

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

**FORM 8-K**

CURRENT REPORT  
Pursuant to Section 13 or 15(d) of  
the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 22, 2017

**DIFFUSION PHARMACEUTICALS INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation)

**000-24477**  
(Commission File  
Number)

**30-0645032**  
(I.R.S. Employer  
Identification No.)

**2020 Avon Court, #4**  
**Charlottesville, Virginia**  
(Address of principal executive offices)

**22902**  
(Zip Code)

**(434) 220-0718**  
(Registrant's telephone number, including area code)

**Not applicable**  
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or Rule 12b-2 of the Securities Exchange Act of 1934.

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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**Item 7.01 Regulation FD Disclosure.**

Attached as Exhibit 99.1 and furnished for purposes of Regulation FD is a presentation to be provided to prospective investors in Diffusion Pharmaceuticals Inc. and certain analysts beginning on Monday, May 22, 2017.

The information in Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1) is being furnished solely to satisfy the requirements of Regulation FD and shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

<u>Exhibit Number</u>	<u>Description</u>
99.1	Diffusion Pharmaceuticals Inc. Presentation.

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: May 22, 2017

**DIFFUSION PHARMACEUTICALS INC.**

By: /s/ David G. Kalergis

Name: David G. Kalergis

Title: Chief Executive Officer

## Forward-Looking Statements

**Diffusio<sub>2</sub>n**  
Pharmaceuticals Inc.

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This presentation contains forward-looking statements within the meaning of U.S. securities laws that are intended to be covered by the safe harbors created by those laws. These statements include, but may not be limited to, our operating and growth strategy, including our product development plans and capital requirements. Such statements may be identified by the use of forward-looking terminology, such as “may,” “will,” “could,” “should,” “believe,” “expect,” “future,” “potential,” “anticipate,” “intend,” “plan,” “estimate,” or the negative or other variations of these words or comparable terminology. The outcome of the events described in these forward-looking statements is subject to significant risks, including those disclosed in our periodic reports filed with the Securities and Exchange Commission. Actual results could differ materially from the forward-looking statements made in this presentation. Although we believe that the assumptions underlying the forward-looking statements are reasonable, any assumptions could be inaccurate, and therefore, there can be no assurance that the forward-looking statements included in the this presentation, will prove to be accurate. In light of the significant uncertainties inherent in the forward-looking statements included herein, the inclusion of such information should not be regarded as a representation by the Company or any other person that the objectives and plans of the Company will be achieved. Further, the statements contained herein speak only as of the date hereof and we undertake no obligation to revise such forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

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# Diffusion<sub>2</sub>n

Pharmaceuticals Inc.

*Better Treatments for Cancer*

**David Kalergis, CEO**  
[dkalergis@diffusionpharma.com](mailto:dkalergis@diffusionpharma.com)

May 19, 2017  
[www.diffusionpharma.com](http://www.diffusionpharma.com)

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## Combating Cellular Oxygen Deprivation to Treat Unmet Medical Needs

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- First-in-class small molecules that safely re-oxygenate oxygen deprived (hypoxic) tissue by a novel mechanism; acts alone or with other treatments
- Multiple opportunities in unmet medical needs across \$ billion markets
- Initial oncology focus uses lead molecule TSC to enhance the efficacy of radiation and chemotherapy:
  - Glioblastoma brain cancer; Phase 2 successfully completed, with 380% 2-year survival improvement in inoperable patients; Granted Orphan Drug Designation
  - Metastatic brain cancer; Granted Orphan Drug Designation
  - Metastatic pancreatic cancer; Phase 2 program design guided by FDA and world experts
- Other Phase 2-ready hypoxia-related follow-on indications, supported by compelling clinical and preclinical data:
  - Stroke, in cooperation with UCLA
  - Peripheral arterial disease; Phase 2 study successfully completed
  - Myocardial infarction and emergency medicine
  - Respiratory diseases, including COPD
  - Neurodegenerative diseases
- IP patent portfolio protection through 2031 (including expected extensions)
- Experienced management, directors, advisors and key investors

# Management & Board of Directors

**Diffusio<sub>2</sub>n**  
Pharmaceuticals Inc.

## Executive Management

**David Kalergis, JD/MBA -- CEO, Chair & Co-Founder**

Life sciences serial entrepreneur, former Principal and General Counsel PRA International

**John L. Gainer, PhD -- CSO & Co-Founder**

Professor Emeritus University of Virginia, Chemical Engineering, Inventor of our TSC Technology

**David Jones, MD -- CMO**

Director of Thoracic Oncology Program at Memorial Sloan Kettering Cancer Center, Principal Investigator in 17 oncology clinical trials

**Thomas Byrne, MS, JD -- General Counsel**

Genentech, Amgen, Yale University, UVA

**Ben Shealy, CFA, MBA -- SVP Finance**

John Hancock buy side, DLJ sell side, VP M&A Corporate Software Rebar

## Board of Directors/Key Shareholders

**David Kalergis, JD/MBA -- CEO, Chair & Co-Founder**

**Isaac Blech -- Director/Vice Chair/Key Shareholder**

World Class Biotechnology Entrepreneur; founded leading companies Celgene, ICOS, Pathogenesis, Genetic Systems.

