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): August 18, 2020

JANONE INC.
(Exact Name of Registrant as Specified in Charter)

Nevada	**000-19621**	**41-1454591**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

325 E. Warm Springs Road, Suite 102
Las Vegas, NV 89119
(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: 702-997-5968
(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 (see General Instruction A.2. below):

☐ 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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	JAN	The NASDAQ Stock Market LLC (The NASDAQ Capital Market)

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☐

Item 7.01. Regulation FD Disclosure

On August 18, 2020, executives of JanOne Inc. (the "Company") announced their intention to hold meetings with various third parties and potential investors in the coming months and plan to present the information contained in the presentation attached to this Current Report on Form 8-K as Exhibit 99.1.

The furnishing of the attached presentation is not an admission as to the materiality of any information therein. The information contained in the presentation is summary information that is intended to be considered in the context of more complete information included in the Company's filings with the the U.S. Securities and Exchange Commission (the "SEC") and other public announcements that the Company has made and may make from time to time by press release or otherwise. The Company undertakes no duty or obligation to update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases, or through other public disclosures.

This information is "furnished" and not "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liabilities of that section. It may only be incorporated by reference in another filing under the Securities Exchange Act of 1934 or the Securities Act of 1933 only if and to the extent such subsequent filing specifically references the information incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	Description
99.1	JanOne Inc. Investor Presentation

SIGNATURES

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

JanOne Inc.

By: /s/ Tony Isaac
Name: Tony Isaac
Title: Chief Executive Officer

Dated: August 18, 2020

Exhibit 99.1

JanOne

NASDAQ:JAN

Presentation Created by:

Tony Giordano, Ph.D.
Chief Scientific Officer

Inquiries, Please Contact: 1 (800) 400-2247 | ir@janone.com

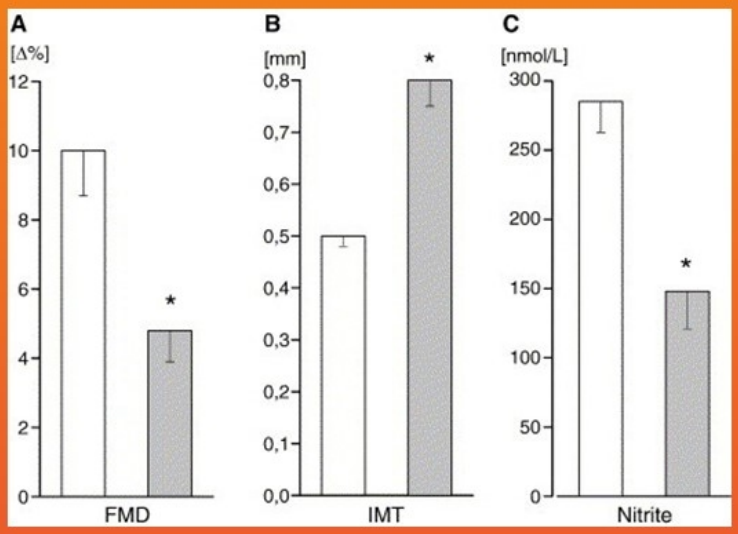
The Nitrite Solution:
Sustained Release Sodium Nitrite

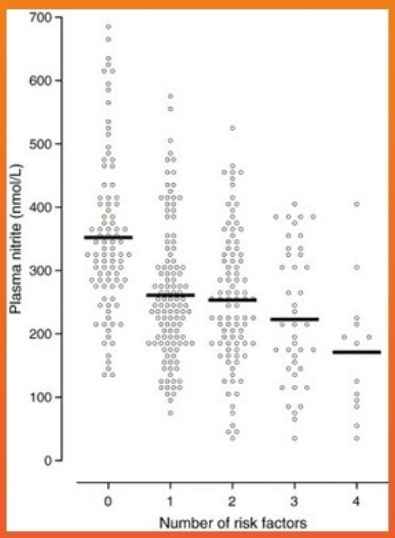
Oral, sustained release formulation of sodium nitrite

- Well established safety profile
- Excellent bioavailability
- Lack of induced tolerance
- Non-narcotic

Does not mask pain, but instead treats the cause of pain by improving tissue and vascular dysfunction.

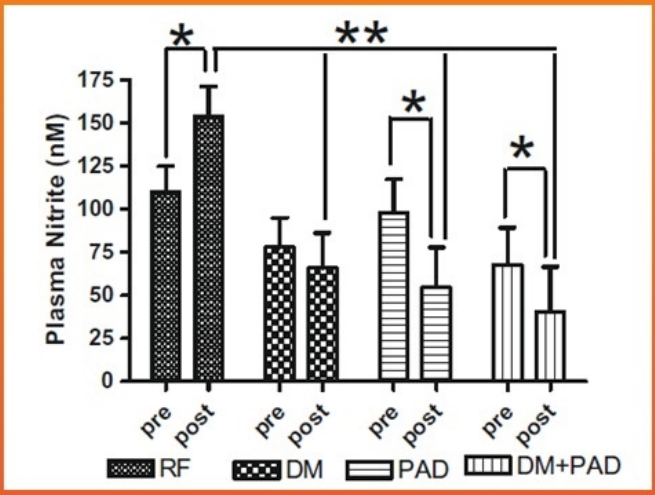
Plasma Nitrite Levels are Negatively Correlated to Cardiovascular Disease





Plasma nitrite levels were inversely related to number of cardiovascular risk factors a subject had and decreased plasma nitrite was associated with decreased flow mediated vasodilation (FMD) and increased intimal medial thickness (IMT) (both indicators of vascular pathology).
-Kleinbongard, et al. (2006) Free Radic Biol and Medicine 40:295-302

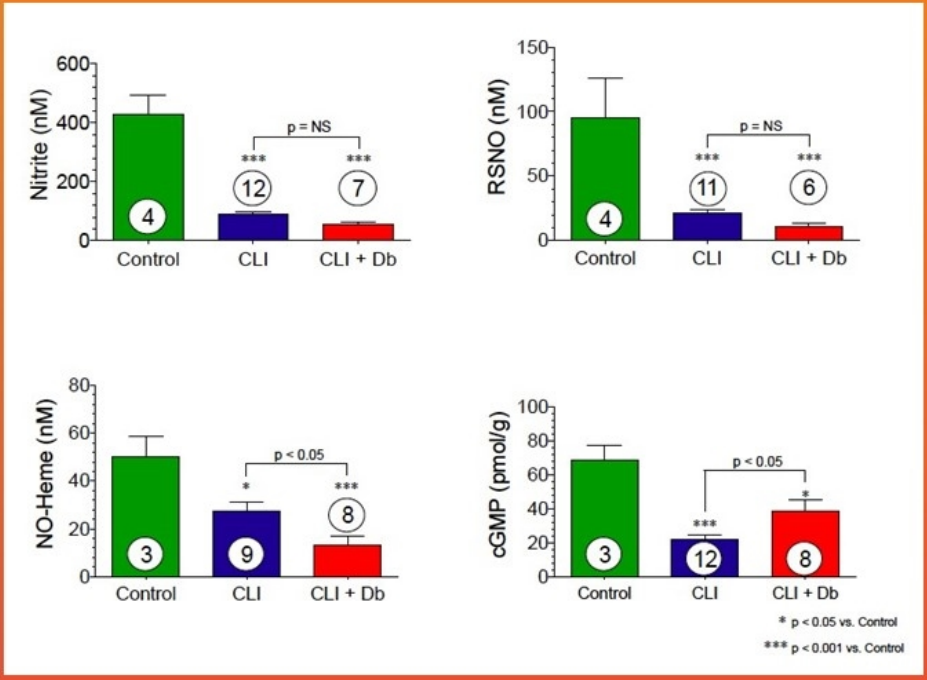
Plasma Nitrite Levels are Reduced In Diabetic and PAD Patients



Exercise is a well known stimulator of eNOS activity, NO production that leads to increased plasma nitrite. In the study by Allen et al, these authors revealed that baseline plasma levels of nitrite were less in patients with diabetes mellitus (DM) or DM + PAD. Importantly, increases in plasma nitrite levels were not observed in either DM, PAD or DM + PAD patients after supervised exercise. These data reveal that baseline nitrite availability is compromised in DM patients and that supervised exercise is unable to increase plasma nitrite levels but actually results in a ***decrease*** in nitrite highlighting a physiological deficiency of this molecule.

