, OS patients have not seen improvement in prognosis with available treatments. **IVT-8086 has received orphan and rare pediatric designation from the FDA for the treatment of metastatic osteosarcoma.** Innova's platform technology is initially focused on targeting cancers including pediatric osteosarcoma, sarcomas, breast cancer, multiple myeloma and pancreatic cancer, however given that this pathway is common across solid and hematological malignancies there are options to treat other cancers. The opportunity for this anticancer therapy as a monotherapy and in combination with other chemotherapy agents will expand across other solid and hematological malignancies. Data to date has demonstrated compelling efficacy with no adverse effects with our therapy in these indications both as monotherapy and in combination in animal *in vitro* and *in vivo* models.

There are currently no diagnostics that have broad implications for assessing early-stage cancer across various solid and hematological malignancies. Measurement of SFRP2 in blood has the potential to be the first diagnostic for early detection across multiple cancers, along with use as a monitoring test for confirming remission and possible reoccurrence of cancer in patients.

Financing and Exit Strategy

A total of approximately $11M in non-dilutive funds has been obtained to date to fund the development of the humanized monoclonal antibody (IVT-8086), including key activities such as preclinical mechanistic studies, animal tumor model studies assessing efficacy and safety across several solid tumors, clinical validation studies, and expanding IP.

Innova is currently raising an initial financing of US$15M to support activation of the IND and initiation of Phase 1, with a second financing anticipated within a year of $25M to support the proposed clinical development program with our lead candidate, IVT-8086, in multiple cancers both as monotherapy and in combination. The financing will also be used to develop our diagnostic which will be used in the clinical program.

The options for substantial exits for the cancer therapy and diagnostic are broad, including partnering/collaboration once clinical data is obtained, partnering in specific territories, or continued expansion of cancer indications to increase value of the program. Regardless of the pathway, the market value for a broad effective therapy of this type would be in excess of $5-10 B, with the value of an effective early cancer diagnostic test in excess of $1B.