ナノバブル酸素供給　－　赤血球が酸素をとどけづらい組織にまで酸素を供給する新技術

NuvOx Pharma

１．原理；High Pressure homogenization装置でナノレベル（250～300nm)でエマルジョン化したDDFPe (Dodecafluoropentane nano-emulsion)は２８°Cで気化するので、体内に点滴投与されたのち、ナノバブルに変化しますが、血液内に溶け込んだ状態を保持します。この時、酸素分子はDDFPeへの非常に高い溶解性によりバブルに吸収された状態を保ち末梢組織、梗塞部位下流への高い酸素運搬能力を示す。

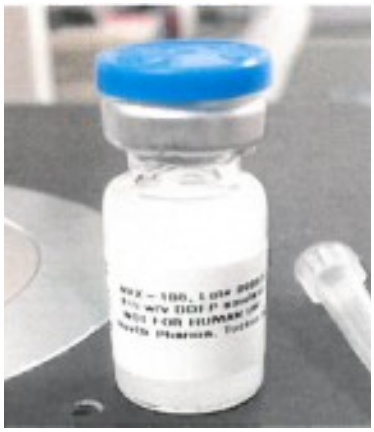
２．用途；１）がん放射線治療の補助療法（がん細胞細胞内の酸素分圧を高めることにより、放射線療法の効果が上がる）

２）心筋梗塞や脳梗塞患者への急性期投与ならびに補助療法

３．溶液100mlあたりの酸素含量；

DDFPe 投与を0.6ml/kgとすると、1回に40ml程度を静脈注射することとなる。DDFPe の酸素結合能力がヘモグロビンの200倍なので、40mlだと1600mlの酸素を含有することになる。ヘモグロビンが末梢組織へ1分間あたり1000mlの酸素を運搬しているので1600mlが上乗せされる。

半減時間；９０分



４．剤型・保存；5ml ～10mlの瓶、４℃で１年以上、室温で１年以内

５．投与法・投与量；静脈注射、放射線治療では純酸素吸入可能。

放射線治療ー0.1ml /kg, その他ー0.1～0.6ml/kg

６．組織酸素分圧上昇曲線（持続時間）；２時間以上

７．承認；欧州で許可済み、米国ではGlioblastoma（膠芽細胞腫）に対するがん放射線治療の補助として使用するオーファンドラッグとして認可済み。

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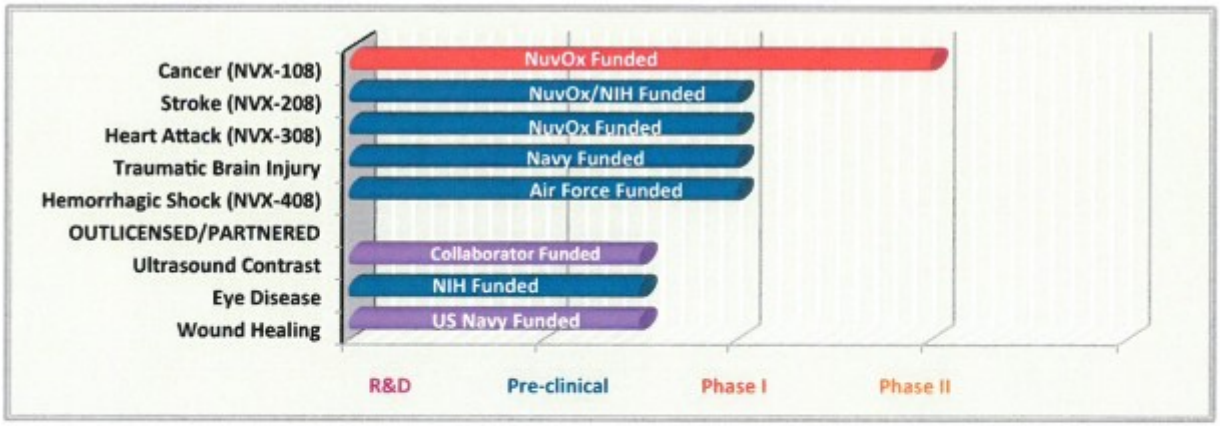
８．パイプライン；

NuvOx Pipeline



- **NVX-108 Cancer:** Over 400% increase in tumor pO_2 with
  - Four (4)-fold increased survival in prostate tumor model treated with radiotherapy (RT)
  - Two (2)-fold increased survival in pancreatic cancer model treated with RT
  - Complete reversal of radiation resistance in hepatoma model.
- **NVX-208 Stroke:** Reduced brain damage 85% in animal models for stroke.
- **NVX-308 CV:** Reduced heart damage 80% in animal model for heart attack.
- **NVX-408 Hemorrhagic Shock:** 100% survival in porcine for hemorrhagic shock.
- **NVX-428 Traumatic Brain Injury:** Demonstrated increased cerebral oxygenation

Figure 1. Below, shows the effect of NVX-108 on tumor oxygen level in a pancreatic tumor xenograft in mice. The tumor pO_2 level was at zero until administration of NVX-108.

