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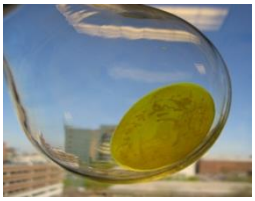
ST-001 NanoFenretinide

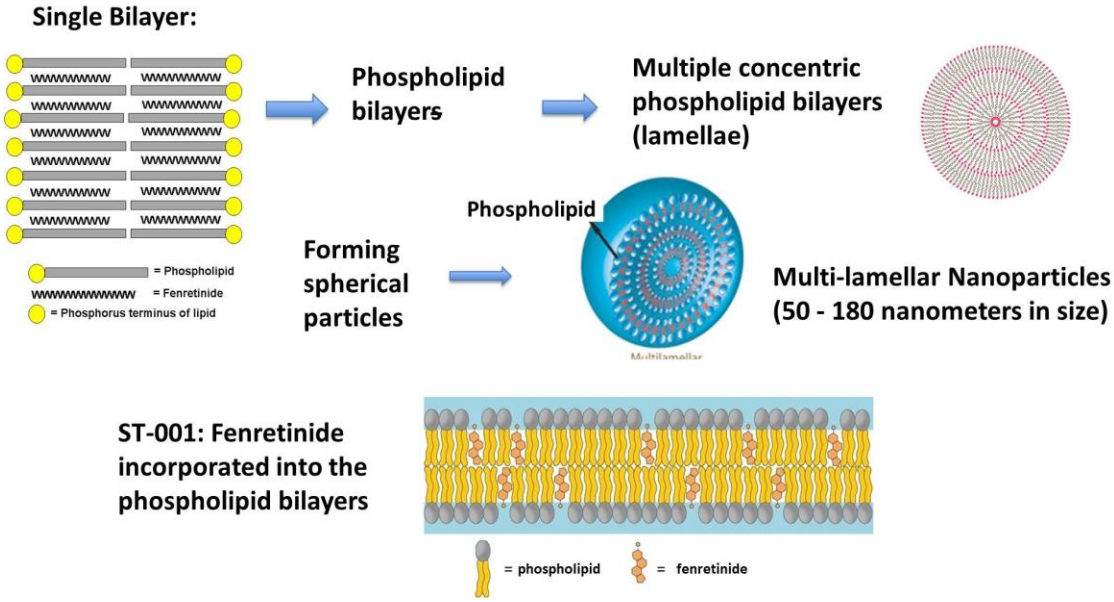


ST-001 Manufacture

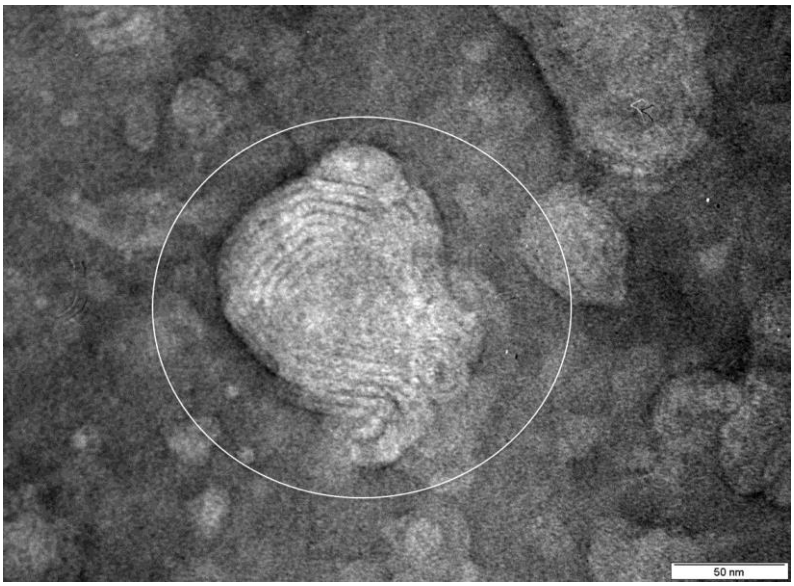
SciTech's lead compound, ST-001, is a small-molecule immune oncology nanoFenretinide cancer drug employed as an aqueous nanoparticle suspension for IV administration. The ST-001 nanoFenretinide drug is comprised of fenretinide in a patented combination with carefully selected phospholipids (inactive ingredients). The phospholipids, comprising ST-001, were chosen because of their extensive use in humans and are recognized as safe for IV use by the FDA. Moreover, they were chosen because of their unique chemical and physical properties, that when combined with those of fenretinide, yielded an integrated, robust structure that contained much higher concentrations of fenretinide. The nature and relative proportions of all the ingredients (composition of matter covered in our patents), that are assembled and manufactured in a very specific manner defines the unique attributes of ST-001.