**John L. Gainer, PhD -- CSO & Co-Founder**

**Alan Levin -- Director**

Pharma Financial Executive, Former EVP & CFO of Endo Health Solutions, Former SVP & CFO of Pfizer

**Robert Adams, JD -- Director**

Former partner at Nixon & Vanderhye, Specialty US Patent and International Patent Licensing

**Mark T. Giles, JD -- Director**

Sole managing member of private investment company, Former chair & CEO of Virginia National Bank

**Frank Yu -- Shareholder**

Founder and CEO, Ally Bridge Group, a leading China-global cross-border healthcare-focused investment group.

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Diffusion Pharmaceuticals' Scientific  
Advisors

**Guy M. Chisolm, PhD, SAB Chair**

Professor, (ret.) Department of Cellular and Molecular Medicine;  
Vice Chair of Lerner Research Institute at Cleveland Clinic

**Gene H. Barnett, MD., MBA, FACS**

Director, Rose Ella Burkhardt Brain Tumor and Neuro-Oncology  
Center, Cleveland Clinic Neurological Institute

**William R. Hiatt, MD**

Professor for cardiovascular research at the University of  
Colorado School of Medicine, Division of Cardiology with a  
clinical and research focus in vascular medicine

**Karen C. Johnston, MD, MSc**

Harrison Distinguished Professor, Chair of Neurology at  
University of Va. Leads Phase III Shine ischemic stroke trial

**Jeffrey L. Saver, MD, FAHA, FAAN, FANA**

Director of the UCLA Stroke Unit, and Professor and SA Vice-  
Chair of Neurology at the David Geffen School of Medicine

**Kathleen A. Welsh-Bohmer, Ph.D., ABPP-CN**

Director of the Joseph and Kathleen Bryan Alzheimer's Disease  
Research Center (Bryan ADRC) at Duke Medical Center



# Diffusio<sub>2</sub>n

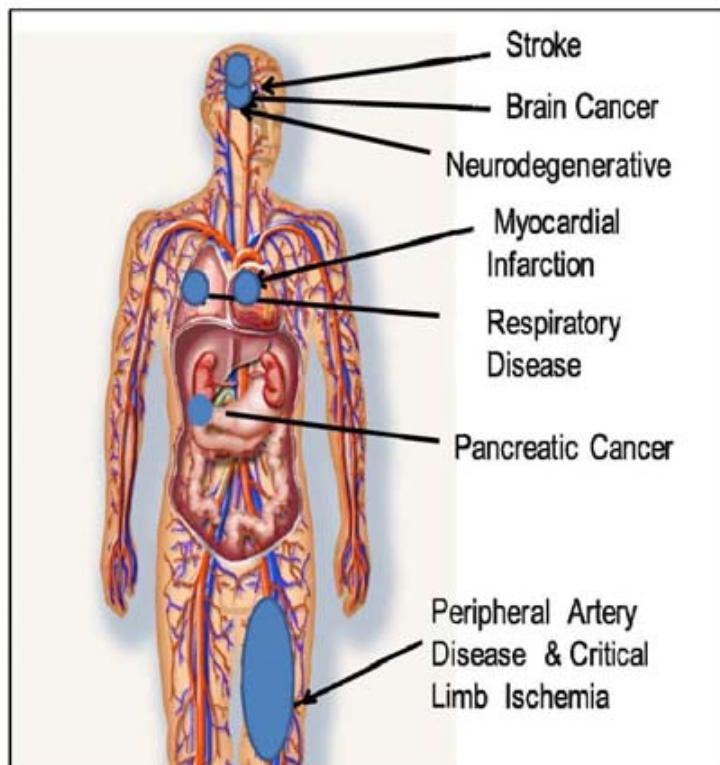
Pharmaceuticals Inc.

## Target Markets

Hypoxia-related conditions, with an initial focus on oncology

# Hypoxia: Cellular Oxygen Deprivation

- Insufficient oxygen supply ("hypoxia") to the body or a region of the body causes major clinical problems in many life-threatening diseases
- Hypoxia is an especially critical obstacle in the treatment of cardiovascular and respiratory diseases, as well as in cancer
- A successful new approach to treating hypoxia would open numerous unmet medical needs in \$ billion markets



- A common feature of many solid cancers
- Caused by tumors outgrowing their blood supply
- Through HIF1 $\alpha$  up-regulation, hypoxia is associated with many negative effects that lead to aggressive tumor phenotypes
  - Increased angiogenesis
  - Increased metastatic potential
  - Increased resistance to treatment
    - Cytotoxic therapy
    - Radiation therapy
- TSC re-oxygenates hypoxic tissue systemically, including cancerous tissue

Cancers with hypoxia-related treatment-resistance:

**Glioblastoma Multiforme**

Worldwide Market \$1B +  
12,000 Patients in the USA  
28,000 Patients worldwide

**Pancreatic Cancer**

Worldwide Market \$3B +  
49,000 Patients in the USA  
100,000 Patients worldwide

**Metastatic Brain Cancer**

Worldwide Market \$5B +  
170,000 Patients in the USA  
375,000 Patients worldwide

Other hypoxic cancers include breast, lung and ovarian

Source of demographic/market data: Cowen & Co., Therapeutics Categories Outlook

# Diffusi<sub>2</sub>n

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TSC Technology, Pipeline  
& Mechanism

# TSC: First-in-Class New Chemical Entity Targeting Hypoxia

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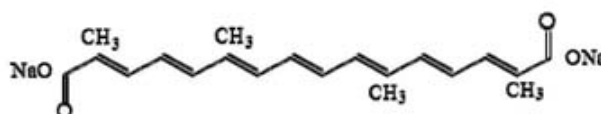
**The Problem:** Hypoxia is an underlying cause of fatality or morbidity in numerous unmet medical needs

**The Solution:** *Oxygen diffusion enhancing compounds* that selectively regulates oxygen's pathway through the body by a novel MOA

**Optimized lead compound:** Trans Sodium Crocetinate (TSC)

- Synthetic small molecule designed to enhance the diffusion of oxygen selectively into hypoxic tissue

TSC is one of a new class of compounds called Bipolar Trans Carotenoid Salts. TSC is the most advanced of these compounds, having been studied in 3 completed clinical trials with 2 more clinical trials planned.