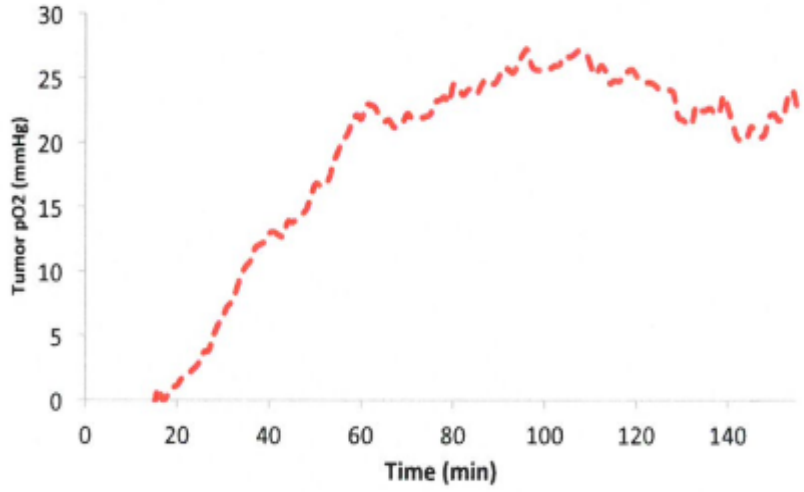


Figure 1. Tumor hypoxia (low oxygen in tumor tissue) is a major impediment to successful tumor treatment. IV administration of NVX-108 increases tumor pO_2 as shown in Figure 1 to left. Radiation treatment (RT) is more effective after administration of NVX-108, **improving survival** in animals treated with RT.

８．特許；

＊ The FDA has designated DDFPe as a Biologic. Designation as a Biologic currently confers 12 years exclusive for 1st in class indication.

＊ NuvOx is the exclusi ve licensee of 4 issued US patents: US5869538 and US6127428 (methods for enhancing transport of gases to tissues), US5876696 and US6245319 (compositions of matter for DDFPe).

＊ NuvOx received notice of allowance for a key composition of matter patent in April, 2014 (US2013/0096204A1).

＊ NuvOx strategy is to strengthen the patent estate surrounding its products.

In 2011 NuvOx filed a patent application for DDFPe microbubbles, which has entered the PCT phase.

In 2012 NovOx filed a patent application for DDFPe in tissue allograft preservation for organ transplantation.

In 2014 NuvOx filed a patent application for DDFPe cancer treatment applications/compositions.

＊ Additional patents are currently being filed strategically to protect the products under development in the Pipeline.

９．Management:

Evan Unger, MD – President & CEO. Dr. Unger has founded three biotech companies. His first company, ImaRx Pharmaceutical, developed 3 FDA approved drugs and was acquired by DuPont yielding a > 20x ROI. Dr. Unger's second company, ImaRx Therapeutics, went public and performed clinical trials in a pioneering new technology to treat stroke. Dr. Unger co-founded NuvOx, in-licensed the core patents and obtained ownership of the regulatory documents for NuvOx key product. Dr. Unger is inventor on 113 issued US patents. He is a board-certified radiologist and has an appointment as professor of radiology and biomedical engineering at the University of Arizona.

Betty R Weaver, CPA - Chief Financial Officer. Ms. Weaver has over 18 years in public accounting with a regional firm in the Dallas/Fort Worth area and as principal of accounting firms in Texas and Arizona. . Ms. Weaver has over 15 years in industry with responsibility for operations, accounting, treasury, facilities, human resources and information technology.

Rajan Ramaswami, PhD – Vice President of Operations. Dr. Ramaswami has over 15 years of experience in leading the Chemistry Manufacturing and Controls (CMC) operations for successful drug development programs at ImaRx Pharmaceuticals Corp and its successor company ImaRx Therapeutics, Inc. As a Chemistry Manufacturing and Control subject matter expert, he has reviewed product development plans, Module 3 section of the IND/NDA for various clients for products ranging from topical/dermal creams/lotions, liquid/solid dose oral formulations, and nano-emulsions and lyophilized powders for intravenous administration Since joining NuvOx, he has assumed the primary responsibility to oversee manufacture of NVX-DDFP nano-emulsions and oversee the research and development efforts of the product pipeline.

Gordon Brandt, MD – Vice President of Regulatory Affairs. Dr. Gordon Brandt has been working with NuvOx since 2012. Dr. Brandt's career in drug, device and biologics development for US and international markets spans more than 30 years. He has led development teams resulting in both NDA and ANDA drug approvals in the US and in centralized marketing authorization for an ultrasound contrast agent in theEU. Dr. Brandt was most recently President and Executive Vice President Clinical/Regulatory at Nastech Pharmaceuticals, a publicly traded biotech company. Previously he led the clinical and regulatory development of EchoGen, a dodecafluoropentane ultrasound product which is the foundation of NuvOx technology.

連絡先；

株式会社 ＢＴＢ Ｊａｐａｎ

〒105-0004

東京都港区新橋５丁目２２－３

ル・グラシエルビル３号館４Ｆ

TEL・FAX : 03-6459-0258

URL : www.btbjapan.com
:担当　菊池　功
kikuchi@btbjapan.com