Nasdaq: DFFN

Diffusion Pharmaceuticals

Enhancing Oxygen,
Fueling Life

Corporate Presentation for
HC Wainwright Global Life Sciences Conference
March 9-10, 2021

Presentation Recording Date: March 5, 2021

Note Regarding Forward-Looking Statements

This presentation (including, for purposes of this Note Regarding Forward-Looking Statements, any accompanying or supplemental oral presentation) includes express and implied forward-looking statements relating to: our product candidates and pipeline; our corporate strategy and product development plans; the prospects and potential of our business and our product candidates, including their safety, effectiveness, and commercial prospects; our ongoing and anticipated clinical trials, other studies, and data readouts therefrom; certain regulatory matters; business development activities, including potential collaborations; certain matters regarding our financial results and securities; milestones, timing, and other expectations regarding any of the foregoing; any other matter that is not a statement of historical fact, including statements regarding our intentions, beliefs, projections, outlook, analyses, or expectations. We may, in some cases, use terms such as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately," or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements.

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Certain information contained in this presentation relates to or is based on studies, publications, surveys, and other data derived from third-party sources and our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and we make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involve a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, although we believe our own internal research is reliable, such research has not been verified by any independent source.

Diffusion Pharmaceuticals Inc. is an innovative biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to the areas where it is needed most.

Diffusio$_2$n
Pharmaceuticals Inc.

Founded in 2001 based on research by Dr. John Gainer at the University of Virginia.

The lead drug candidate, trans sodium crocetinate (TSC) is being developed to enhance the diffusion of oxygen to hypoxic tissues.

Recent Company Highlights

Enhanced Financial Stability

- Raised $34.5M gross proceeds in February from an underwritten public offering, before underwriting discounts, commissions and expenses
- Company prepared for next steps with good cash position, no debt, and a clean balance sheet

Completed COVID Safety Study

- Completed Phase 1b safety and tolerability study in hospitalized COVID-19 patients in February 2021
- Topline data indicated no dose-limiting toxicities or serious adverse events at doses up to 1.5 mg/kg administered q6 hours
- Secondary endpoint data to be available in Q2 2021

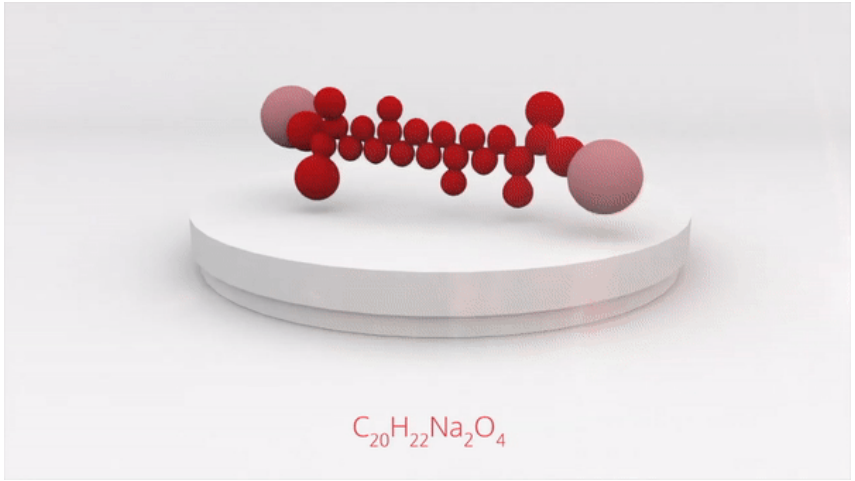
Studies to Demonstrate Effects on Oxygenation

- Three clinical studies planned to demonstrate TSC effect on oxygenation
- Transcutaneous oxygen monitoring ("TCOM") study to start in 1Q 21
- Induced hypoxia study to start in mid-year
- Lung diffusion ("DLCO") study to start mid-year

Trans Sodium Crocetinate (TSC)

Novel Mechanism Targeting Hypoxia

Trans **S**odium **C**rocetinate (**TSC**)



A novel, bipolar synthetic carotenoid designed to enhance the oxygenation of hypoxic tissues.