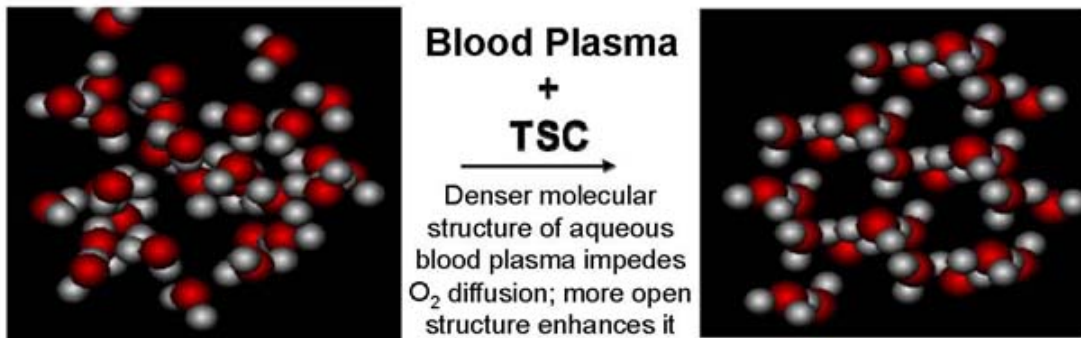
**New Chemical Entity with Novel Mechanism of Action  
that Enhances Oxygen Diffusion to Hypoxic Regions in  
Many Disease Settings**

- ✓ TSC developed at University of Virginia (USA) by Professor John Gainer, Diffusion Pharma's Co-Founder
- ✓ Initially developed under a grant from US Office of Naval Research as an emergency treatment for battlefield casualties suffering life-threatening hypoxia from blood-loss
- ✓ Transitioned to oncology clinical trials as a first focus, based on promising pre-clinical and human safety and efficacy data

## TSC's Mechanism of Action

- First modern drug compound designed to harness the “**cosmotropic**” effect to impart systemic therapeutic benefit
  - When added to an aqueous solution such as blood plasma, cause the aqueous molecules to form more hydrogen bonds with each other
- Additional hydrogen bonds change arrangement of molecular structure of the aqueous portion of blood plasma
  - Oxygen can more easily diffuse into hypoxic tissue due to more open structural arrangement

Denser molecular structure → (additional hydrogen bonds) → more open molecular structure





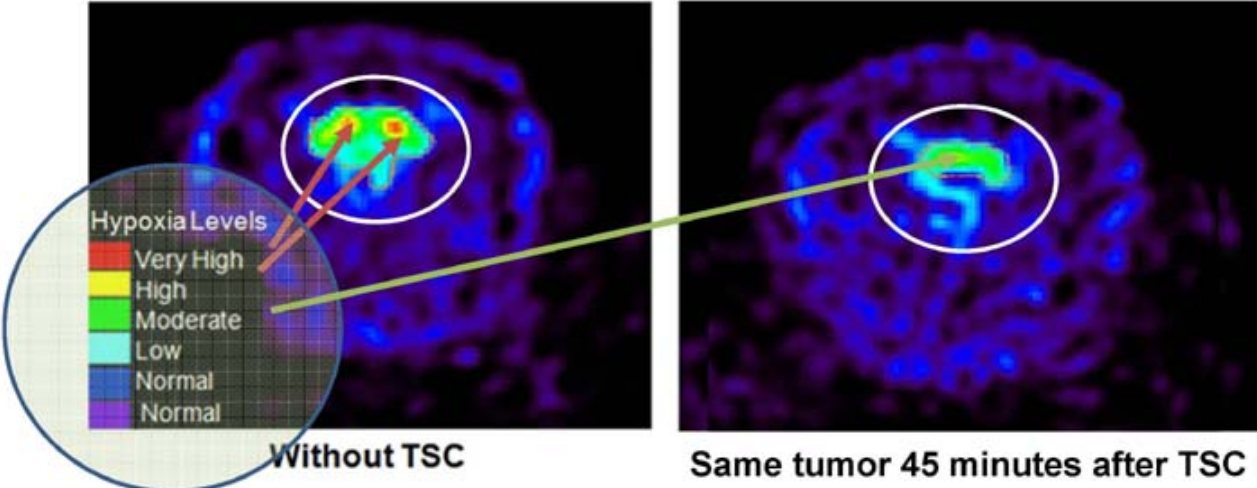
## Mechanism of Action Validated

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- Computer simulation studies demonstrate enhanced diffusion of oxygen
- In vitro studies demonstrate enhanced hydrogen bonding
- Direct oxygen measurement in tissue with PET, LICOX, TCOM
- Hypoxia-related animal models demonstrate improvements in key parameters
- Phase 2 proof of concept trials in PAD and oncology demonstrate favorable safety profile, clinical efficacy, and optimal dosing regimens
- Phase 3 ready