-Allen et al Nitric Oxide 2009 20:231-237

Skeletal Muscle Nitrite and Metabolite Levels are Reduced in Critical Limb Ischemia Patients



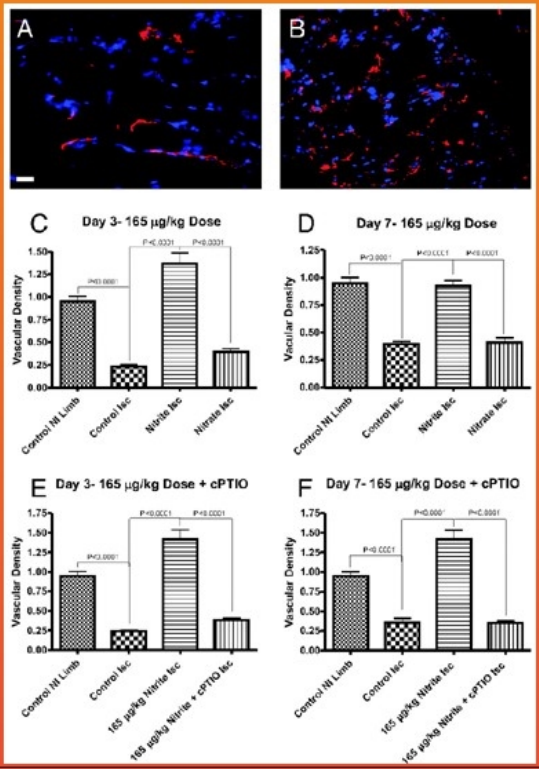
- Skeletal muscle nitrite, nitrosothiol, nitric oxide-heme and cGMP are all significantly reduced in CLI patients.
- Diabetic patients with CLI show even further nitrite reductions.

Sodium Nitrite and Sustained Release Nitrite: Preclinical Data

Nitrite and Sustained Release Nitrite: Preclinical Data

- Highly selective
- Promotes blood vessel growth
- Prevents diabetic nephropathy
- Stimulates wound healing
- Prevents tissue necrosis

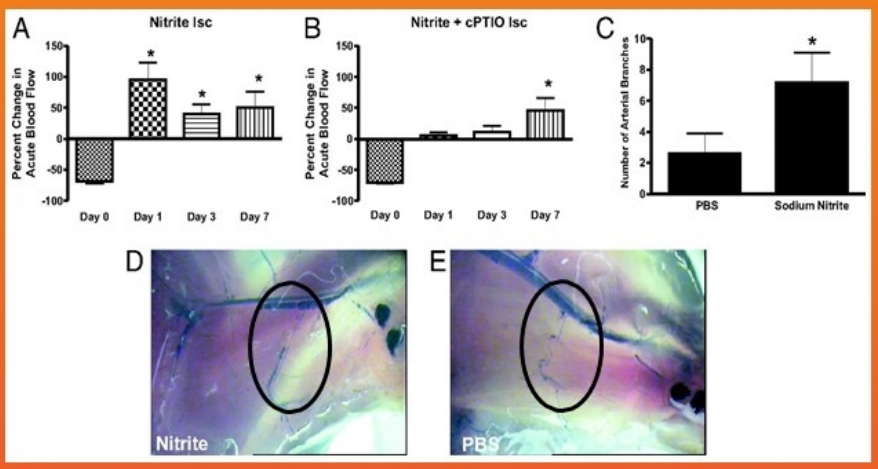
Nitrite Therapy Selectively Increases Ischemic Tissue Vascular Density in an NO-dependent Manner



Chronic sodium nitrite therapy increases ischemic tissue vascular density in an NO-dependent manner. A and B show representative images of CD31 (red) and DAPI nuclear (blue) staining from sodium nitrite and sodium nitrate ischemic gastrocnemius muscle tissue at day 7. C and D report the vascular density of ischemic gastrocnemius muscle tissue at days 3 and 7 for 165 µg/kg sodium nitrite and nitrate treatments, respectively. E and F demonstrate the vascular density of ischemic gastrocnemius muscle tissue at days 3 and 7 from 165 µg/kg sodium nitrite plus carboxy PTIO. (Scale bar, 150 µm.) n = 10 mice per treatment group.

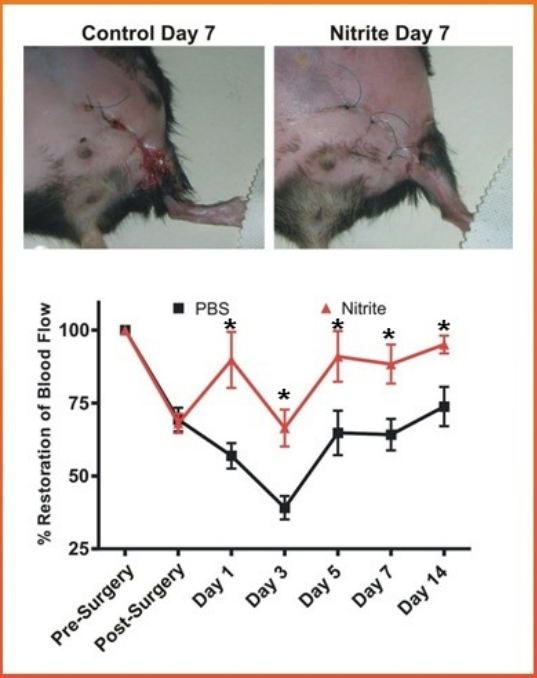
Kumar D. et al. PNAS; 2008; 105:7540-7545.

Nitrite Therapy Augments Arterial Perfusion of Ischemic Tissue



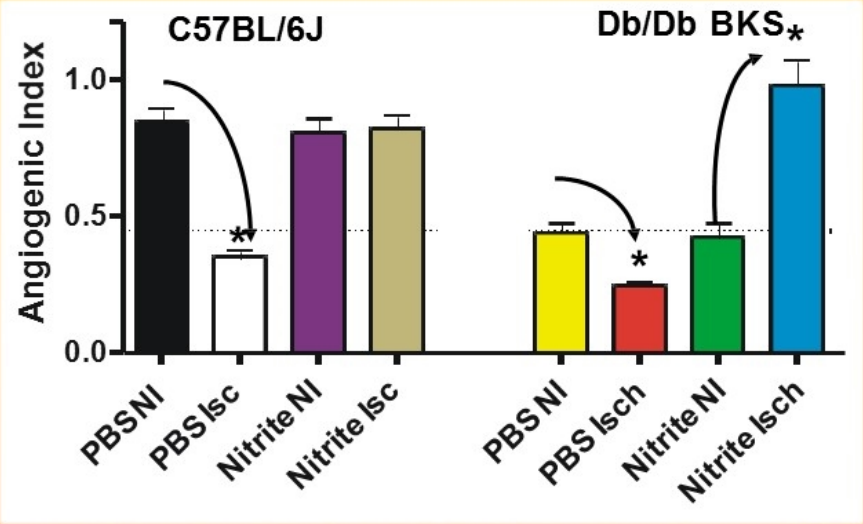
Chronic sodium nitrite therapy acutely increases ischemic tissue blood flow and stimulates arteriogenesis. A and B report 165 µg/kg sodium nitrite-induced acute changes in blood flow of chronically ischemic tissues at various time points with or without cPTIO, respectively. C reports the number of arterial branches between PBS and nitrite therapies. D and E illustrate vascular casting of the arterial vasculature in ischemic hind limbs of day 7 nitrite or PBS-treated mice, respectively.
*, $P < 0.01$ vs. sodium nitrate. n = 10 mice per treatment group.
Kumar D. et.al. PNAS;2008;105:7540-7545

