# NUFS™ (Nanoparticulation Using Fat and Supercritical fluid)

## Bio-Synectics, Inc.


**Contact Information**

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|---|---|
| **Industry Sector** | Biotechnology, Drug delivery, Pharmaceutical |
| **Therapeutic Area** | Oncology |
| **Stage of Development** | Preclinical |

## 1. Summary

- The NUFS™ is a drug delivery platform technology enabling efficient and effective formulation of poorly soluble drug substances. It generates nanoparticles of poorly water soluble substances by utilizing edible solid lipids and the supercritical fluid of CO2.
- The nanoparticulate form of poorly soluble substances generated by the NUFS™ process can be conveniently used for various drug formulations such as oral, intravenous, inhalable, topical, and so on.

## 2. Applications

- In case of oral formulation the technology can be very helpful for solving the problems caused by the poor solubility of drug substances such as poor bioavailability, inter-individual variances, and fed-fasted variances.
- The technology enables convenient intravenous formulations by only nanoparticulate dispersions of drug substances. So it can be used for the reformulation of chemotherapy drugs with harsh surfactants in order to remove the problem of hypersensitivity.

## 3. Market Feasibility

- In pharmaceutics, 90% of active ingredients are in the form of solid particles, so the solubility of the active ingredients is a key factor governing the efficacy of the drug substance.
- It is said that 90% of marketed drugs since 1995 show low solubility and more than 40% of NCEs show very poor solubility.
- The NUFS™ technology can be a strong tool in developing the drug formulation of new chemical entities and also for the reformulation of approved drugs for better efficacy and patient's convenience.

## 4. Type of Business Relationship Sought (include licensing availability)

- The licensing of the NUFS™ technology as a drug delivery system solution.
- The partnership and licensing agreement to perform preclinical, clinical development of NufsDTX™.

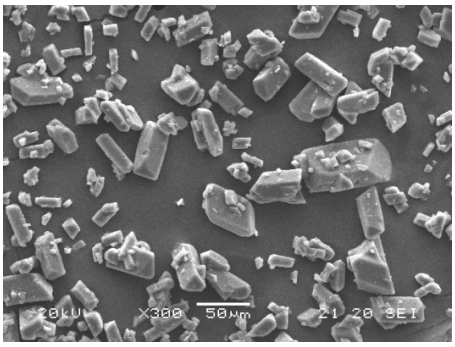
## 5. Technical Advantages

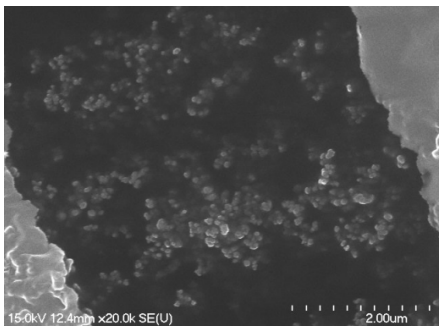
- A platform technology applicable to many poorly soluble substances
  - The competing nanoparticulation technology, wet-milling is known to have the concern of possible contamination from milling media making it difficult to be used for intravenous injectables. But the NUFS ™ process can be used for various formulations such as oral, injectable, inhalable, topical, and so on.

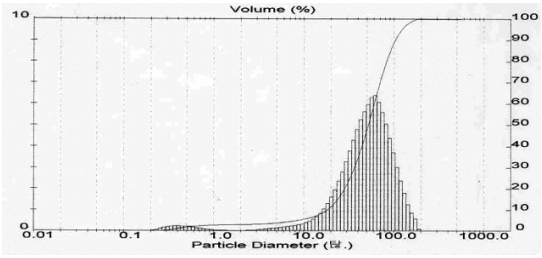
- No safety concern on the carrier
  - The NUFS ™ process only uses FDA approved inactive ingredients without using any special carriers to make nanoparticles.

- Superior nanoparticle characteristics
  - The [Figure 1] below shows the example of nanoparticulation using itraconazole. The NUFS ™ process typically produces very narrowly distributed particles in the range of 100nm~300nm.

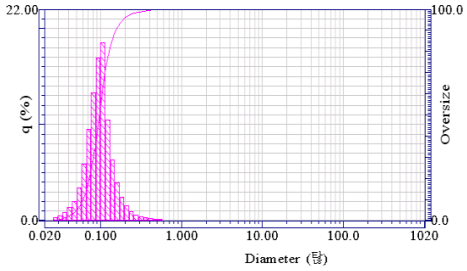
- Easy and cost-effective process
  - As we can get a powder form as the direct output from the NUFS™ process there is no need for drying steps which are typically needed for other technologies such as wet-milling and high pressure homogenization.
  - The technology can be easily incorporated into the cGMP requirements.