Sodium salt of the trans isomer of crocetin, which is derived from saffron.

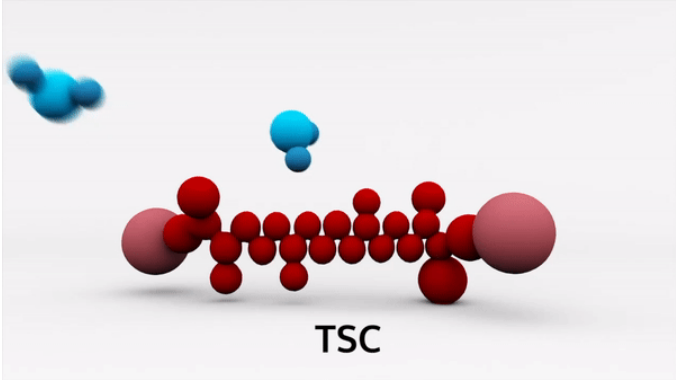
Only the trans isomer is effective in modifying oxygen diffusivity.

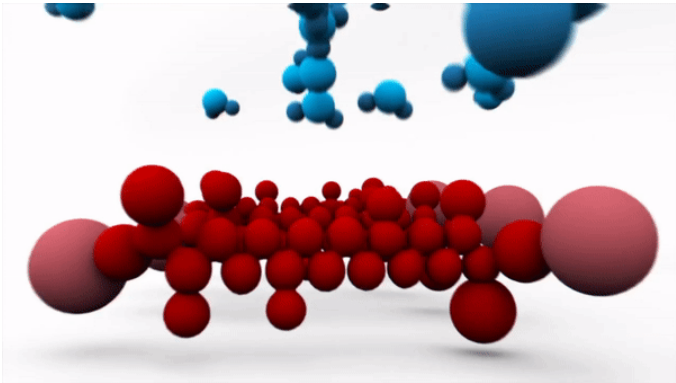
TSC Mechanism of Action

Blood plasma is 90% water. Water molecules are constantly moving in a loosely organized matrix, bound by hydrogen bonds.

Oxygen diffuses passively through plasma from areas of high to low oxygen concentrations, such as from oxygenated red blood cells into tissues where the oxygen is used to power the cells.

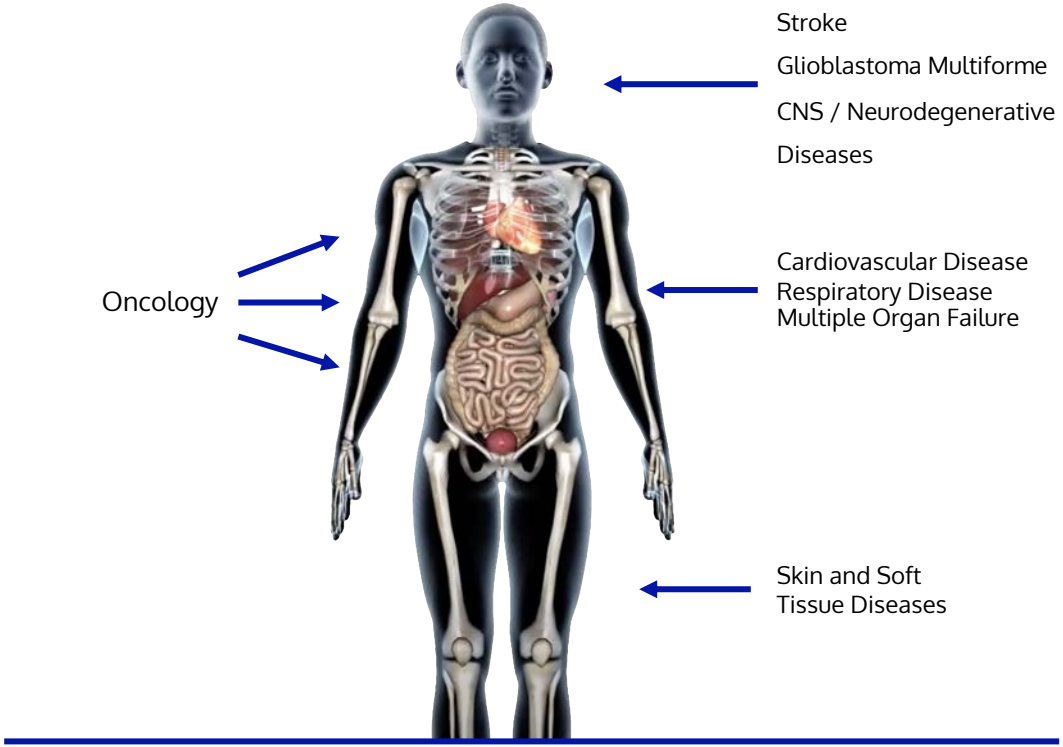
TSC enhances diffusion by increasing the amount of hydrogen bonding, creating a less dense matrix of water molecules.