Nitrite Therapy Restores Diabetic Ischemic Hind-Limb Blood Flow and Promotes Wound Healing



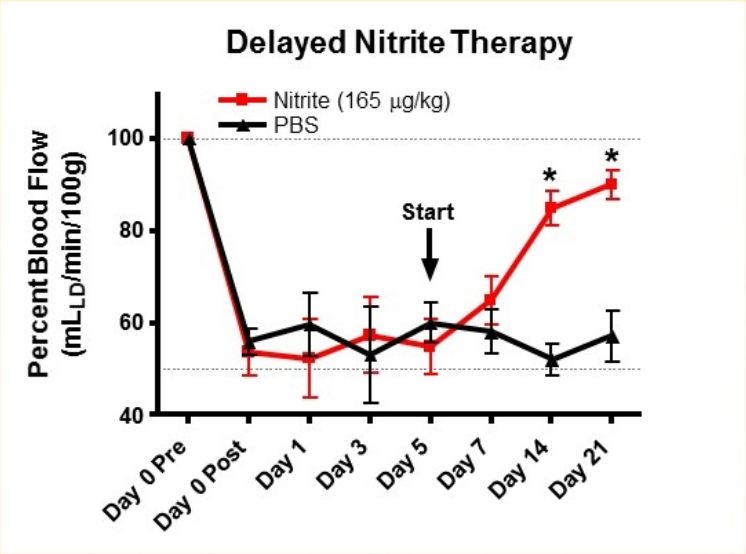
Unilateral femoral artery ligation was performed on 18-20 week old male Db/Db mice. Mice were randomized to PBS or sodium nitrite (165 µg/kg) therapy twice daily via I.P. injection. Laser doppler flowmetry was performed at the indicated time points. Increased wound dehiscence was noted in the PBS treated animals at day 7 but not in nitrite treated animals. (Bir et al Diabetes 2014, 63(1):270-81)

Nitrite Therapy Increases Diabetic Ischemia Induced Angiogenesis



Nitrite therapy prevented ischemia mediated endothelial cell density loss in normal C57BL/6J ischemic limbs. Nitrite therapy significantly restored endothelial cell density in ischemic limbs of diabetic mice to normal C57BL/6J levels compared to PBS therapy of non-ischemic and ischemic conditions. These data suggest that nitrite therapy may be useful in attenuating microvascular rarefaction due to loss of nitric oxide that is observed during metabolic dysfunction (Frisbee JC AJP Integr Comp Physiol 2005 289(2):R307-16; Stepp et al Microcirculation 2007 14(4-5): 311-6)

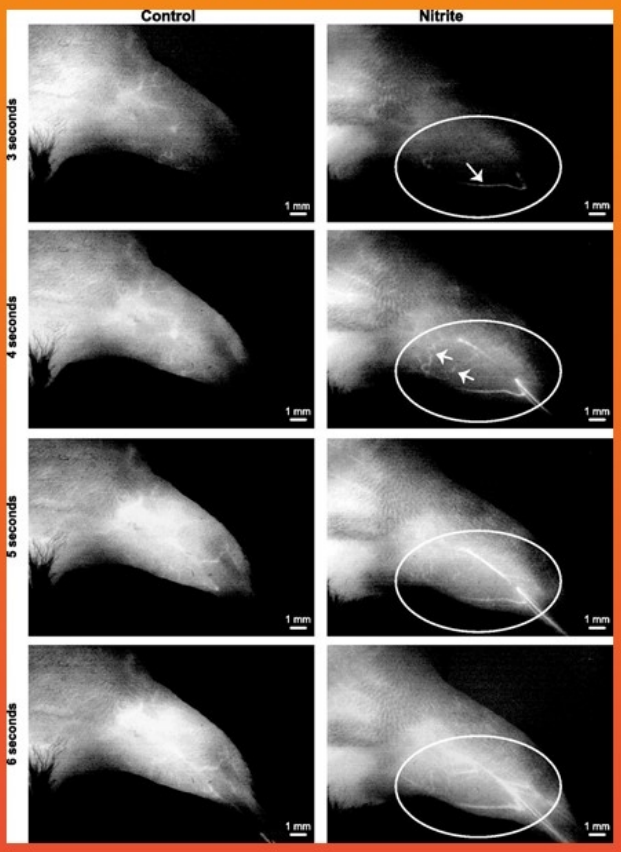
Delayed Nitrite Therapy Restores Ischemic Hind-Limb Blood Flow



Studies were performed to determine whether nitrite mediated therapy would be effective in tissue that had been left ischemic for 5 days after femoral artery ligation. Femoral artery ligation was performed in C57BL/6J mice and the animals randomized to either PBS or sodium nitrite therapy 5 days after artery ligation. Treatments were given b.i.d. via I.P. injection. Ischemic limb blood flow was measured using laser doppler flowmetry. (Bir et al Diabetes 2014, 63(1):270-81)

Delayed nitrite therapy increases SPY angiogram arteriogenesis

Delayed nitrite therapy increases SPY angiogram arteriogenesis. Representative temporal SPY angiogram image stills (3–6 s) are shown at 11 days following ligation and 6 days after beginning therapy (either PBS or sodium nitrite). *Left*: PBS control angiogram. *Right*: sodium nitrite angiogram following injection of ICG. $n = 5$ animals per cohort. Circles identify limb anatomical regions of vascular blush, whereas arrows indicate perfused vessels that progressively occur over time.
Bir S C et al. Am J Physiol Heart Circ Physiol 2012;303:H178-H188

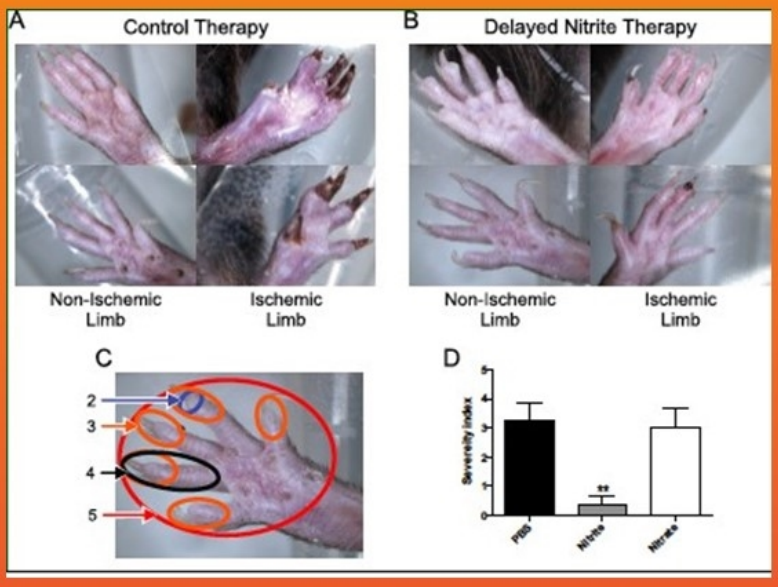


Nitrite Therapy Prevents Diabetic Nephropathy in Rats

	Control	Diabetic	Diabetic + Nitrite
Serum Glucose	105	363	344
Nitrite/Nitrate	11.5	2.5	11.0
Renal Collagen	2.7	5.7	3.3
Blood Urea Nitrogen (BUN)	19.2	98.2	34.6
Serum Creatinine	0.6	1.7	0.8
Urine Protein	5	84	20
Serum Cholesterol	61	160	157