# TSC Reduces Brain Tumor Hypoxia

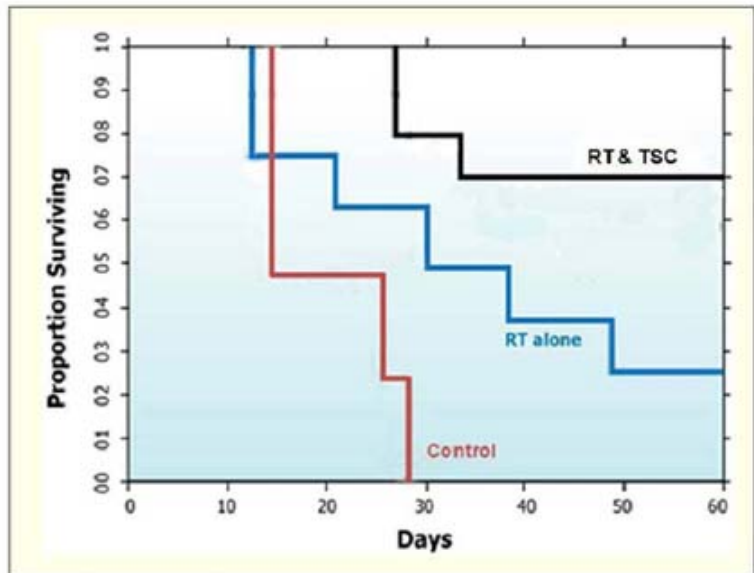
Allows better results with radiation and chemotherapy



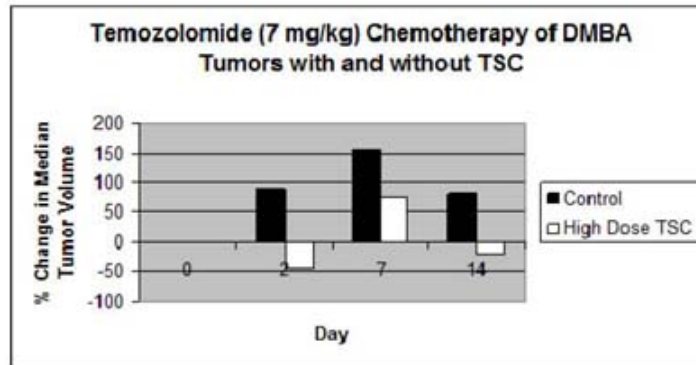
PET scan showing hypoxia levels in rat brain tumor, before and after TSC.

## TSC with Radiation Therapy Triples Survival in Animal Models

- Rat glioblastoma cells implanted in rat brains
- On day 10, rat brains received radiation therapy
- TSC increased survival from 28% to 73%
- Tumor remission seen in TSC survivors



**Sheehan J, et al.** Trans sodium crocetinate sensitizes glioblastoma multiforme tumors to radiation. *J Neurosurg* 108:972-978, 2008.  
See also, **Sheehan J, et al.** TSC with Radiation and Temozolomide; *J Neurosurg* 113:234-239, 2010.



- In animal models, TSC significantly enhances the effectiveness of chemotherapy with temozolomide, even in the absence of concurrent radiation.
- Supports dosing TSC concurrent with the six-month long “Temo only” phase of first line GBM treatment.
- Provides opportunity for a possible better Phase 3 trial result.

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## Oncology Clinical Programs

**First Targeting Treatment Resistance in Solid Cancers  
Using TSC**

Glioblastoma Multiforme  
Metastatic Brain Cancer  
Pancreatic Cancer

### About TSC

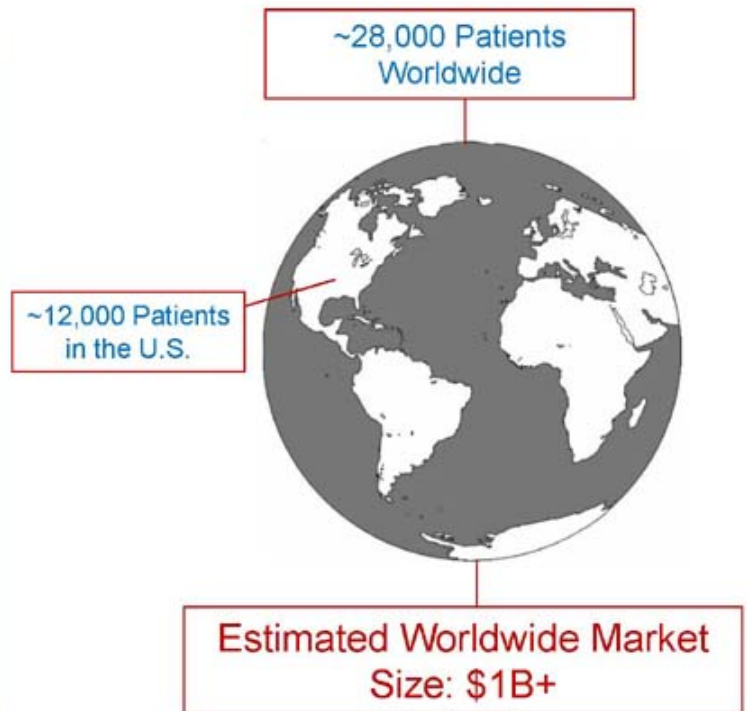
- Administered via bolus IV
- Tested in 148 human subjects in Phase 1 & 2 trials
- No dose-limiting side effects or serious adverse events reported
- CMC: Phase 3 scale-up in process
- FDA: Two open INDs (Cardio-Renal and Oncology)
- FDA Orphan Drug Designation granted in multiple indications