TSC: Potential to Treat Hypoxia-related Conditions

- Hypoxia is associated with the pathophysiology of many acute and chronic conditions
- TSC's novel mechanism of action enhances oxygenation
- In vivo oxygenation and functional effects observed in preclinical models
- Safe and well-tolerated in more than 180 subjects treated in clinical studies



Significant Global Intellectual Property Portfolio

Patents covering compositions, formulations, and uses of product candidates in major markets

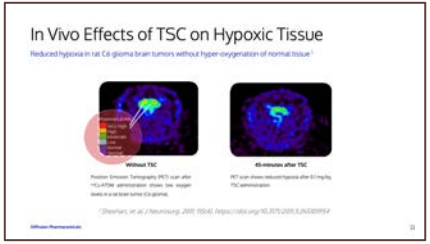
- 16 U.S. patents issued, more than 30 non-U.S. patents issued, and over 20 applications pending worldwide including major markets such as the United States, European Union, Japan, and China
- Normal life (i.e., no adjustments or extensions) of key patents related to composition of matter of TSC extends to 2026, with potential patent term extensions to 2031
- TSC Orphan Drug designations (GBM and metastatic brain cancer) and Hatch-Waxman Act exclusivity period may provide up to 7 years of additional protection
- Normal life of TSC oral formulation patents extends to 2031, with potential patent term extensions to 2036

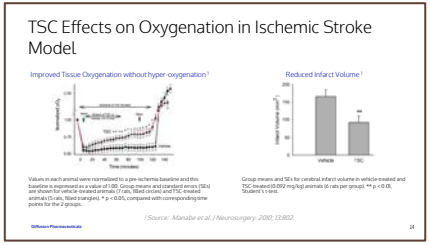
TSC Development

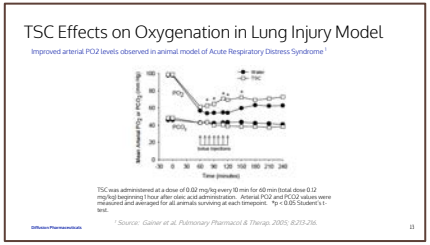
Completed Studies

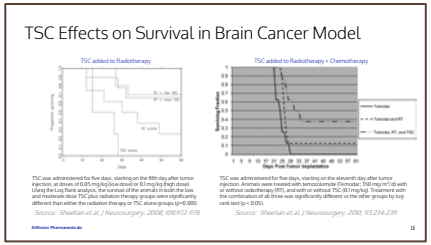
Preclinical Effects of TSC on Oxygenation