ST-001 is designed to deliver a 15-fold higher drug to lipid ratio and a >6x concentration of the API than conventional IV formulations achieving therapeutically effective doses without the toxic side effects observed with other delivery systems – a benefit previously unattainable. Recent discovery of the API's immunotherapeutic effect, in which a reactivated natural immune response compliments the previously understood safe, direct, chemotherapeutic effect (functioning as dual mechanisms of action), has added materially to its value as a versatile therapeutic.

Given below is a graphical representation of the ST-001 molecular architecture depicting the 2D to 3D self-assembly of the phospholipid-fenretinide complex from bilayers to spherical concentric multilayers (lamellae).



The multi-lamellar structure of the ST-001 nanoFenretinide particle is readily evident in the electron microscopy image provided below.



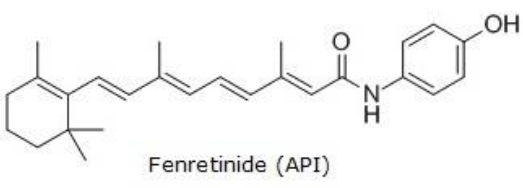
The versatility of the SciTech technology is illustrated below where new drug products "ST-00X" (for IV and topical administration) may be generated by changing the phospholipids to accommodate different drugs (API).

ST-001 = Fenretinide Bilayer Matrix **ST-00X = API Bilayer Matrix**

Given below is SciTech's current drug product pipeline:

ST-001 – Intravenous fenretinide formulation for the treatment of NHL.
ST-002 – Topical formulation for the treatment of various skin cancers and bed sores.
ST-003 – Intravenous formulation for the treatment of small cell lung cancer (SCLC).
ST-004 – Intravenous formulation for the treatment of metastatic breast cancer (MBC).
ST-005 – Intravenous formulation for the treatment of neuroblastoma (pediatric cancer).
ST-006 – Intravenous formulation for the treatment of T-cell acute lymphoblastic leukemia (T-ALL).

Fenretinide (API)



Fenretinide (API)

API's Chemical Structure and Properties - Fenretinide (4-hydroxy(phenyl)retinamide; 4-HPR) is the active pharmaceutical in SciTech's ST-001 formulation. It is a synthetic retinoid derivative related to vitamin A (retinol). Fenretinide is a relatively small molecule (Chemical Formula: $C_{26}H_{33}NO_2$; Molar Mass: 391.546 g/mol) that has been extensively studied and well characterized (PubChem CID: 5288209). It is essentially insoluble in water (water solubility: 0.00119 mg/mL) but significantly more soluble in organic solvents and lipids.

API's History - McNeil Laboratories first developed fenretinide as an anti- cancer drug in the early 1980s. Subsequent drug studies by Johnson & Johnson (J&J), the National Cancer Institute (NCI) and others have generated a large body of data available for public use. These earlier studies demonstrated fenretinide's safety and efficacy as a therapeutic

agent. The history of fenretinide is a fitful series of discoveries about its unique therapeutic properties followed by clinical trials to evaluate these properties using suboptimal pharmaceutical compositions that happened to be available.

The substantial body of medical literature shows that fenretinide has significant anticancer activity in experimental and clinical settings. The drug destroys cancer cells by selectively inducing apoptosis. Clinically, the drug is effective at treating and preventing cancer when blood plasma levels reach the minimum therapeutic threshold for several days. Because of the poor systemic bioavailability of fenretinide, it has not hitherto been possible to achieve that minimum therapeutic threshold safely and so it has not been possible to achieve the drug's full therapeutic potential.

Fenretinide's performance has been well scrutinized in humans. Particularly noteworthy studies include the following: (1) A large study of breast cancer chemoprevention (approx. 3000 patients, 5 year study) demonstrating fenretinide to be well tolerated in humans; (2) NCI case report confirming tumor response in an advanced cutaneous T-cell lymphoma patient (CTCL) - an early efficacy signal; (3) ASCO paper confirming therapeutic responses in the treatment of CTCL and angioimmunoblastic T-cell lymphoma (AITL) that also highlights the shortcomings of the competition's product, and (4) Phase II clinical study showing fenretinide to be well tolerated in patients with small cell lung cancer (SCLC) as well as a stabilization of the disease in 30% of the patients.