### TSC Advantages

- Cosmotropic: Imparts greater molecular order to blood plasma
- Facilitates diffusion of oxygen into hypoxic tissue
- Mechanism does not require blood brain barrier penetration
- Does not hyper-oxygenate normal tissue
- Safely treats hypoxia-related conditions such as stroke and respiratory
- Increases tumor-killing power of radiation and chemotherapy

# Glioblastoma Market Overview

- Life-threatening cancer of glial cells in the brain with an average life expectancy post-diagnosis < 2 years
- Standard of care is radiation and chemotherapy (temozolomide)
- One of the most hypoxic cancers, causing significant resistance to both radiation and chemotherapy
- Phase 1/2 clinical trial with TSC plus radiation and chemo showed safety and increase in overall survival



Source of demographic/market data: Cowen & Co., Therapeutics Categories Outlook

# Glioblastoma Phase 2 Clinical Trial Successfully Completed

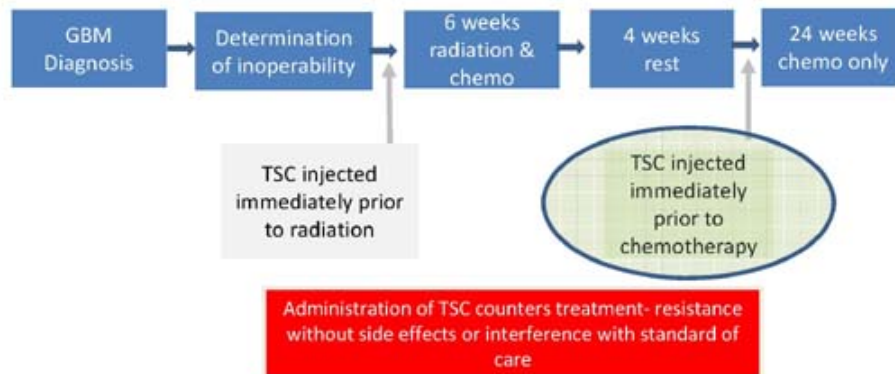
Design	Results
<ul style="list-style-type: none"><li>▪ 59 newly diagnosed GBM patients enrolled at 18 cancer centers</li><li>▪ Open label, historical control study</li><li>▪ TSC dosed 3X/week for 6 weeks concurrent with standard radiation and chemotherapy</li><li>▪ Patients stratified for analysis:<ul style="list-style-type: none"><li>- Surgery for tumor removal</li><li>- No surgery (inoperable/biopsy only)</li></ul></li><li>▪ Primary endpoint: survival at 2 years</li><li>▪ Other endpoints: tumor status, performance, quality of life (Q of L)</li></ul>	<ul style="list-style-type: none"><li>▪ <b><i>Results reported in the <u>Journal of Neurosurgery</u></i></b></li><li>▪ <b><i>Clean safety profile, no serious adverse events attributed to TSC; no negative effects on Q of L</i></b></li><li>▪ <b><i>Tumor regression in many patients; 11 target tumors reported “undetectable”</i></b></li><li>▪ <b><i>Overall survival increased by 37% at 2 years</i></b></li><li>▪ <b><i>Survival of “inoperable” patients increased by 380% at 2 years</i></b></li></ul>



- Focus resources on a Phase 3 trial requiring the fewest patients with highest chance of success
- 380% survival increase in inoperable patients at 2 years is a strong signal, increasing chance of reproducibility
- With inoperables identified as a highly-responsive subset in Phase 2, we will concentrate on that subset in Phase 3
- Inoperable patients are currently excluded from major clinical trials, highlighting the unmet need and making that patient population available for the TSC Phase 3 trial

- GBM End-of-Phase 2 meeting held at FDA headquarters
- Single Phase 3 Study could serve as the basis for approval
- Extensive Phase 3 trial design guidance received:
  - Phase 3 study of TSC as first line treatment with radiation/chemo in newly diagnosed primary brain cancer patients
  - Randomized, controlled, multi-center pivotal study
  - Primary clinical endpoint is survival based on time-to-event
  - Significant flexibility to increase TSC dosing exposure based on Phase 2 study results and supporting animal toxicology
- Phase 3 focused on inoperable patient population
- Enrollment targeted to begin in 2017