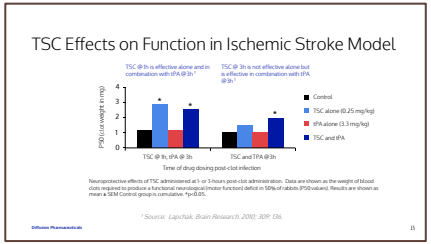
- ✓ Reduced hypoxia in rat C6 glioma brain tumors without hyper-oxygenation of normal tissue
- ✓ Improved survival in rat C6 glioma model when added to radiotherapy with or without chemotherapy
- ✓ Improved tissue oxygenation without hyper-oxygenation and reduce infarct size in rat ischemic stroke model
- ✓ Functional benefit in rabbit ischemic stroke model (with or without tPA at 1 hr; with tPA at 3 hrs)
- ✓ Improved arterial PO2 levels in rat model of Acute Respiratory Distress Syndrome











TSC Clinical Experience

Previously Completed Clinical Studies

Study 100-001 Healthy Volunteers

- n=30 normal healthy volunteers (NHV)
- Single, ascending, intravenous (iv) dose (0.1 to 5 mg/kg) safety and pharmacokinetics
- Maximum tolerated dose (MTD) and pharmacokinetics (PK) characterized for single iv dose

Study 100-301 PAD

- n=48 pts with peripheral artery disease (PAD) and claudication
- Double-blind, placebo-controlled, single, ascending dose (0.25 to 2 mg/kg iv) safety, PK and efficacy
- No dose-related adverse events (AEs), PK characterized and preliminary physical improvement signal

Study 100-202 GBM

- n=59 pts with newly diagnosed glioblastoma multiform (GBM)
- Open-label, add-on of TSC (0.25 mg/kg) to standard of care (SOC) radiation + chemotherapy
- No dose-related AEs
- Survival of biopsy-only subset comparable to complete resection

Study 100-206 GBM

- n=19-pts with newly diagnosed, biopsy-only GBM
- lead-in of Phase 3 randomized controlled trial (RCT) to evaluate four escalating dose cohorts (0.25, 0.5, 1.0, and 1.5 mg/kg) administered 3x weekly with SOC
- No dose-related AEs

Mohler et al. Vasc Med. 2011; 16:346.

Gainer et al. J Neurosurg. 2017; 26 (2):460.

TSC Clinical Experience

Recently Completed Clinical Study in Hospitalized Patients with COVID-19 (Study 100-303)

Study Design

- Open-label, ascending dose study of intravenous TSC in hospitalized COVID-19 patients
- National Institute of Infectious Diseases, Bucharest, Romania
- Patients dosed every 6 hours for up to 15 days
- Primary Endpoint: Safety and Tolerability after 5 days of dosing
- Secondary Endpoints: repeat-dose PK/pharmacodynamics (PD), blood O2, multiple clinical endpoints

Topline Results

- First two patients dosed on September 10, 2020
- Completed dosing of the twenty-fourth and final patient on February 9, 2021
- No dose-limiting toxicities were observed among any patients who received doses of 0.25 mg/kg, 0.5 mg/kg, 1.0 mg/kg, or 1.5 mg/kg every 6 hours
- Results of secondary endpoint analyses are anticipated to be completed and announced by 2Q 2021