From Arya et al (2011) Mol Cell Biochem 354:57-66

Nitrite Therapy Prevents Tissue Necrosis in Aged Db/Db Mice



Delayed sodium nitrite (165 ug/kg) or control PBS therapy was stated 5 days post femoral artery ligation in 9 month old Db/Db mice. Nitrite therapy significantly prevented tissue necrosis (panel B) compared to control PBS therapy (panel A). Panel D reports tissue necrosis severity as a function of degree of limb and digit involvement. Nitrite therapy but not PBS control or sodium nitrate significantly prevented tissue necrosis. (Bir et al Diabetes 2014, 63(1):270-81)

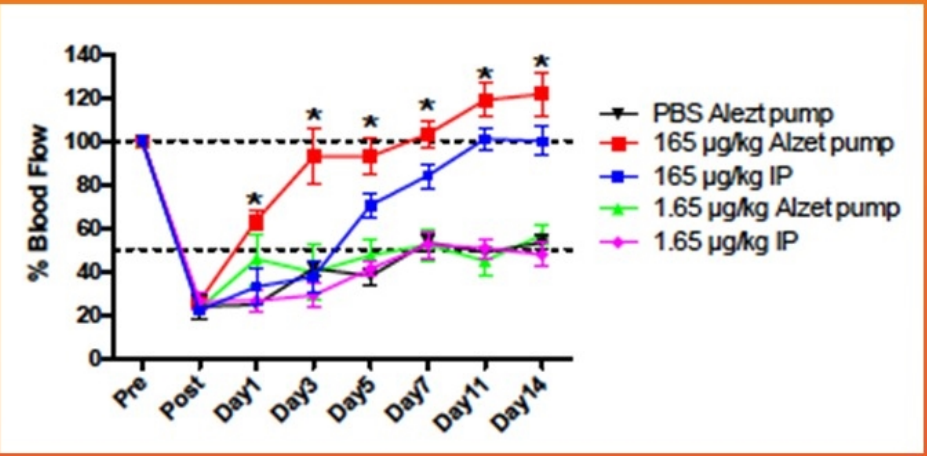
Nitrite and Hind Limb Ischemia Summary

- Single one-time nitrite therapy does not stimulate angiogenesis.
- Delayed nitrite therapy effectively restores ischemic tissue blood flow.
- Nitrite therapy is effective in a wide range of pathologies involving alterations of angiogenesis including diabetes, wound healing and tissue necrosis.
- Beneficial effects center on enhancing angiogenesis, endothelial cell proliferation, and arteriogenesis.

Development of JAN101: A Sustained Release Formulation of Sodium Nitrite

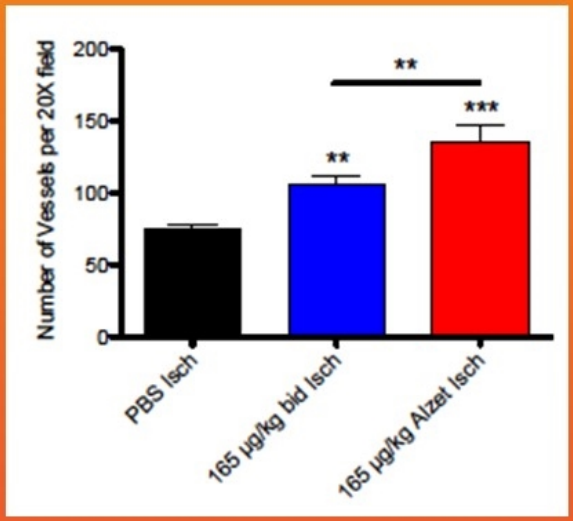
- Animal data supports improved efficacy.
- Sustained release formulation have been developed at the University of Iowa.
- One of these formulations has been scaled up for manufacturing and used in clinical studies.

Sustained Nitrite Delivery is Superior to Bolus Nitrite Injection for Ischemic Limb Blood Flow Restoration



Ischemic limb blood flow was measured using laser doppler flowmetry on mice with alzet minipump implantation versus I.P. injection. These data clearly reveal that sustained nitrite delivery using alzet minipumps quickly increased and sustained ischemic limb blood flow compared to nitrite I.P. injection that was more gradual. Interestingly, continuous lower dose nitrite delivery using minipumps was not effective at restoring blood flow above that of PBS therapy or I.P. injection route.

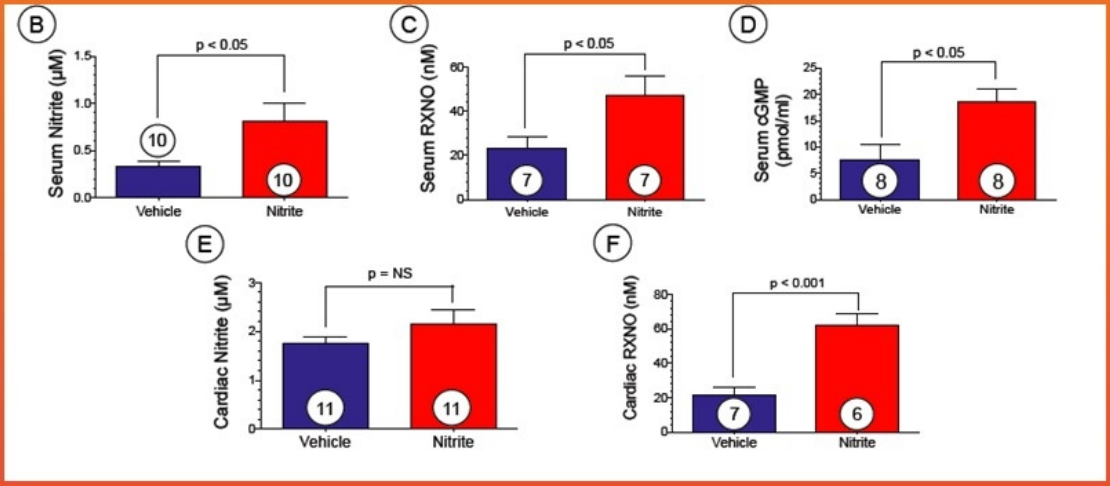
Sustained Nitrite Delivery is More Potent for Ischemic Vascular Growth



Ischemic tissues were harvested at day 5 to determine whether continuous nitrite therapy augmented ischemic vascular growth over b.i.d IP injection of sodium nitrite. Both nitrite delivery formats significantly increased vascular density in the ischemic limb. However, alzet minipump delivery of nitrite significantly increased vessel density over that of nitrite b.i.d. IP injection of nitrite. **p<0.01 versus PBS, ***p<0.001 versus PBS, line with **p<0.01 165 ug/kg alzet vs 165 ug/kg bid injection, n=6.