**[Original particle size : mean 80㎛]**




**[After NUFS™ : mean 100 nm]**

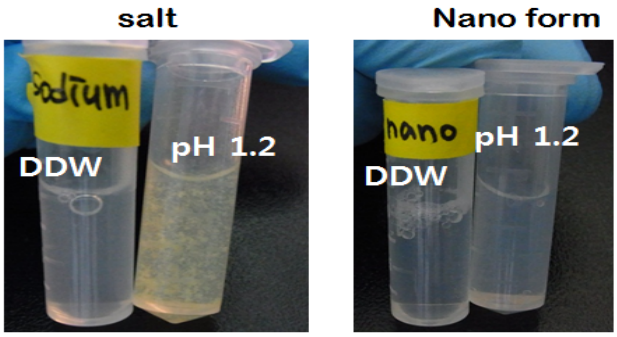
[Figure 1] An example of NUFS™ process

## 6. Technical Highlighted Summary

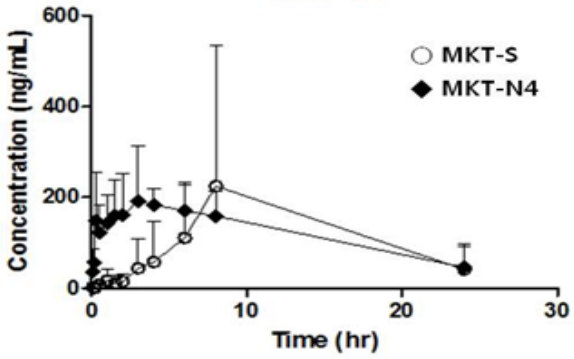
- The example of reformulation of SINGULAIR®(montelukast sodium) as a nanoparticulate free base form shows that the the NUFS™ technology can be used to decrease the inter-individual drug absorption variances and shorten the time for drug absorption not only to enhance the bioavailability.

  - [Figure 2] shows that the sodium salt form of the original drug precipitates in the acidic condition of stomach, but the nanoparticulate form keeps stable status.

- [Figure 3] shows that by the free base nanoparticulation we can expect similar bioavailability (AUC and $C_{MAX}$), faster absorption($T_{MAX}$), and decreased variance($CV_{AUC}$) compared with the original drug.



