



Targeted Transient Ribosomal Inhibition (TTRI)

Summary: TTRI is a non systemic platform therapeutic that silences expression of every protein involved in the underlying etiology and pathology of a disease condition in a target tissue mass. Topical, Inhalable, or Transdermal delivery is used and the drug is retained where applied. The therapeutic effect is targeted Antiproliferative, Anti-Inflammatory, and Antiviral activity. Normal cells in the target tissue are not harmed when using Non-Ablative regimens, and Ablative regimens (prolonged, uninterrupted, IC100) can be used to achieve disease reversal (e.g. COPD, RA). NexGen believes TTRI will set an unbeatable potency standard versus single protein target technologies such as Antibody and RNAi. For example, topical TTRI will silence all ~100 viral and inflammatory proteins in a Herpes Lesion. Inhalable TTRI will silence all 10 influenza viral proteins and all related inflammatory proteins (cytokines and leukotrienes), preventing mortality from strains such as H5N1. TTRI will also set an unbeatable safety standard, as the targeted therapeutic doses used are thousand of times smaller than the systemic NOEL dose in humans. The technology is covered by 5 issued and 1 pending US patents.

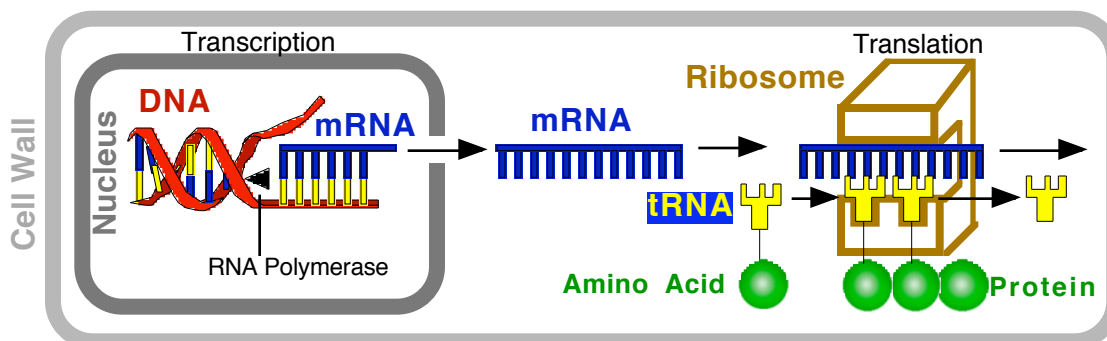
Clinical Data Summary: The data is consistent with the known MOA of binding to the peptidyl transferase site on ribosomes and transiently interfering with translation of RNA into proteins (RNAi / PSR). **Antiproliferative activity** (not targeted) was characterized in 7 Phase II human clinical trials against cancer. The drug is a cytostatic requiring prolonged administration for ablative effect. **Antiviral activity** (ex vivo, human cells, HSV): The drug inhibited de novo synthesis of all viral proteins and inhibited viral DNA synthesis as a secondary effect of protein synthesis inhibition (viral DNA polymerase synthesis inhibition). **Anti-inflammatory activity:** demonstrated in contact hypersensitive mice. **Dermal PK** (topical application, human skin, ex vivo): 97% - 99% retained in the epidermis and dermis. **Systemic safety** (NOEL from Phase human trials by IV): Targeted doses are thousands of times smaller than the systemic NOEL (no observable effect level).

Primary Markets:

Disease	US Cases	ASP	US Market (\$ in Mil.)	Therapeutic Advantage
Psoriasis	7,500,000	\$ 250	\$ 1,875	Topical Anti-Inflammatory, Antiproliferative
Herpes Lesions	120,000,000	\$ 20	\$ 2,400	Topical Antiviral, Anti-Inflammatory
Age Spots			\$ 2,000	Ablative Reg. - Topical Apoptotic
Acne	17,000,000	\$ 71	\$ 2,000	Topical Antiproliferative, Anti-Inflammatory
COPD - Chr. Bron.	9,800,000	\$ 500	\$ 4,900	Inhalable Anti-Inflammatory, Antiproliferative or Ablative Reg.-Ablation of Solid Obstructions
Asthma	16,400,000	\$ 250	\$ 4,100	Inhalable Anti-Inflammatory
Influenza			\$ 500	Inhalable Antiviral, Anti-Inflammatory
Rheum. Arthritis	2,500,000	\$ 500	\$ 1,250	Transdermal Anti-Inflammatory, Antiproliferative or Abl.Reg. - Reversal of Synovial Overprolif.
Cellulite		\$ 250	\$?	Ablation of Sub Cutaneous Fat Cells

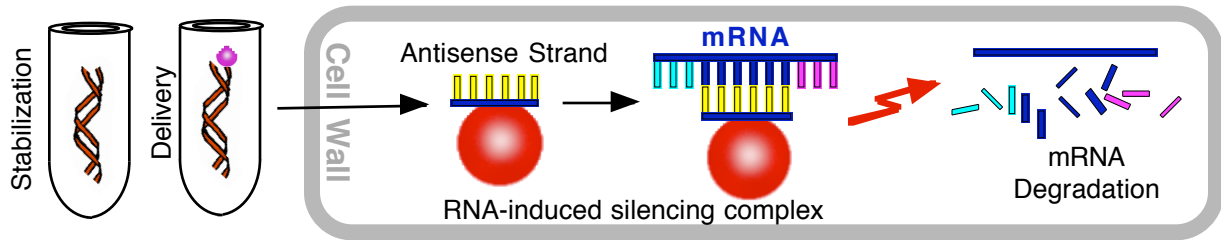
The Competition: TTRI is better suited for disease conditions involving synthesis of a broad spectrum of proteins, whereas traditional RNAi or Antibody technologies are better suited for disease conditions driven by a single protein. A brief background is necessary to understand the difference as well as to understand our IP strategy.

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

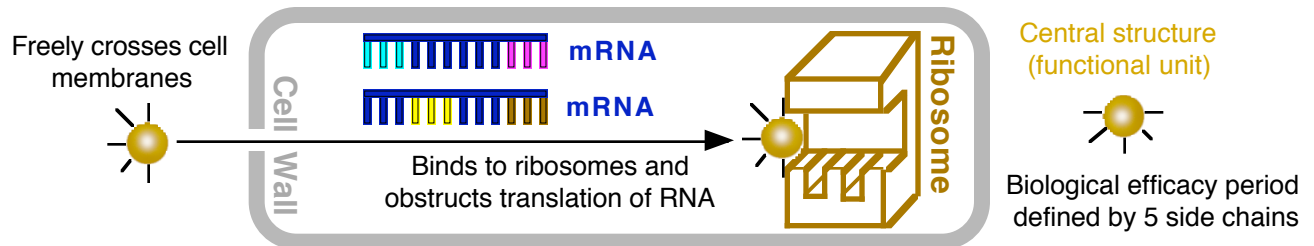


Synthesis of a single aberrant protein or overexpression of single normal protein results in certain disease conditions. Disease conditions can also involve hyperactive synthesis of a broad spectrum of proteins, such as happens with inflammation mediated cell hyperproliferation, viral infections with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

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.



TTRI is better suited for disease conditions that involve synthesis of a large spectrum of proteins and TTRI does not require any stabilization or new delivery technology. TTRI does not require determining which proteins need to be silenced, as it silences them all. Drug concentration defines degree of Protein Synthesis Restriction (e.g. IC50, IC80, 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. It is ideally suited for topical, inhalable, and transdermal administration. Sustained IC100 for up to 3 days does not harm normal cells (non ablative regimens) and beyond that may be used to achieve a desired level of ablation (ablative regimens).



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, Influenza)

Business Plan / Roadmap: The plan envisions clinical development of the existing compound (DAS), while simultaneously funding parallel development of synthetic variants to extend patent protection beyond the 2021 - 2029 expiry of the existing patents. The 4 Phase I human trials of DAS remove systemic safety as an issue. The initial focus is to obtain 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, in order to eliminate any competitive efficacy risk.