## Phase 3 GBM Pivotal Trial Design ("Inoperable" Strategy)

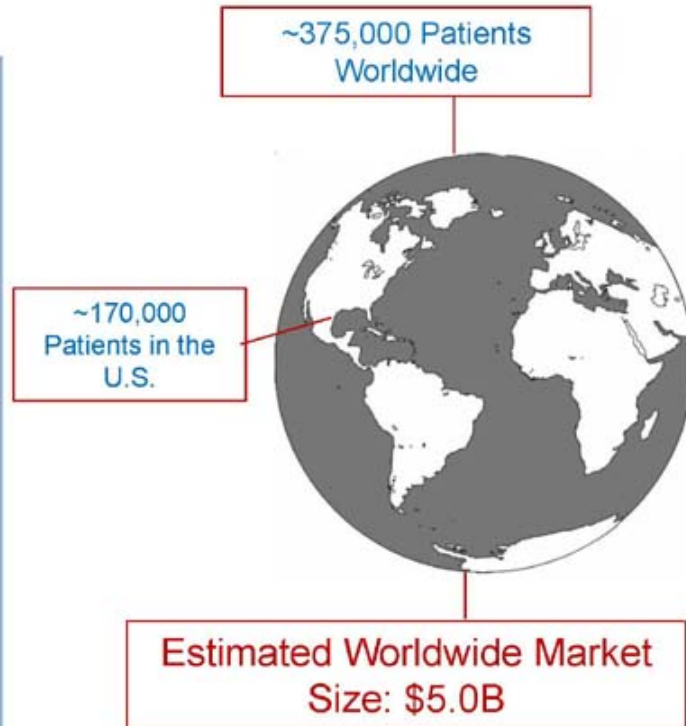


### DESIGN

- Randomized, placebo-controlled
- Primary endpoint is overall survival; secondary endpoints are tumor status, performance, Q of L
- 230 newly diagnosed inoperable GBM patients (about 115 TSC treated/115 control) at up to 100 sites in US, EU and Asia
- TSC dosing treatment period covers 36 doses spaced over entire period of "initial treatment"
- Dosing plan: TSC dosed 3X/week for first 6 weeks concurrent with standard radiation and chemotherapy; 1 month patient rest; 3X/week for the first week of the following 6 months

# Metastatic Brain Cancer

- Life-threatening cancer that has metastasized to the brain
- Average life expectancy post-diagnosis of < 1 year
- Standard of care is radiation only
- One of the most hypoxic cancers, causing significant resistance to radiation treatment
- No approved drug for metastatic brain cancer
- TSC granted FDA Orphan Designation



Source of demographic/market data: Cowen & Co., Therapeutics Categories Outlook

## Animal Model of Brain Metastases Shows Significant Efficacy

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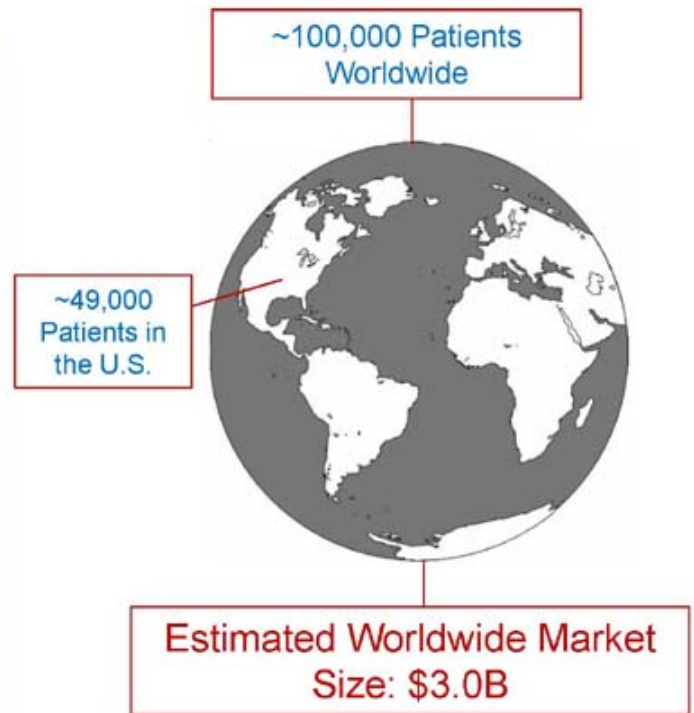
	At 30 Days	At 45 Days	At 60 Days
No Treatment (% Surviving)	0%	0%	0%
Radiation Only (% Surviving)	65%	40%	25%*
Radiation + TSC (% Surviving)	80%	70%	70%**

*J Neurosurg* 108:972-978, 2008.

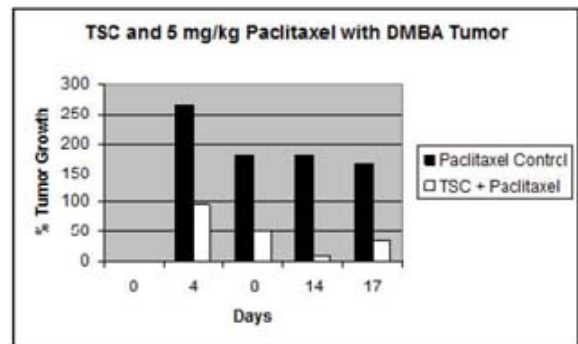
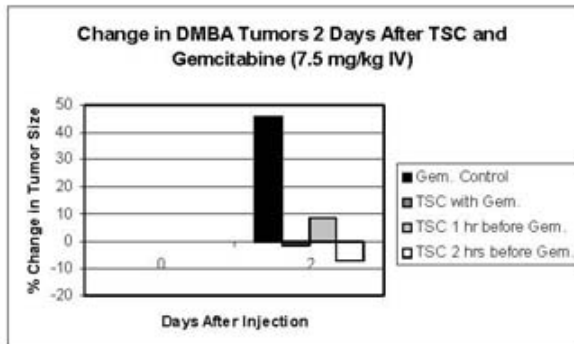
- Cancer cells implanted in rat brains simulate metastases.
- All untreated animals dead within 30 days. (0% survival.)
- \*Radiation-only treatment group had 25% survival at 60 days. MRI shows substantial tumor remaining.
- \*\*Radiation plus TSC treatment group had 70% survival at 60 days. Complete tumor remission in TSC survivors, based on MRI.