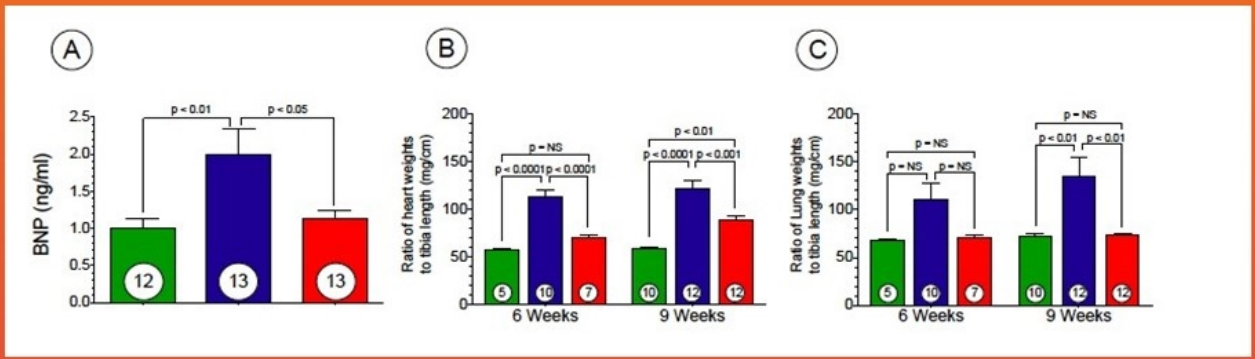
Sustained Nitrite Delivery Increases Levels of Circulating Nitrite and Metabolites

- Serum nitrite, nitrosothiol and cGMP all increased in nitrite treated animals.
- Cardiac nitrite levels are not changed but nitrosothiol levels are increased.



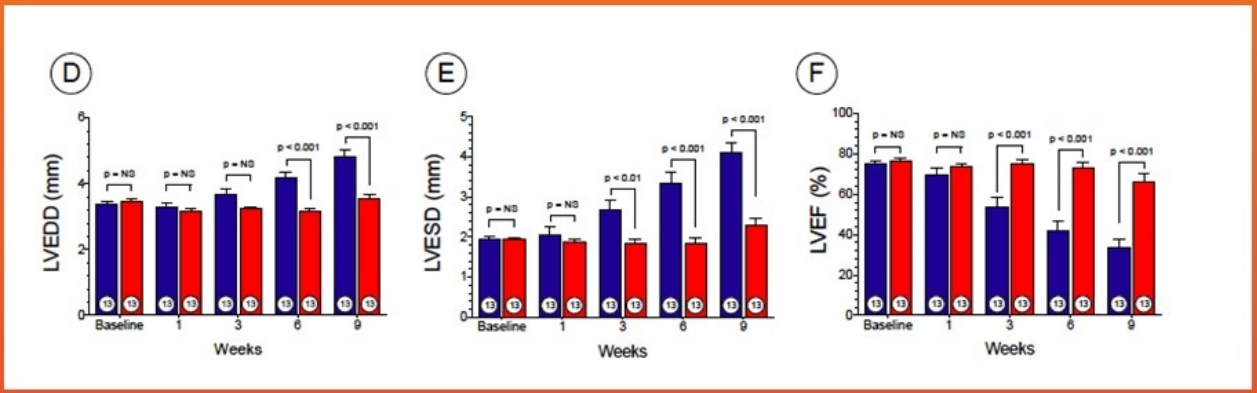
Sustained Nitrite Therapy Prevents Cardiac Dysfunction

- Brain Natriuretic Peptide (BNP) is a peptide produced in the heart and are increased in heart failure (Panel A). BNP remains low after nitrite therapy (Panel A).
- During heart failure the heart hypertrophies or increases in size. Nitrite therapy prevents hypertrophy (Panel B).
- Lungs also hypertrophy during heart failure, and nitrite prevents this (Panel C).



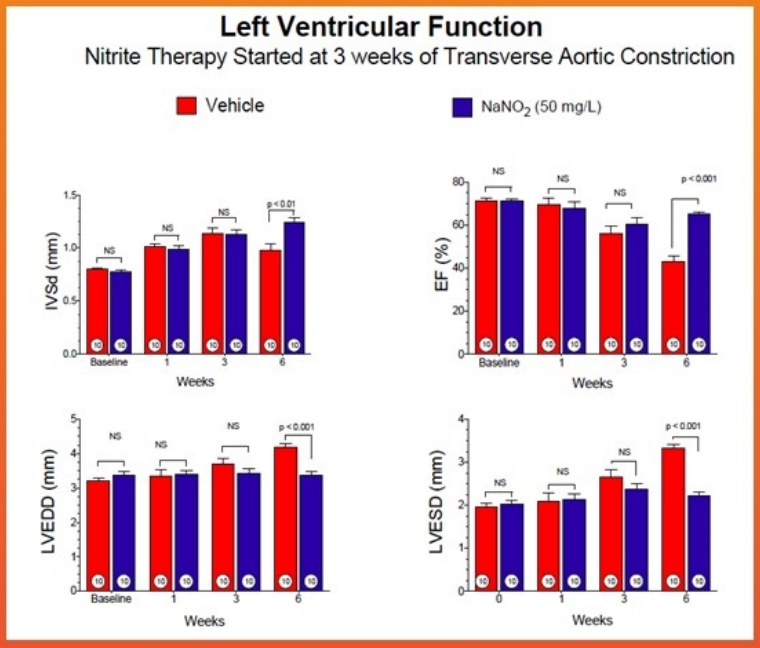
Sustained Nitrite Therapy Prevents Cardiac Dysfunction, cont.

- Diastolic and systolic cardiac dilatation are increased in heart failure. Nitrite significantly inhibited this (Panels D and E).
- A major problem in heart failure is a significant drop in the Ejection Fraction. Nitrite prevented this drop (Panel F).



Delayed Nitrite Therapy also Improves Cardiac Function

- Nitrite therapy was delayed for 3 weeks following the Transverse Aortic Constriction.
- A major problem in heart failure is a significant drop in the Ejection Fraction. Nitrite prevented this drop (Panel F).



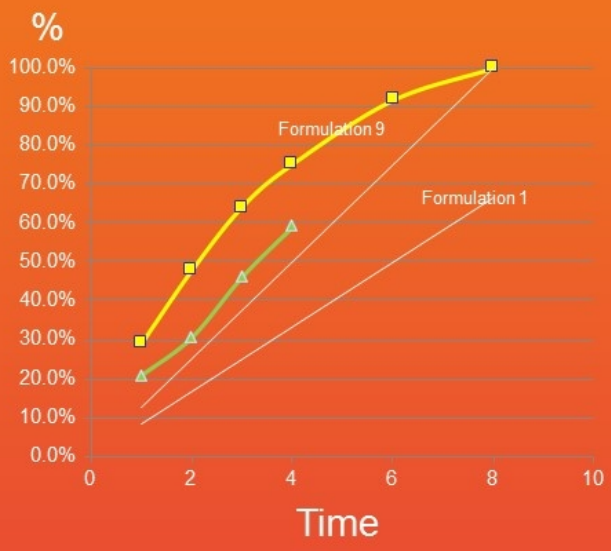
Summary of Sustained Release Animal Data

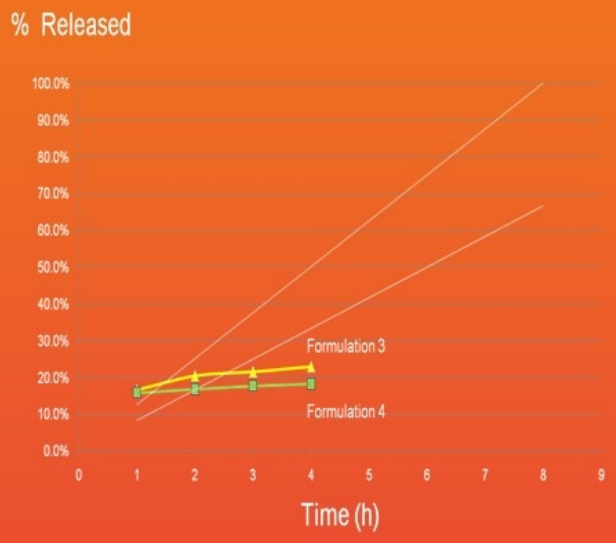
- Sustained release of nitrite resulted in faster and more robust angiogenesis in Hind Limb Ischemia model of PAD.
- Sustained release of nitrite resulted in improved cardiac function in Transverse Aortic Constriction model of heart failure, whereas bolus release was inactive.