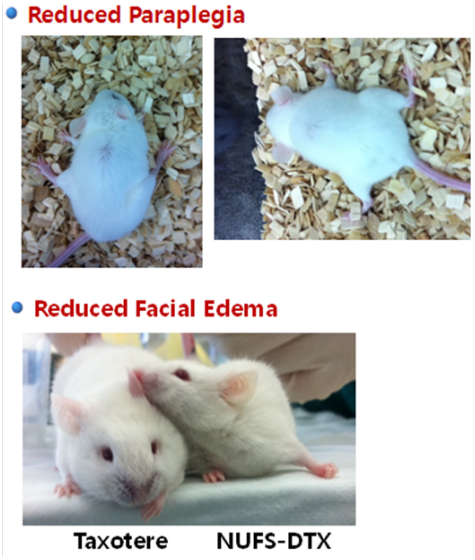

[Figure 2] Comparison of precipitation



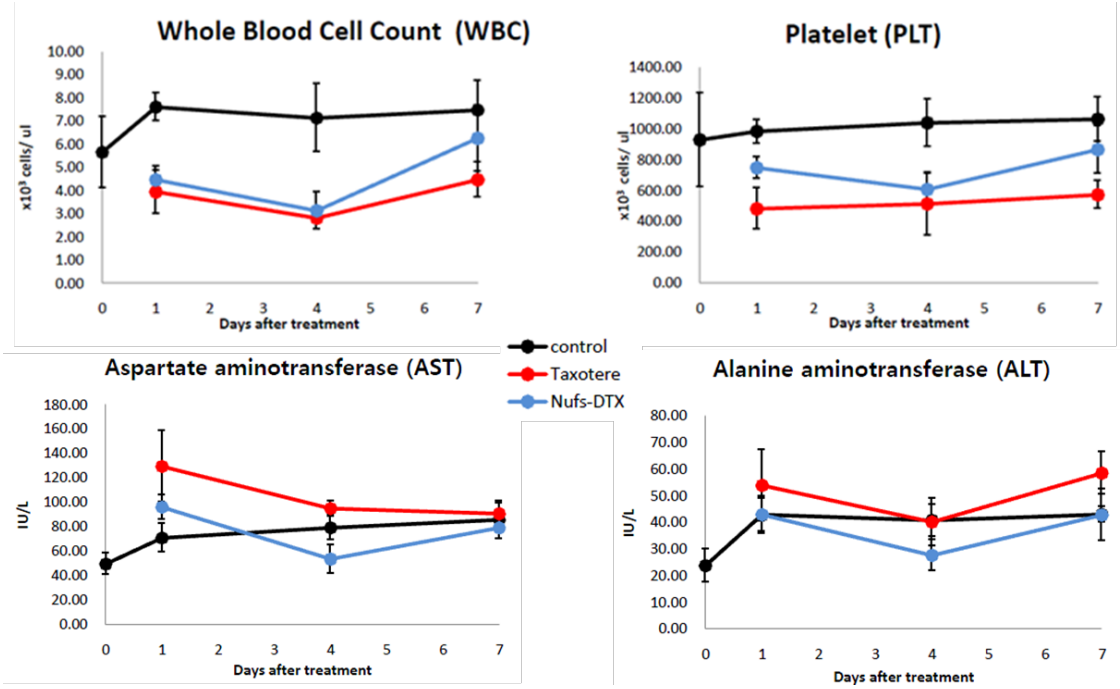

| Drug Formulation | $AUC_{0-24}$ (ng·hr/mL) | $CV_{AUC}$ (%) | $T_{max}$ (hr) | $C_{max}$ (ng/mL) |
|---|---|---|---|---|
| MKT-S (n=9) | 2748.0 ± 2722.4 | 99.1 | 6.0 ± 2.6 | 267.2 ± 291.2 |
| MKT-N4 (n=7) | 2975.8 ± 433.9 | 14.6 | 3.0 ± 2.0 | 266.2 ± 74.8 |

- We applied the NUFS™ technology to develop the toxic surfactant free form docetaxel (NufsDTX™). By performing various animal test we confirmed that NufsDTX™ has the similar anti-cancer efficacy with the original drug TAXOTERE® and as can be seen in the following pictures the reformulation provides very low toxicity profiles compared to the TAXOTERE®.

| Comparison | NUFS-DTX (vs Taxotere) |
|---|---|
| Mortality rate | Lower |
| Clinical signs | Reduced and delayed paraplegia |
| Body weight changes | Almost no reduction in low dose |
| CBC, Chemistry | No distinction |
| Organ weight | Less reduction |
| Histopathology | Less toxicological lesions |




[Figure 4] Comparison of overall toxicity



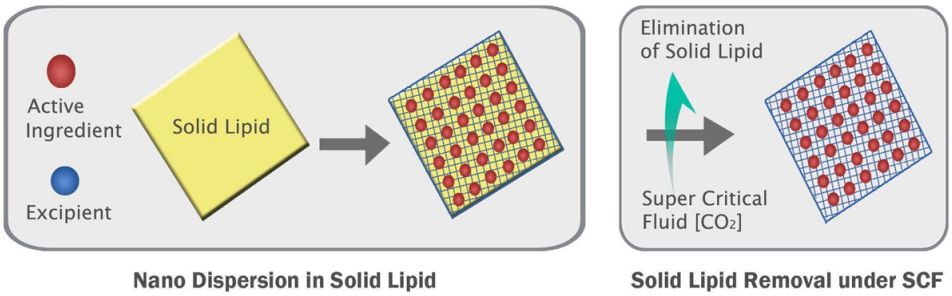

[Figure 5] Hematologic toxicity and hepatotoxicity

## 7. Mechanism (MOA)

- The NUFS™ technology is composed of the following two steps.

[Step 1] The nanoparticles of an active ingredient are generated within the mixture of solid lipids

[Step 2] By applying the supercritical extraction process the solid lipids are removed and the nano-dispersible powder of the active ingredient is acquired.




[Figure 6] NUFS$^{IM}$ process

## 8. Patent Information and Status

The patents for the NUFS$^{TM}$ technology are registered or in the process of registration in major countries including US, Europe, China, Japan, Canada, Australia, India, and Korea.

## 9. Patent Number(s)

| Title | Appl. Number | Country | Status | Asignee |
|---|---|---|---|---|
| Method for preparing nano-scale or amorphous particle using solid fat as a solvent | PCT/KR2004/002914 (2004.11.11) | Korea | Registered | Bio-Synectics |
| | | U.S.A | Registered | |
| | | Europe | Published | |
| | | China | Registered | |
| | | Japan | Registered | |
| | | Australia | Registered | |
| | | Canada | Published | |
| Method for preparing nano-scale particle of active material | PCT/KR2007/002172 (2007.5.3) | Korea | Registered | Bio-Synectics |
| | | U.S.A | Published | |
| | | Europe | Registered | |
| | | China | Published | |
| | | Japan | Registered | |
| | | Australia | Published | |
| | | Canada | Published | |
| | | India | Published | |

## 10. Key Words

Drug Delivery, Nanoparticle, Nano Drug Delivery, Nanoparticulation, Drug Formulation, Docetaxel, Docetaxel nanoparticle, Taxane nanoparticle

## 11. Company Description

- Bio-Synectics, Inc. is a biopharmaceutical company incorporated in 2004. Based on the patented nanoparticulation technology we develop drug delivery solutions for partnering pharmaceutical companies and also we are working on our own pipeline of incrementally modified drugs. Other business activities of Bio-Synectics, Inc. include the manufacturing and sales of value added nutraceutical and cosmetic ingredients.
- CEO : Kab-Sig Kim, Ph.D.
- Paid-in Capital : KRW 1,290,000,000