# Pancreatic Cancer Market Overview

- Life-threatening cancer of the pancreas with an average life expectancy post-diagnosis < 1 year
- Emerging standard of care is radiation and chemotherapy
- One of the most hypoxic cancers, causing significant resistance to both radiation and chemotherapy
- TSC shown pre-clinically to be a powerful potentiator of current SOC first line pancreatic cancer treatment regimen (gemcitabine plus nab-paclitaxel)



Source of demographic/market data: Cowen & Co., Therapeutics Categories Outlook, Feb 2015



- In various animal models, TSC significantly enhances the standard-of-care chemotherapies used in the treatment of pancreatic cancer (gemcitabine and paclitaxel.)
- For gemcitabine, administration of TSC at 2 hours prior to chemo causes significant tumor volume reduction
- For paclitaxel, administration of TSC significantly slowed tumor growth.
- Note: Both gemcitabine and paclitaxel were developed and FDA-approved under programs led by members of the Diffusion Scientific Advisory Board.

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## Other Indications



**Pre-clinical data supports TSC as a treatment for other hypoxia-driven conditions such as:**

- Stroke and myocardial infarction
- Peripheral artery disease (PAD)
- Neurodegenerative diseases (such as Alzheimer's or Parkinson's) involving death of neurons
- Respiratory diseases, including COPD
- Emergency medicine, including hemorrhagic shock
- And others

Having a proven safety from our oncology clinical trials we can begin additional studies in Phase 2 for the above indications.

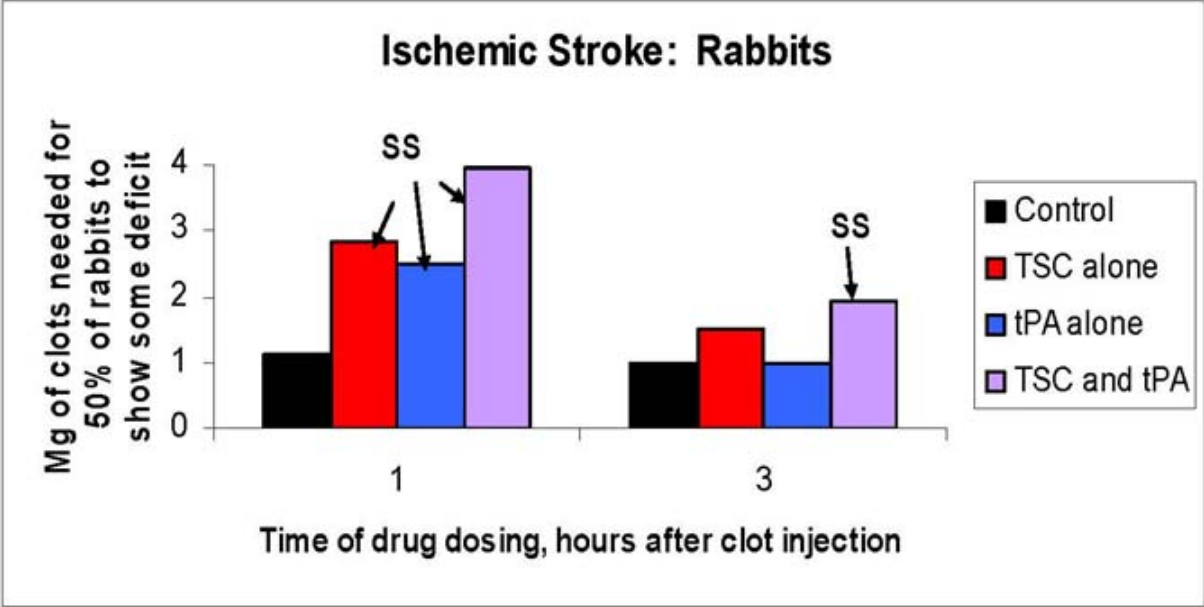
# Stroke

- Stroke is restricted blood flow to the brain, caused by a clot (ischemic) or a bleed (hemorrhagic).
- The resulting hypoxia drives the destruction of neurons, leading to impairment and death.
- tPA can only be use in ischemic stroke; can be fatal in hemorrhagic, delaying treatment time.
- TSC shows safety and efficacy in both ischemic and hemorrhagic stroke.
- Stroke clinical trial design being advised in co-operation with leading clinicians.



Source of demographic/market data: Cowen & Co., Therapeutics Categories Outlook

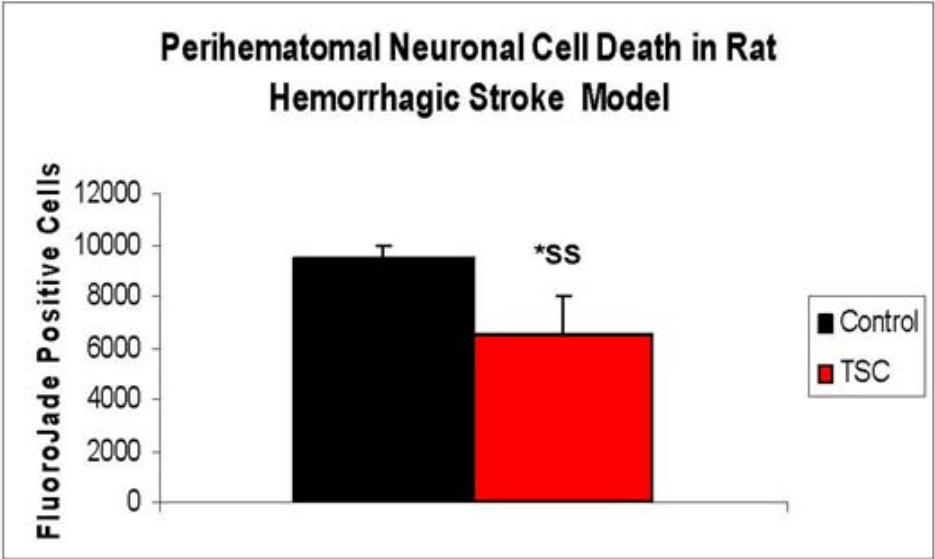
# TSC Shows Safety and Efficacy in Ischemic Stroke



