



## Executive Summary - Targeted Full Spectrum RNAi / PSR

**Summary:** The available clinical data strongly suggests that the Targeted Full Spectrum (tfs) RNAi / PSR (Protein Synthesis Restriction) platform technology will set an unbeatable potency standard for RNAi technologies. The primary addressable markets are estimated at just under \$ 20 billion in the US. Because tfsRNAi / PSR does not require stabilization or delivery technologies like other forms of RNAi, and because one of the compounds has already been evaluated for systemic safety in humans, tfsRNAi / PSR can be brought to market rapidly, with low risk, to establish an unbeatable potency standard in the primary indications. The technology is covered by 5 issued and 1 pending US patents. The therapeutic effect of tfsRNAi / PSR is targeted Antiproliferative, Anti-Inflammatory, and Antiviral activity, with a large margin of systemic safety.

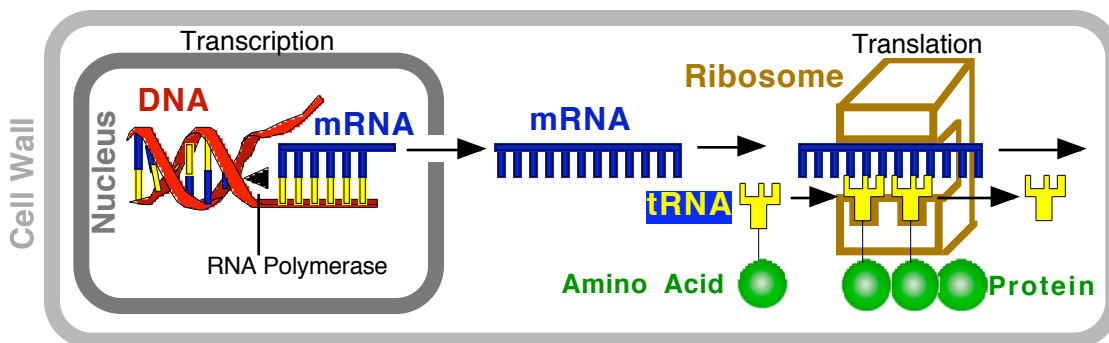
**Clinical Data Summary:** The data is consistent with the known MOA of binding to ribosomes and interfering with translation of RNA into proteins. The **Antiproliferative activity** of RNAi / PSR (not targeted) was characterized in 7 Phase II human clinical trials against cancer. The drug is a cytostatic requiring prolonged administration for cytotoxic effect. The **Antiviral activity** was characterized ex vivo in human cell lines infected with herpes virus. The drug inhibited de novo synthesis of all viral proteins as well as inhibited viral DNA synthesis as a secondary effect of protein synthesis inhibition (viral DNA polymerase synthesis inhibition). The **Anti-inflammatory activity** was demonstrated in vivo, in contact hypersensitive mice. A 30 ng topical dose resulted in a 44% reduction in inflammation. The **dermal PK** was characterized in 2 studies, ex vivo, human skin. The compounds tested localized virtually completely in the epidermis and dermis ( 97% - 99%). **Systemic safety** was characterized in 4 Phase I human clinical trials by intravenous infusion. The IC100 doses proposed for targeted dermal, pulmonary, and transdermal indications range from hundreds of times to hundreds of thousands of times smaller than the human systemic NOEL dose (no observable effect level dose).

### Primary Markets:

	US Cases	Annual ASP	Addressable US Market (\$ in Mil.)	Therapeutic Advantage
Psoriasis	7,500,000	\$250	\$1,875	Targeted Anti-Inflammatory, Antiproliferative
Herpes Oral Lesions/yr	40,000,000	\$20	\$800	Targeted Antiviral, Anti-Inflammatory
Herpes Genital Lesions/yr	80,000,000	\$20	\$1,600	Targeted Antiviral, Anti-Inflammatory
Anti-Aging Exfoliation			\$2,000	Targeted Antiproliferative (Exfoliation Regimen)
Acne	17,000,000	\$71	\$2,000	Targeted Antiproliferative, Anti-Inflammatory
COPD - Chr. Bronchitis	9,800,000	\$500	\$4,900	Targeted Anti-Inflammatory, Antiproliferative
Asthma	16,400,000	\$250	\$4,100	Targeted Anti-Inflammatory
Rheumatoid Arthritis	2,500,000	\$500	\$1,250	Targeted Anti-Inflammatory, Antiproliferative
Macular Degen. (wet /yr)	200,000	\$2,500	\$500	Targeted Anti-Proliferative
<b>RNAi / PSR Totals</b>			<b>\$19,025</b>	