As a safer analog of vitamin A, fenretinide entered the clinic as a low strength formulation in corn oil loaded into a soft gel cap (100-mg) designed for chemoprevention studies, and clinical studies reported efficacy, especially in premenopausal women, but fenretinide failed to displace tamoxifen in this setting, and interest waned. Fenretinide acquired a reputation as a chemotherapeutic agent based on reports of its ability to induce apoptosis, distinguishing it mechanistically from natural retinoids, and NCI CTEP sponsored dose-escalation Phase 1 trials to establish its MTD and safety profile. However, without re-formulation to deliver the higher doses, it was perhaps not surprising that chemotherapeutic plasma levels could not be achieved due to limits on oral bioavailability. The recommended Phase 2 Dose (RP2D) of fenretinide was set at 900 mg/m^2 bid, not defined by toxicity but rather by the dose associated with achieving maximum possible Cmax and AUC in >80% of patients. Unfortunately, the achievable Cmax was 2-3 fold below concentrations needed for apoptosis in preclinical models, and Phase 2 results were predictable: modest disease stabilization but not regression in SCLC and no significant activity in renal cell cancer, associated with sub-therapeutic intratumoral drug levels in biopsies. A Phase II study in ovarian cancer reported an association between efficacy and a steady state plasma concentration >9 microM, but concluded that formulations with improved bioavailability were still needed. An investigational oral formulation of fenretinide complexed with Lym-X-Sorb, a commercial lipid product from BioMolecular Products Inc., only modestly improved oral bioavailability in pediatric patients (average Cmax of 21 microM) with predictable modest efficacy. Similar results were obtained from a Phase 1 trial of the fenretinide:LXS complex in adult patients, leading the authors to state in the abstract "Better fenretinide formulations are needed to… achieve the consistent systemic exposures associated with activity in preclinical models". However, this Phase 1 report did note that 1 of 2 CTCL patients experienced disease stabilization with improvement in pruritus and resolution of skin infections despite poor drug bioavailability.

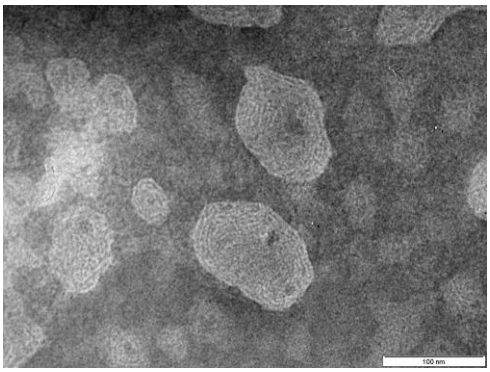
The experience to date suggests an inherent limitation on oral bioavailability of fenretinide, so it seemed prudent to pursue injectable formulations that will circumvent the problem altogether. The first IV formulation was developed and patented under the NCI-RAID program: an IV emulsion formulation of 2 mg per cc fenretinide. In the Phase 1 trial, clinical responses were reported in three patients, not including a transient response in NHL at a low dose level (reported at ASH 2007), and it is striking that these three cases were T cell NHL: one case of CTCL and two cases of angioimmunoblastic lymphoma.

Responses in the Phase 1 Clinical Trial of emulsion-fenretinide, qdx5 CIVI q3wk (ASH 2007, Abstract #2581) (highlighted dose level is RP2D)			
Dose Level mg/m2/day	**Diagnosis**	**Response**	**Toxicities by Dose Level**

905	angioimmunoblastic T-cell lymphoma	4+ month unconfirmed CR (6+ month CR)	2 of 5 pts Grade 4 hypertriglyceridemia that resolved after stopping the infusion
1280	CTCL HDACi- and bexarotene-refractory	10+ month molecular CR	1 of 5 pts Grade 4 hypertriglyceridemia
1810	angioimmunoblastic T-cell lymphoma	8+ month PR	2 of 3 pts Grade 4 hypertriglyceridemia

The case report of the durable CTCL response described a 28 year old female presenting at the NCI clinic with stage IV Sézary Syndrome after 3 cycles of CHOP and one cycle of gemcitabine, during which Sézary cells appeared. At the NCI, she received three protocols over nine months with mixed response: standard bexarotene, a phase II HDAC and a phase II immunotoxin. In stark contrast, six cycles of fenretinide-emulsion achieved a confirmed tumor response, and 26 cycles achieved sustained CR and no evidence of pruritic plaques or erythema. Significantly, this CTCL patient had prior, unsuccessful bexarotene and HDAC therapies, indicating lack of cross-resistance of fenretinide.

The CTCL case is an early efficacy signal of fenretinide in MF/SS, analogous to the serendipitous efficacy signals in MF/SS patients from Phase 1 trials of bexarotene, vorinostat and romidepsin described above that eventually led to their approval as CTCL therapies, and this early efficacy signal is the rationale for proposing CTCL as the disease target of ST-001. The efficacy signal of romidepsin in CTCL that arose from a NCI Phase 1 trial was pursued with a definitive Phase 2 trial, so an important question is why the early efficacy signal of emulsion-fenretinide was not similarly pursued into Phase 2. The reason appears to be the severe hypertriglyceridemia (Grade 4) associated with the efficacious dose levels, and the fact that 2 of 3 clinical responses, including the SS patient who did not experience this toxicity, occurred at dose levels at or above the Recommended Phase 2 Dose (RP2D) of 905 mg/m2/d (highlighted in Table). These findings point to the strategy to finally realize the clinical potential of fenretinide: IV administration coupled with the highest possible strength formulation to minimize any contribution of the load of lipid excipients to hypertriglyceridemia (the emulsion was 2 mg per cc). SciTech dropped its pursuit of emulsions when it became clear that it was limited to strengths <6 mg per cc (unpublished data), and instead launched a R&D program to design a lipid carrier-based approach specifically to support high strength fenretinide formulations.