TSC Development

Planned Studies

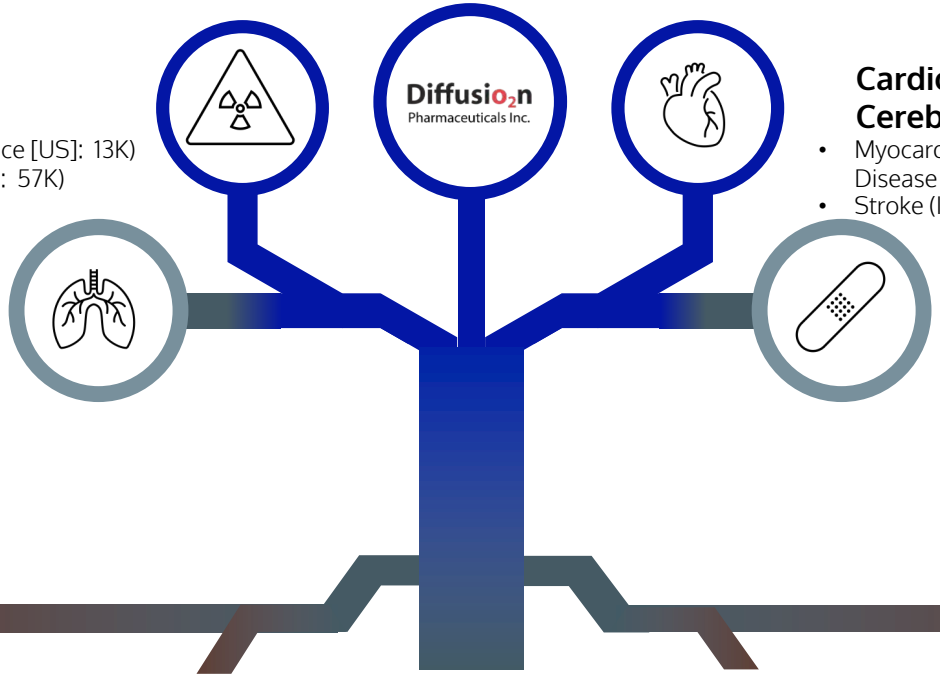
TSC Opportunities

Oncology

- Glioblastoma Multiforme (Incidence [US]: 13K)
- Pancreatic Cancer (Incidence [US]: 57K)

Respiratory

- Pneumonia (Incidence [US]: 1.3M)
- ARDS (Incidence [US]: 190K)
- COVID-19 (Incidence [US]: 20M)



Cardiovascular/ Cerebrovascular

- Myocardial infarction, Vascular Disease (Incidence [US]: 1 M)
- Stroke (Incidence [US] : 800K)

Skin / Soft Tissue

- Chronic wounds (Prevalence [US]: 6.5M)
- Burns (Incidence [US]: 1.1M)
- Acute Infections (Incidence [US]: 1.6M)

Supportive Data

Preclinical Safety and Efficacy Data	Single and Repeat Dose Safety and Tolerability	Preliminary Clinical Signals – PAD and GBM	Demonstrate Improved Oxygenation, Optimize Dose-Response

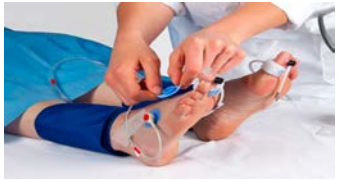
Planned Clinical Study: "*TCOM*"

Transcutaneous Oxygen Monitoring (TCOM, tcpO2)

- Simple, non-invasive, reliable, repeatable measure of local oxygen tension in tissue below the skin
- Objective measure of oxygen release and diffusion into tissues from vasculature, allowing direct assessment of tissue hypoxia
- Used to evaluate severity of peripheral artery disease, mapping of amputation level, assess likelihood of wound and amputation healing, predict benefit of hyperbaric therapy (HBOT)
- Direct measure of O2 released through the skin, not a pulse oximeter

Protocol Design

- Randomized, placebo-controlled, single ascending dose study in healthy volunteers to measure the exposure-response relationship of TSC and oxygenation
- All subjects on 100% O2 pre/post TSC dose
- TCOM measurements pre/post TSC dose
- Identify dose, time to increase in tcpO2 after TSC dose, magnitude of effect, duration of effect
- Start 1Q 21, with topline data by 2Q 21 to inform dose selection for subsequent trials