Demonstrable Advantage: Non Ablative regimens (IC100, transient or sustained IC50, IC80 etc...) can be used to silence or attenuate expression of every protein involved in the underlying etiology and pathology of the selected indications, which would set an unbeatable potency standard against single protein target technologies such as RNAi or Antibody. Ablative regimens (prolonged, sustained IC100) would reverse certain disease conditions versus just inhibiting them (e.g. COPD, RA). Delivery of the drug only where needed, retention of the drug in the tissue to which it is applied without going systemic, and total doses used that are hundreds to hundreds of thousands of times smaller than the systemic NOEL dose, should set an exceptional safety standard.

Competitive Landscape: The current lack of fast, decisive efficacy makes many markets easy targets for TTRI. The competitive landscape, by indication, is provided below:

COMPETITIVE LANDSCAPE (1 of 2)

Current lack of fast, decisive efficacy makes many markets easy targets:

- **TTRI Non Ablative Regimens** quickly **inhibit synthesis of every protein underlying the etiology and pathology of the disease**.
- **TTRI Ablative Regimens** can be used to **expedite removal of undesirable accumulations of cell populations**.

<u>DRUG</u>	<u>Route</u>	<u>NAME</u>	<u>DRUG TYPE OR ACTION</u>	<u>COMPANY</u>	<u>PRESCRIBING INFO. / CLINICAL OUTCOMES</u>
HERPES LESIONS					
Zovirax	Top.	acyclovir	Antiviral: DNA polym. inhib.	Sanofi-Av.	reduces duration of lesion from 5 days to 4.5 days
Denavir	Top.	penciclovir	Antiviral: DNA polym. inhib.	New Am.	reduces duration of lesion from 5 days to 4.5 days
Abreva	Top.	docosanol	Antiviral: envelope fusion inh.	Glaxo	mean healing time of 5.7 days vs. 7.3 days
TTRI-NonAbl.	Top.	DAS/analog	Antiviral + Anti-inflammatory	NexGen	to be determined
Valtrex	Oral	valacyclovir	Antiviral: acyclovir pro drug	Glaxo	12 mo: 34% recurrence free vs. 4% placebo
Famvir	Oral	famciclovir	Antiviral: penciclovir pro drug	Novartis	12 mo: 29% recurrence free vs. 6% placebo
PSORIASIS					
Tazorac	Top.	tazarotene	retinoid pro drug	Allergan	3 mo: 0-3% normal skin, 3-5% min. psoriasis
Davonex	Top.	calcipotriene	vitamin D3 Analog	Warner	2 mo: 11% no psoriasis, 50% marked improvement
Taclonex	Top.	calcip. + betam.	vit.D3 + corticosteroid	LEO	1 mo: 48% no to min. vs 26% betam, 17% calcip.