ST-001 NanoFenretinide Particles

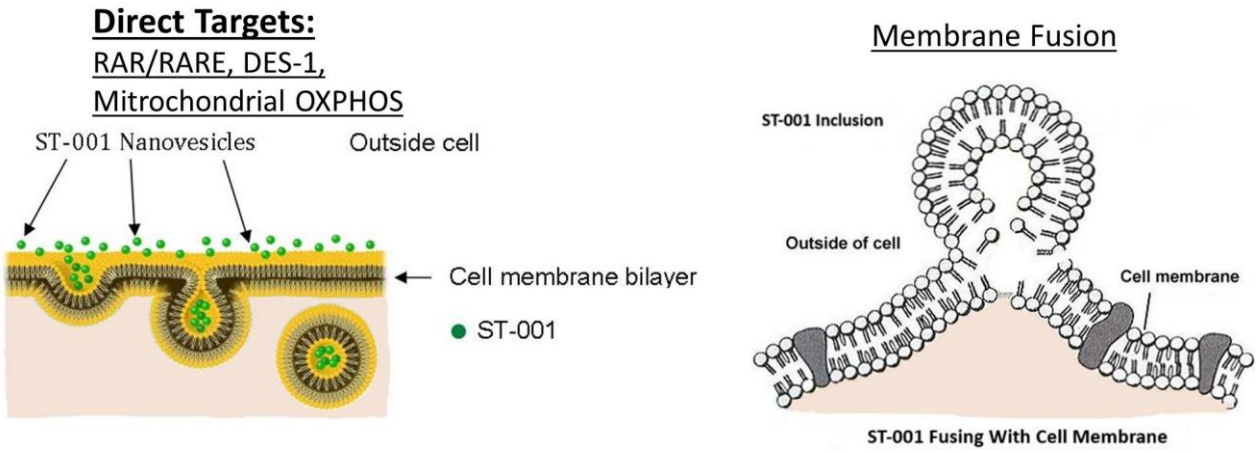
McNeil and J&J transferred the development rights of fenretinide to the National Cancer Institute (NCI) after they were beaten to market by Tamoxifen. Subsequently, the NCI, as well as others, struggled for years to overcome fenretinide's inherent poor solubility problem resulting in low bioavailability - **limitations successfully overcome by SciTech's drug formulation product (ST-001) and of great interest to pharma.** Fenretinide is currently in the public domain and the NCI has specifically made the cGMP manufactured API available to SciTech *gratis* for further use and development. **J&J** continues to follow the company's development path and **has formally expressed an interest in engaging in collaboration to develop SciTech's ST-001 "franchise"once any human therapeutic response is confirmed.** They would like to engage us in studying its use in treating small cell lung cancer (SCLC). This position is based on J & J's assessment that prior clinical data suggests that an enabled fenretinide product will likely be a viable therapeutic candidate for the treatment of SCLC. It is our opinion that this speaks elegantly to the potential of ST-001 and the prospect of interesting deal exit events materializing.

Mechanism of Drug Action - There is ample evidence in the scientific literature that demonstrates that fenretinide is selectively cytotoxic and destroys cancer cells by inducing apoptosis (programmed cell death). It has been shown that

fenretinide generates several apoptosis-mediating agents such as ceramides, reactive oxygen species (ROS), and ganglioside.

Recently, fenretinide has been shown to reactivate the immune system in the treatment of lymphoma. The fact that fenretinide induces multiple apoptosis mediators and a likely immune response has served as the basis of predictions regarding its efficacy in so many different types of cancer. The most common side effects reported with oral, lower dose fenretinide use include skin dryness and night-blindness, which are both reversible upon cessation of the fenretinide treatment.

Given below is a graphical representation of ST-001 drug delivery and mechanism of action.



- Once inside the cancer cell fenretinide affects multiple biochemical pathways ultimately causing cell death via apoptosis
- These pathways include retinoid receptors, oxygen radicals and inhibition of ceramide (unlike retinoic acid)*
- Systemic ST-001 nanoparticles may enter cells like Exosomes and Ectosomes

*Kalemkerian, G.P., et al., Growth inhibition and induction of apoptosis by fenretinide in small-cell lung cancer cell lines. J Natl Cancer Inst, 1995. 87(22): p. 1674-80.