Thus, sustained release nitrite should improve efficacy in human subjects and reduce side effects since high CMax will be eliminated.

Development of Sustained Release Formulations: *in vitro* Dissolution

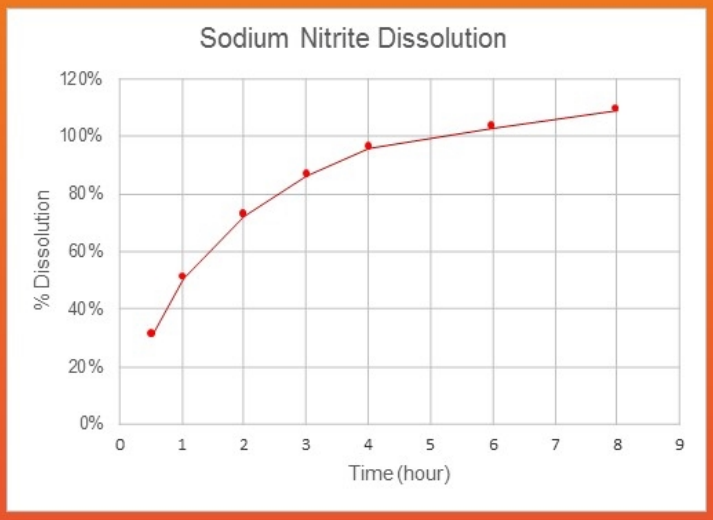
- Development of various sustained release formulations was carried out in Dr. Douglas Flanagan's lab at the University of Iowa
- A number of the formulations resulted in very good in vitro release kinetics



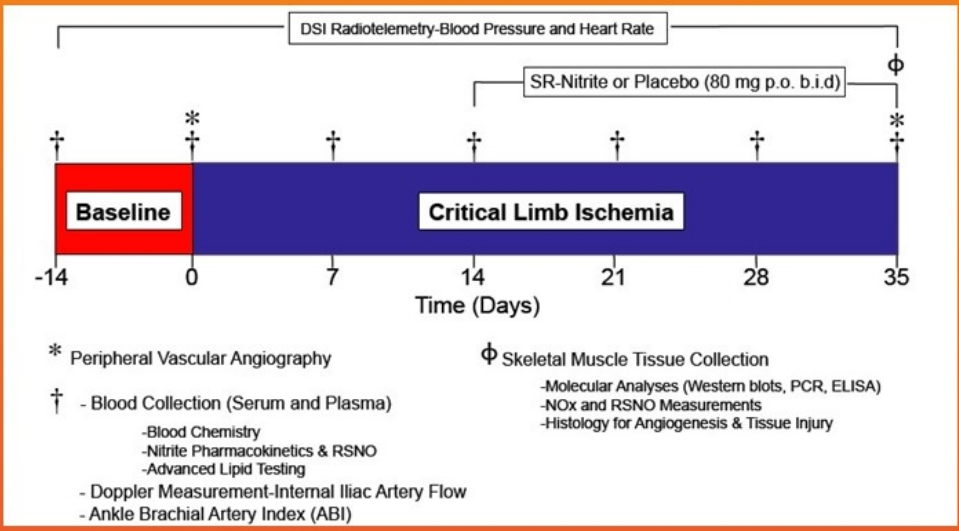


Manufacturable Formulation Developed

- Composition
  - 80 mg sodium nitrite
  - HPMC
  - Lactose
  - PVP k30
  - magnesium stearate.
- Testing carried out
  - Purity (uv spec)
  - Dissolution
  - 24-hour release



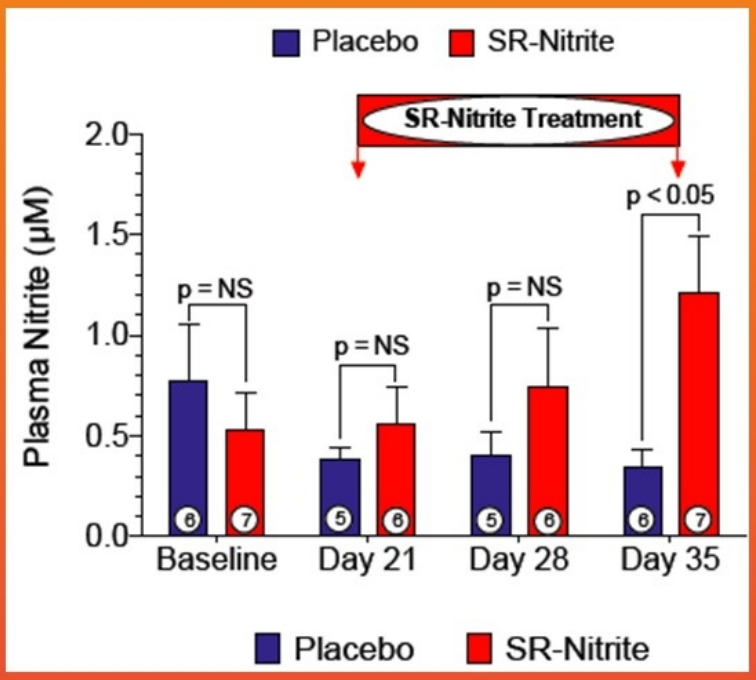
80 mg Sustained Release Tablets Manufactured Tested in CLI Model in Ossabaw Pigs



- Ossabaw pigs fed a high cholesterol diet to induce obesity and diabetes
- Common and external iliac arteries occluded for 14 days
- Randomized to placebo or 80 mg JAN101 (sustained release)
- Femoral blood pressure and doppler ultrasound measured weekly

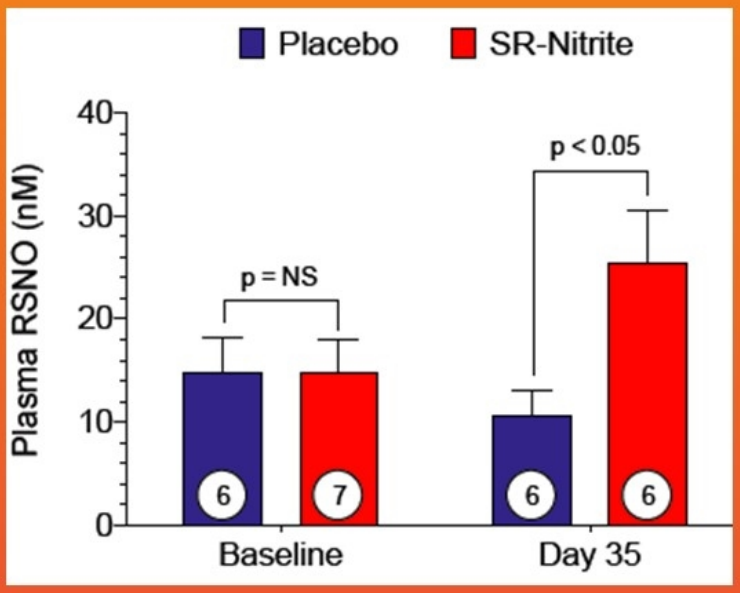
Sustained Release Nitrite Increases Plasma Circulating Levels of Nitrite

- Following occlusion of the artery, plasma nitrite levels dropped in control animals.
- Nitrite treatment increased nitrite levels over time.