Clobex	Top.	clobetasol p.	Anti-inflam: corticosteroid	Galderma	1 mo: 37% had no to min. psoriasis
Drithox, etc...	Top.	anthralin	Antiprolif: mitochon. Inhib.	several	Anthralin(Curtis, '85): 1 mo: 35% "clearing", 35% sig. imp.
TTRI-NonAbl.	Top.	DAS/analog	Anti-inflam + Antiprolif.	NexGen	to be determined
TTRI-Abl.Reg.	Top.	DAS/analog	Anti-inflam. + Ablation	NexGen	Apoptotic Epidermal Ablation Regimen - TBD
Stelara	Inject.	ustekinumab	Anti-Inflam: IL12, IL23 MAB	J&J-Centocor	3 mo: 59%-73% clear to min (2 studies, 2 doses)
Enbrel	Inject.	etanercept	Anti-inflam: TNF Blocker	Amgen, Pfizer	3 mo: 32% / 47% (25 / 50 mg BIW) clear or min.
Remicade	Inject.	infliximab	Anti-inflam: TNF Blocker	J&J-Centocor	week 10: 75%-90% clear to min v. 1-10% placebo
ACNE					
Retin-A Micro	Top.	tretinoin	vitamin A	J&J-OrthoN.	3 mo: 32%-45% lesion count drop vs. 16-23% vehicle
Aczone	Top.	dapsone	antibacterial	Allergan	3 mo: 35% -45% no to min. acne vs 28%-32% vehicle
Azelex	Top.	azelaic acid	antibacterial + skin thinning	Allergan	Thiboutot, '08: 70% reduc. vs. 77% perox, 63% clindamycin
Clindagel	Top.	clindamycin	antibacterial	Galderma	3 mo: 38% lesion count drop vs. 27% for vehicle alone
Differin	Top.	adapalene	retinoid	Galderma	3 mo: 44%-52% lesion count drop vs. 33-37% vehicle
Tazorac	Top.	tazarotene	retinoid pro drug	Allergan	3 mo: 42%-44% lesion count drop vs. 21-24% vehicle
Epiduo	Top.	adap.+peroxi.	retinoid +antibacterial	Galderma	3 mo: 30% clear/almost vs. 20% adap., 22% perox., 11% gel
TTRI-Abl.Reg.	Top.	DAS/analog	Skin Thinning + Anti-inflam.	NexGen	to be determined
AGE SPOTS - Actinic Keratosis					
Zyclara	Top.	imiquimod	Unknown: Immune Activator	Graceway	2 mo: 26% - 46% complete clearance (2 studies)
Solaraze	Top.	diclofenac	COX & DNA synth. inhibitor	PharmaDerm	3 mo: 34% - 47% cure (2 studies), 2 mo: 31%, 1 mo: 14%
Efudex	Top.	fluorouracil	Antiprolif: S-Phase cytotoxic	Valeant	62.5% cure rate (Medscape)
Metvixia	Top.	aminolevulinic	Light activated cytotoxic	Galderma	83%-86% cure vs. 29%-52% w/vehicle only (2 studies)
TTRI-Abl.Reg.	Top.	DAS/analog	Skin Ablation + Anti-inflam.	NexGen	Apoptotic Epidermal Ablation Regimen - TBD
Cryotherapy	Surgcl.	liquid nitrogen	necrotic cell destruction		39% - 83% cure rate (Medscape)
Excision	Surgcl.	curette/blade	necrotic cell destruction		
Fraxel	Surgcl.	Thulium laser	laser destruction	Solta	83.5% decrease in lesions after 2 - 4 treatments