Planned Clinical Study: *"Induced Hypoxia"*

Rationale

- The partial pressure of oxygen (PaO2) decreases with altitude – 21% at sea level, to <12% at 15K feet
- Altitude induced hypoxia can produce a physiological insult which is exacerbated by exercise
- Worsening hypoxia will decrease exercise performance and can lead to pulmonary edema and altered mental status
- Enhanced oxygen delivery may delay or mitigate onset of hypoxia induced symptoms at any altitude

Protocol Design

- Phase 1, single center, randomized, placebo-controlled, cross-over treatment trial in normal healthy volunteers.
- Two "induced hypoxia" sessions per subject at simulated altitude (15K ft) in single day, with intervening rest
- Aerobic exercise during each session at altitude
- Subjects receive either TSC or control before each exercise session (randomized by session)
- Clinical endpoints: vital signs, ECG telemetry, PaO2, SaO2, VO2, safety
- Start 2Q 21, with topline data by 3Q 21

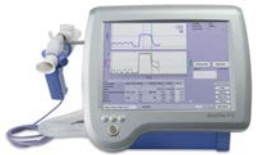
Planned Clinical Study: "*DLCO*"

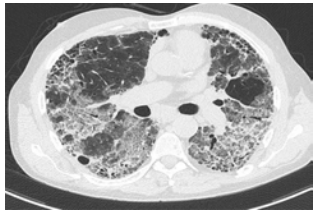
Diffusing Capacity of the Lungs (DLCO or TLCO)

- A pulmonary function test that measures gas (carbon monoxide, CO) diffusion from lungs to the bloodstream where CO binds hemoglobin (Hgb)
- Single breath test, in-office, non-invasive, repeatable
- Standard screening tool as part of work-up for pulmonary disease etiology
- Serially monitored outpatient (for improvement vs progression)
- Diffusion capacity can be profoundly reduced in Interstitial Lung Disease (ILD), COPD, Heart Failure, Pulmonary Hypertension

Anticipated Protocol Design

- Phase 1b, single center, dose ranging, single dose study in patients with ILD
- Endpoints: pre-dose baseline DLCO and six-minute walk test, followed by post dose serial DLCO readings and six-minute walk test
- Start 2Q 21, with topline data by 3Q 21





Planned Clinical Studies: Summary

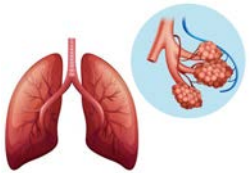
Value Proposition

- Preclinical data suggest broad potential as a treatment for hypoxia-related conditions
- Formulated for intravenous administration
- Safe and well-tolerated in over 180 subjects in clinical studies with single or multiple daily doses
- No evidence of drug:drug or drug:disease interactions, supporting use in conditions that require polytherapy for disease management

Next Steps

- Execute clinical studies in experimental models of oxygenation
- TCOM study anticipated to start in 1Q2021
- VO2 study anticipated to start by 3Q2021
- DLCO study anticipated to start by 3Q2021
- Identify indications where medical need, mechanism of action, formulation, and probability and timing of development success converge

Planned Clinical Studies: Clinical Relevance



DLCO
(O2 Uptake in ILD Pts)

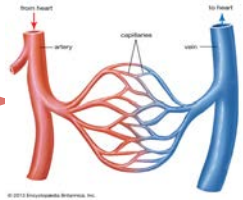
- Interstitial Lung Disease
- ARDS / Pneumonias
- Pulmonary Embolus
- COPD/emphysema

TCPO2
(O2 Delivery in NHVs)

- Wounds
- Peripheral Vascular Disease
- Ischemia/Reperfusion Injury
- Tumor Sensitization