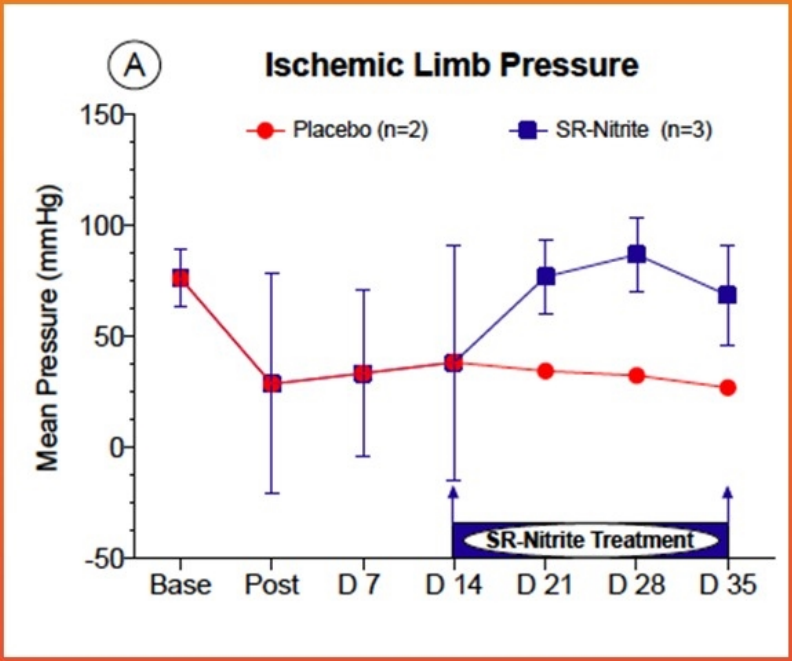


Sustained Release Nitrite Increases Circulating RSNO

- RSNO is a down stream marker of nitric oxide activity.
- Following occlusion of the artery, plasma RSNO levels in placebo animals dropped slightly.
- Nitrite treatment significantly increased RSNO levels indicating an increase in nitric oxide activity.



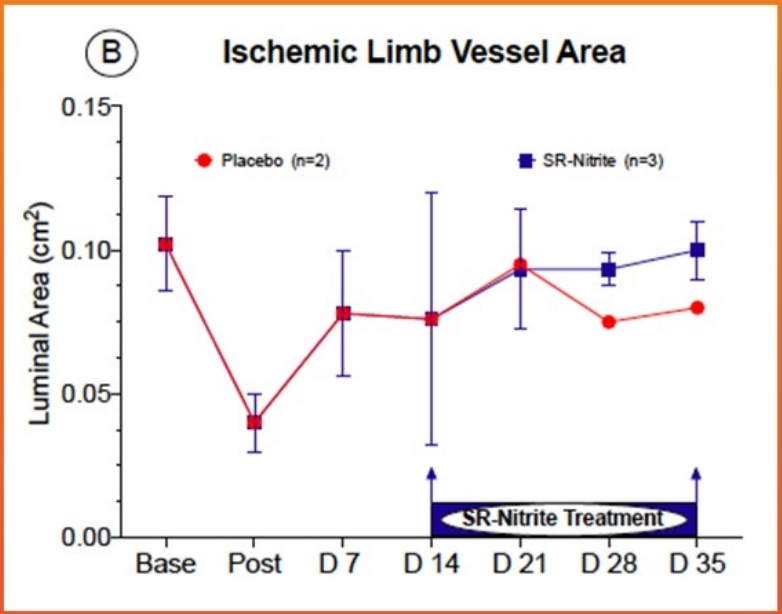
Sustained Release Nitrite Treatment Results in a Trend of Increasing Mean Arterial Pressure



- Following occlusion of the artery, mean arterial pressure in the ischemic limb drops and remains down due to reduced blood flow.
- Nitrite treatment increased mean arterial pressure.
- Vasodilation would lead to drop in blood pressure so increase likely due to arteriogenesis.

Sustained Release Nitrite Treatment Results in a Trend of Increasing Luminal Artery Area

- Doppler ultrasound was used to measure superficial femoral artery vessel area.
- Following occlusion of the artery, luminal area was reduced.
- Nitrite treatment increased luminal area.

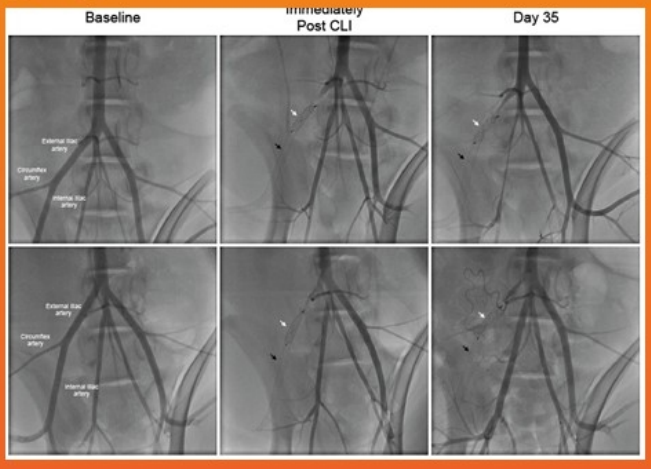


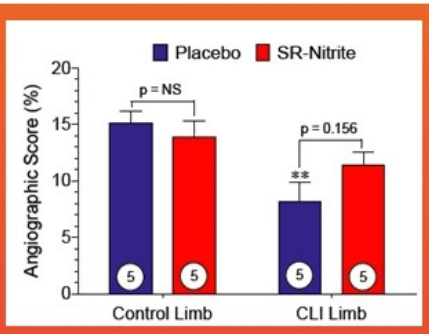
Sustained Release Nitrite Treatment Results in a Trend toward Increasing Angiogenesis

- Representative, magnified-view contrast angiography was carried out at different times following occlusion.
- Hind limb vessel density was acquired by angiographic score of the magnified-view contrast angiographic images .
- Quantitative angiographic analysis revealed a significant reduction in perfusion of the CLI limb ($p < 0.01$) in the placebo group when compared to the control limb; however, no reduction was observed in the Nitrite treated animals.