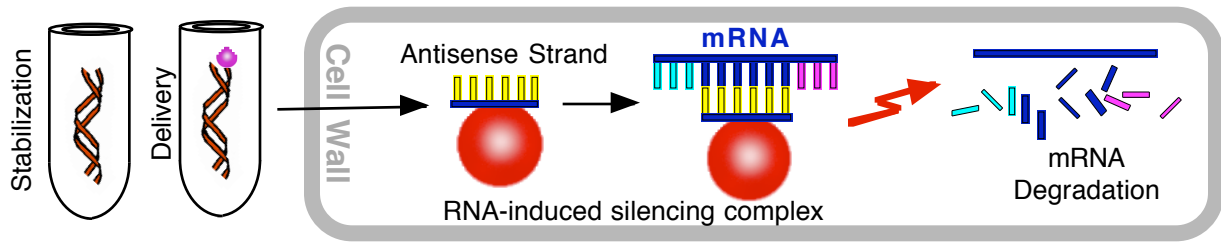
**The Competition:** In context of RNAi technologies, tfsRNAi / PSR is better suited for disease conditions involving synthesis of a broad spectrum of proteins, whereas other RNAi technologies focus on a single protein. A brief background is necessary to understand the difference as well as to understand our IP strategy.

RNA function is summarized below. Drugs that interfere with or inhibit RNA interfere with or inhibit protein synthesis.

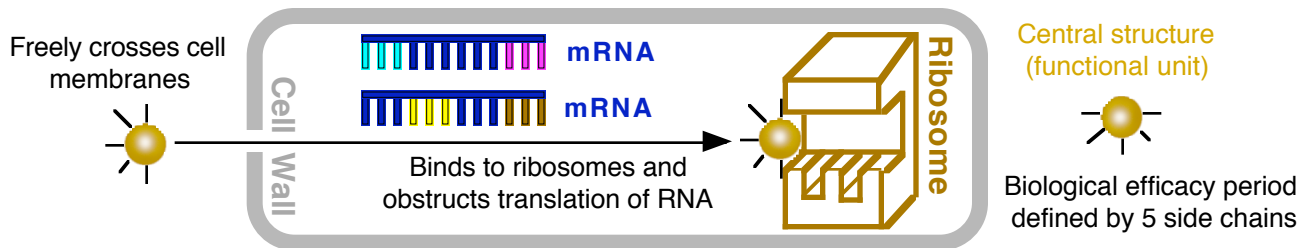


Synthesis of a single aberrant protein or overexpression of single normal protein results in certain disease conditions. Disease conditions can also involve hyperactive synthesis of a broad spectrum of proteins, such as happens with cell hyperproliferation, inflammation, and viral infections.

**siRNA** uses Antisense technology to target a specific mRNA sequence and hence inhibit synthesis of a single protein. siRNA requires stabilization and delivery technologies, which are a major impediment to its commercialization.



**tfSRNAi / PSR** is better suited for disease conditions that involve synthesis of a large spectrum of proteins and does not require any stabilization or delivery technology. Drug concentration defines degree of PSR (e.g. IC50, IC 80, IC100). Side chain combinations define intracellular inactivation time, hence biological efficacy period, which can be from hours to days. The compound localizes where applied and its blood insolubility keeps it out of general circulation, making it ideally suited for topical, inhalable, and transdermal administration, without the need for any targeting technology.



**Patent Summary:** The availability of 5 side chain sites makes innumerable synthetic variants possible, making composition of matter patents fairly meaningless from a protection standpoint. The issued method of use patents provide protection against the use of any natural or synthetic variant for the following indications:

- U.S. Pat. 6,346,251 - Psoriasis Treatment Method
- U.S. Pat. 6,355,251 - Epidermal Exfoliation Method ( Age Spots, Warts, skin rejuvenation, etc...)
- U.S. Pat. 6,559,178 - Apoptotic Chemosurgery Method (Ablation of Non Malignant Cell Populations)
- U.S. Pat. 7,012,091 - Pulmonary Anti-Inflammatory
- U.S. Pat. 7,015,244 - COPD Treatment Method
- US App. 12/321,717 - Dermal and Pulmonary Anti-Infective, Anti-Inflammatory (Herpes, Acne, Avian Flu)

**Business Plan / Roadmap:** The plan envisions using the existing compound, while simultaneously funding parallel development of synthetic variants, to extend patent protection beyond the 2021 - 2029 expiry of the existing patents. Because the existing compound has been evaluated in 4 Phase I human trials for systemic safety, and targeted therapeutic doses are hundreds of times smaller than the systemic NOEL dose, it removes human safety as an issue. Statistically, only around 20% of drug candidates make it past Phase I (Safety) and 40% make it past Phase II (initial efficacy). Removing Safety as an issue greatly boosts the probability of success. One could additionally improve the probability of success by obtaining 10 -20 Phase II type data points per indication in a country that does not require a redo of Phase I for a change in route of administration.

**Demonstrable Advantage:** The product can be brought to market rapidly, and at low risk, because it does not require stabilization or delivery technologies and has already been evaluated in humans for systemic safety. The product should set an unbeatable potency standard relative to other RNAi technologies because it inhibits the full spectrum of protein synthesis required to drive the underlying disease condition in the tissue targeted for treatment.

**Exit Point / Return on Investment:** To develop the 8 top indications through Phase II would cost roughly \$ 90 million, at which point each successful indication should value out at ~ \$ 200+ million, by sale to big pharma.