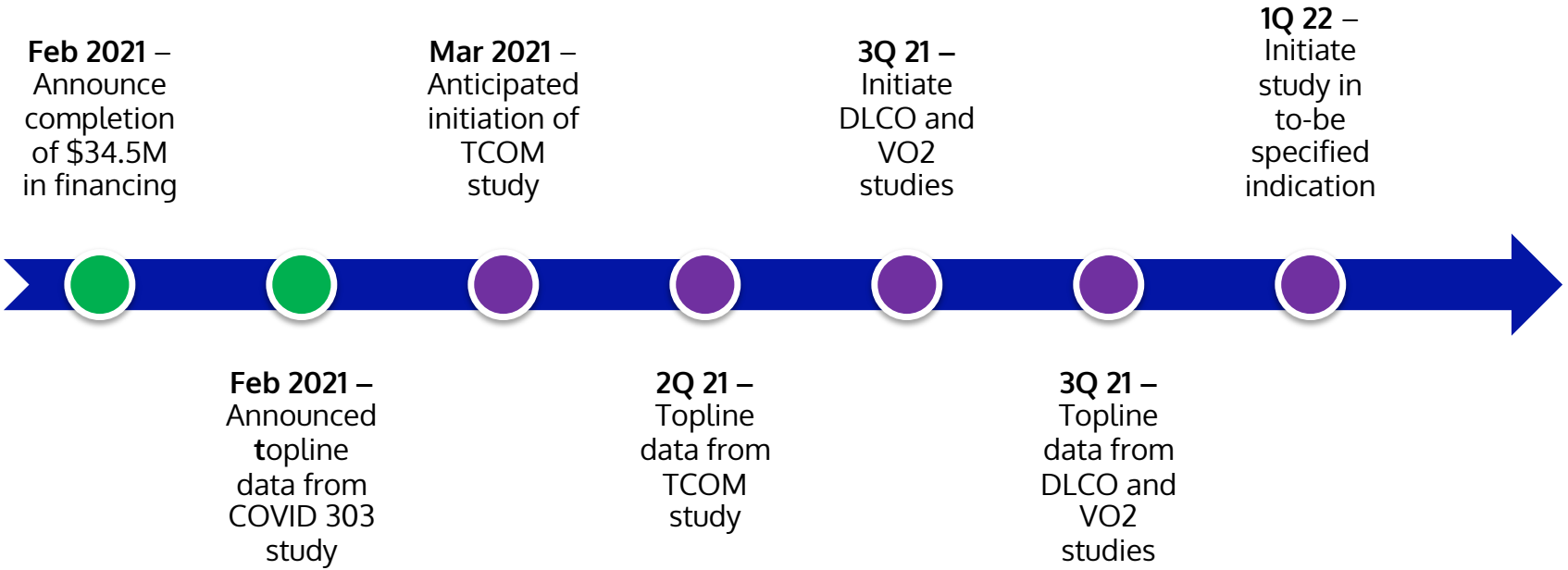
Induced Hypoxia
(VO2 and PaO2 in NHVs)

- Anemia
- Major surgeries
- Physical Performance



Corporate Highlights

Near-term Milestones



Financial Highlights

As of September 30, 2020	
Cash, Cash Equivalents and Short-Term Investments	$21,910,183
Long-Term Debt/Debt for Borrowed Money	$0
As of February 18, 2021	
Shares of Common Stock Outstanding	101,677,093
Potentially Dilutive Shares Outstanding [1]	9,023,1971
Fully Diluted Shares of Common Stock Outstanding	110,700,290

1. The number includes shares of common stock, underlying warrants and options outstanding as of February 18, 2021. The weighted average exercise prices of such warrants and options are $8.09 per share and $8.28 per share, respectively.

Investment Highlights

TSC's novel mechanism of action targets hypoxic conditions, an area of high unmet medical need

Topline data from trial in hospitalized COVID-19 patients indicates TSC safety and tolerability when dosed every 6 hours up to 1.5 mg/kg

Safe and well-tolerated in over 180 subjects included in clinical trials

Near-term initiation of clinical studies to demonstrate the effects of TSC on oxygenation

Significant, recent financing enhances financial stability and extends cash runway through projected completion of an anticipated Phase 2/2b study

Continued investment in strong global IP portfolio

Thank you