COMPETITIVE LANDSCAPE (2 of 2)

DRUG	Route	NAME	DRUG TYPE OR ACTION	COMPANY	PRESCRIBING INFORMATION / CLINICAL OUTCOMES
AGE SPOTS - Mottled Hyperpigmentation					
Average	Top.	tazarotene	retinoid pro drug	Allergan	24 wks: 42% - 54% had 1 grade impr. vs. 17%-30% vehicle
TTRI-NonAbl.	Top.	DAS/analogue	Tyrosinase/melanin downreg.	NexGen	to be determined
TTRI-Abl.Reg.	Top.	DAS/analogue	Melanocyte Ablation	NexGen	Ablation of Melanocytes - TBD
COPD - Chronic Bronchitis					
Advair	Inhal.	flutic.+ salem.	corticosteroid+beta-adr.agon.	Glaxo	24 wks: FEV improvement: 17% sustained, 27% Post Dose
Spiriva	Inhal.	tiotropium	anticholinergic	Boehringer	1 yr: sustained +FEV 28%-31%, (0.28 -0.31L) after 1 wk.
Symbicort	Inhal.	budes. +form.	glucocorticoid+beta-adr.agon.	AstraZeneca	9% Post Dose +FEV,1.4 "events/yr" vs.1.8-1.9 plcbo./formoterol
TTRI-NonAbl	Inhal.	DAS/analogue	Anti-inflam. + Antiprolif.	NexGen	to be determined
TTRI-NonAbl	Inhal.	DAS/analogue	Antiviral + Anti-inflammatory	NexGen	For COPD patients with viral lung infections - TBD
TTRI-Abl.Reg.	Inhal.	DAS/analogue	Lung Thinning + Anti-inflam.	NexGen	Ablation of Solid Obstructions -TBD
ASTHMA					
Advair	Inhal.	flutic.+ salem.	corticosteroid+beta-adr.agon.	Glaxo	12 wks: +FEV of 25% vs. 15% fluticasone, 5% salmeterol
Singulair	Oral	montelukast	Anti-inflam.: leuk. rcpr. antag.	Merck	12 wks: +FEV of 13%(0.32L) vs. 4%(0.1L) placebo
Pulmicort	Inhal.	budesonide	Anti-inflam: corticosteroid	AstraZeneca	12 wks: +FEV of 0.29 L vs. 0.1L for placebo
Symbicort	Inhal.	budes.+ form.	corticosteroid+beta-adr.agon.	AstraZeneca	+FEV of 9% post dose, 87% within 5 minutes
Flovent	Inhal.	fluticasone p.	Anti-inflam: corticosteroid	Glaxo	12 wks: +FEV of 9% - 11% at endpoint (3 studies)
TTRI-NonAbl.	Inhal.	DAS/analogue	cytokine,leukotri. downreg.	NexGen	to be determined
TTRI-NonAbl.	Inhal.	DAS/analogue	Antiviral+Anti-inflammatory	NexGen	For Asthma patients with viral lung infections -TBD
INFLUENZA					
Tamiflu	Oral	oseltamivir	Antiviral: neuraminidase inhib.	Roche	1.3 day reduction in median time to none to mild symptoms
Relenza	Inhal.	zanamivir	Antiviral: neuraminidase inhib.	Glaxo	up to 1 day less to imprmt. in symp., but not stat. significant
TTRI-NonAbl	Inhal.	DAS/analogue	Antiviral+Anti-inflammatory	NexGen	to be determined
RHEUMATOID ARTHRITIS					
Methotrexate	inject.	methotrexate	Antiprolif: S-Phase Cytotoxic	Hospira	12 mo ACR 70 (70% improve): 17%(Enbrel pi), 27%(Humira pi)
Enbrel	inject.	etanercept	Anti-inflam: TNF Blocker	Amgen,Pfizer	12 mo: Enbrel: 22% ACR 70, Enbrel + MTX: 40% ACR 70
Remicade	inject.	infliximab	Anti-inflam: TNF Blocker	J&J -Centocor	54 wks: Remicade+MTX: 11%-37% ACR 70 vs. 2 -21% MTX
Kineret	inject.	anakinra	Anti-inflam: IL1-R Antag.	Biovitum A.B.	6 mo: 1% - 6% had ACR 70 vs 1% - 2% placebo (study 1 & 3)
Humira	inject.	adalimumab	Anti-inflam.: TNF Blocker	Abbott	1 yr, ACR 70: 26% Humira, 27% MTX, 46% Humira+MTX
Rituxan	inject.	rituximab	CD20 Antibody (B-Cell Tox.)	Genentech	R+MTX 24 wk: ACR 70: 8-12% vs 1 - 11% MTX (study 1 & 2)
Orencia	inject.	abatacept	T-Cell activation inhibitor	BMS	3 mo ACR 70: 6%, ORN+MTX: 6 mo. 20-32% vs 7-20% MTX
Actemra	inject.	tocilizumab	Anti-inflam: IL-6 rcpr. block	Genentech	24 wk. ACR 70: 28% vs 15% MTX; 13% - 22% Actemra + MTX
Celebrex	oral	celecoxib	Anti-inflam: COX-2 inhibitor	Pfizer	no meaningful efficacy data disclosed in pi.
TTRI-NonAbl	transD	DAS/analogue	Anti-inflam. + Antiprolif.	NexGen	to be determined
TTRI-Abl.Reg.	transD	DAS/analogue	Anti-inflam+Synovial Ablat.	NexGen	Ablation of Chronic Synovial Overproliferation - TBD