SS = statistical significance

Lapchak; *Brain Research*; Vol. 1309;pp 136-145; 2010

# TSC Shows Safety and Efficacy in Hemorrhagic Stroke



SS = statistical significance

# Diffusion<sub>2</sub>n

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## Business Overview

- Issued and pending patents cover:
  - Composition of matter of drug product
  - Use of TSC for the treatment of cancer in combination with radiation and/or chemotherapy
  - Treatment of hypoxic conditions including stroke, heart attack, respiratory conditions and neurodegenerative diseases
- 14 patents issued in US & 46 issued abroad, including Asia
- Patents cover the major markets with key patent life until 2026, plus expected extensions until 2031
- Orphan Drug Designations seven-year exclusivity periods provide additional protection in the US
- Formulation patent provides protection for the TSC oral drug product until 2031, with possible extensions

## Upcoming Key Milestones

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### **230 Patient Glioblastoma Multiforme (GBM) Phase 3**

2017 – Study Start-up and Begin Treating Patients

2018-2019 – Complete Enrollment

2019 – Interim Data Readout (Potential)

2020 – Complete Study Conduct

Data collection, analysis and regulatory interaction will then occur over the following 12 to 18 months.

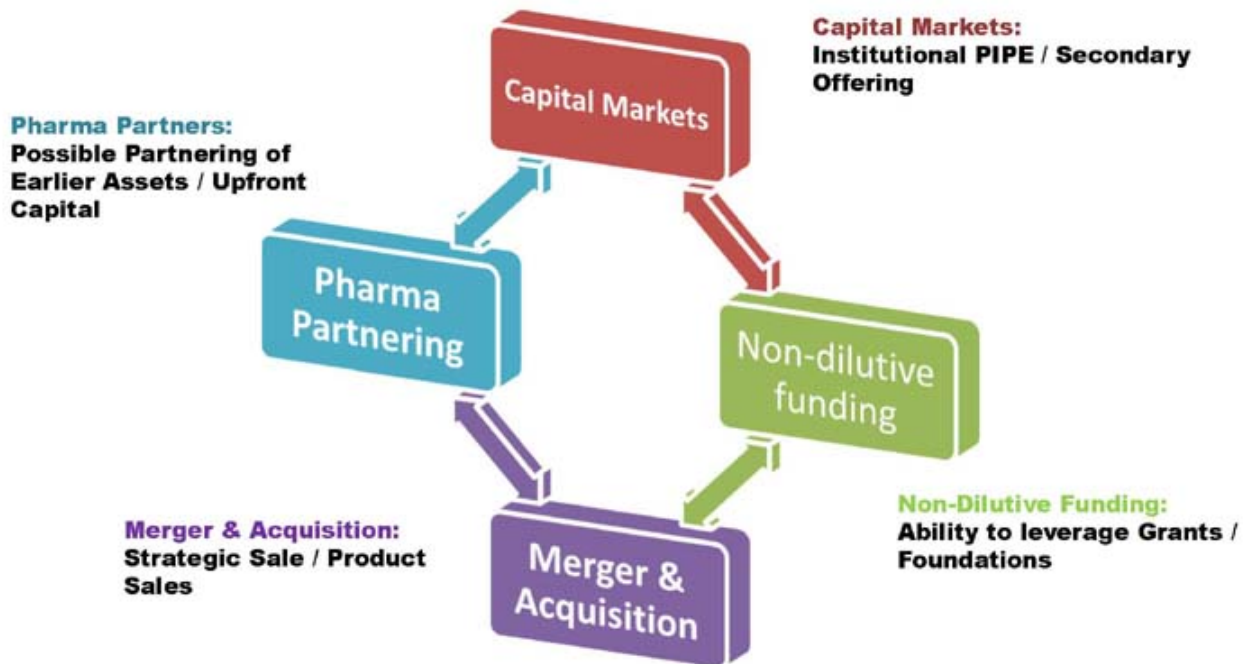
### **Possible Partnering – 2017**

Stroke Indication

## Financial Overview

- Total capital invested to date: \$88 million
- Current cash on hand: \$20 million
- Became a public entity effective 1/8/2016 through a merger with RestorGenex Corp
- Trades as Diffusion Pharmaceuticals Inc. (Ticker: NASDAQ DFFN)
- Financials – See Diffusion 10-K Annual 2016 on the Company's website at [www.diffusionpharma.com](http://www.diffusionpharma.com)





## Combating Cellular Oxygen Deprivation to Treat Unmet Medical Needs

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- First-in-class small molecules that safely re-oxygenate oxygen deprived (hypoxic) tissue by a novel mechanism; acts alone or with other treatments
- Multiple opportunities in unmet medical needs across \$ billion markets
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- IP patent portfolio protection through 2031 (including expected extensions)
- Experienced management, directors, advisors and key investors

# Diffusion<sub>2</sub>n

Pharmaceuticals Inc.

*Better Treatments for Cancer*

**David Kalergis, CEO**  
[dkalergis@diffusionpharma.com](mailto:dkalergis@diffusionpharma.com)

May 19, 2017  
[www.diffusionpharma.com](http://www.diffusionpharma.com)