Placebo

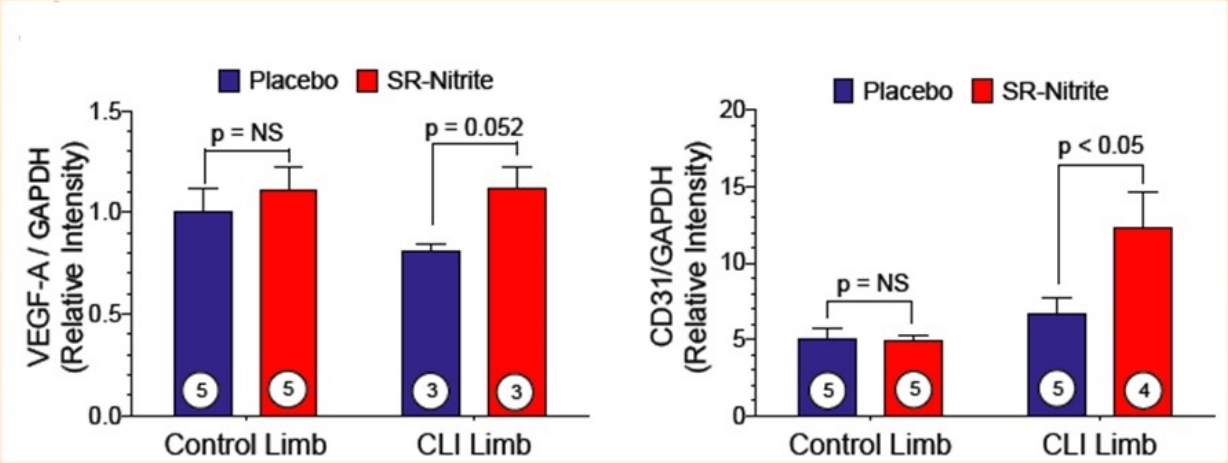
Nitrite





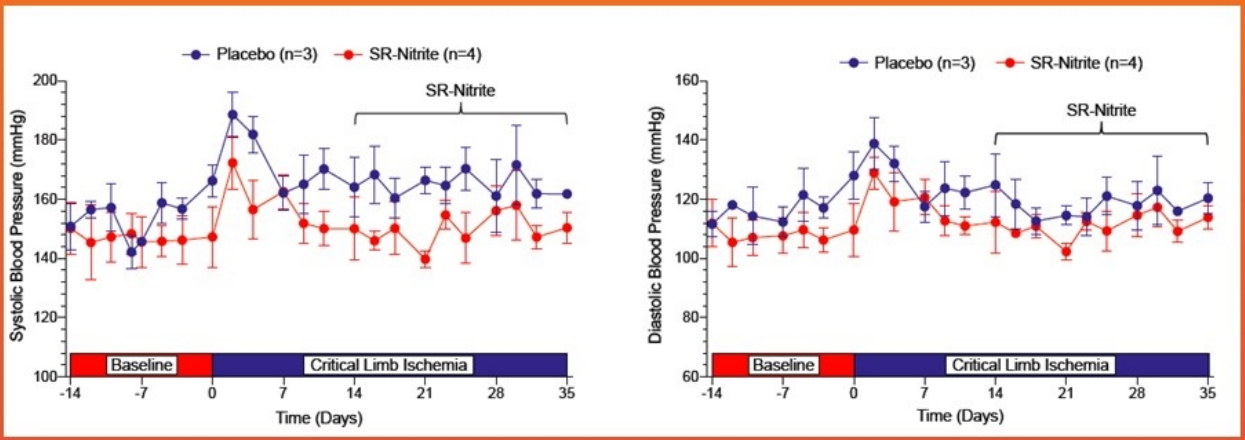
Sustained Release Nitrite Treatment Increases Markers of Angiogenesis

- VEGF mRNA levels are significantly increased ($p < 0.05$) in the ischemic limb following Nitrite treatment and protein levels show a strong trend towards increasing.
- CD31 mRNA levels show a trend towards increasing following Nitrite treatment ($p=0.051$) and the protein levels are significantly increased.



24 Hour Telemetry Showed No Change in Systolic or Diastolic Blood Pressure following Treatment with Sustained Release Nitrite

Ossabaw pigs fed a high-fat diet result in a hypertensive phenotype. Graphical representation of daily AM and PM averages of blood pressure and heart rate using radiotelemetry in the conscious animal was measured starting 14 days prior to critical limb ischemia surgery and continued for 35 days post.



Summary of Sustained Release Nitrite Formulation Work

- Various formulations developed with strong *in vitro* dissolution properties
- The manufactured formulation resulted in positive observations in Ossabaw pig CLI study
  - No change in blood pressure
  - Significant increase in biomarkers of angiogenesis
  - Strong trend toward actual increase in angiogenesis
- Have established GMP manufacturing protocols for sustained release nitrite (40 and 80 mg)

Sodium Nitrite & Sustained Release Sodium Nitrite: Clinical Data

But wasn't Arg supposed to induce angiogenesis and treat PAD via NO, and failed in Clinical Trials?

Arg

- MOA
  - Converted to NO via eNOS
- Active
  - In healthy tissue (requires healthy endothelial cells)

Nitrite

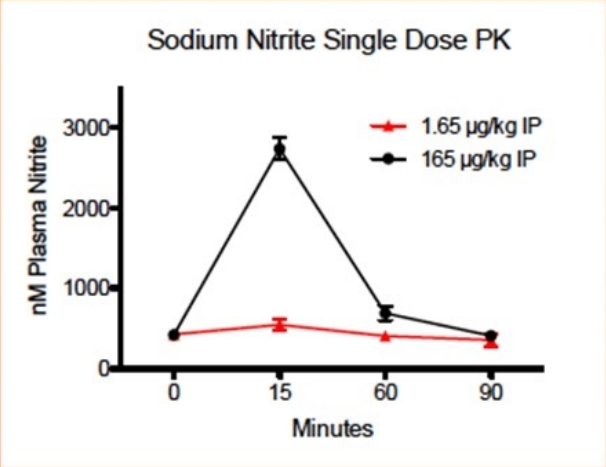
- MOA
  - Chemically reduced to NO in ischemic tissue
- Active
  - In unhealthy, low oxygen, tissue

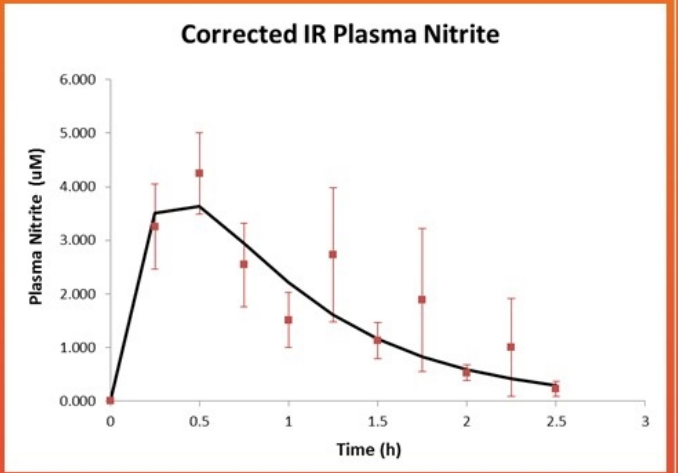
Phase I Sodium Nitrite Clinical Trial

- IND approved by the FDA
- Trial completed (PI: Frank Greenway, Pennington)
- To assess the safety of a single dose, 80 mg, of sodium nitrite provided orally
  - Methemglobin: Nitrite know to increase methemoglobin, which can impair oxygen transport
  - Blood pressure: Nitrite can act as a vasodilator, resulting in an unsafe drop in blood pressure.

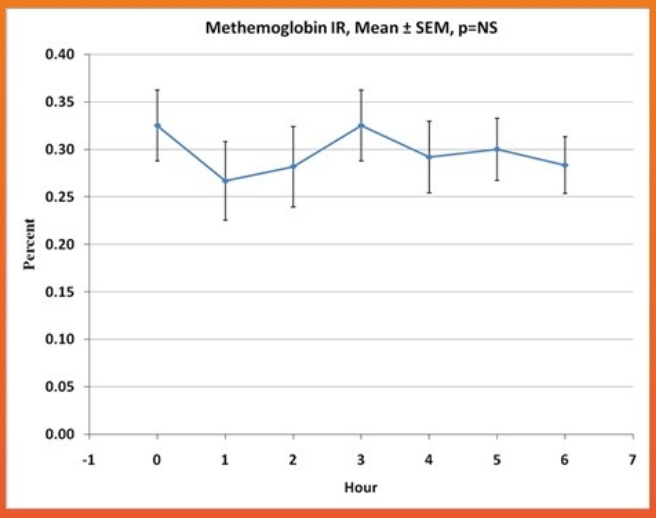
Blood Levels Correspond to Effective PK Observed in Mice

- In mouse studies, a C_{max} of ~2.7 μM with rapid clearance provided for twice daily resulted in activity described in animal studies
- In the Phase I study, a single oral administration of nitrite resulted in a C_{max} of ~4.1 μM, with rapid clearance





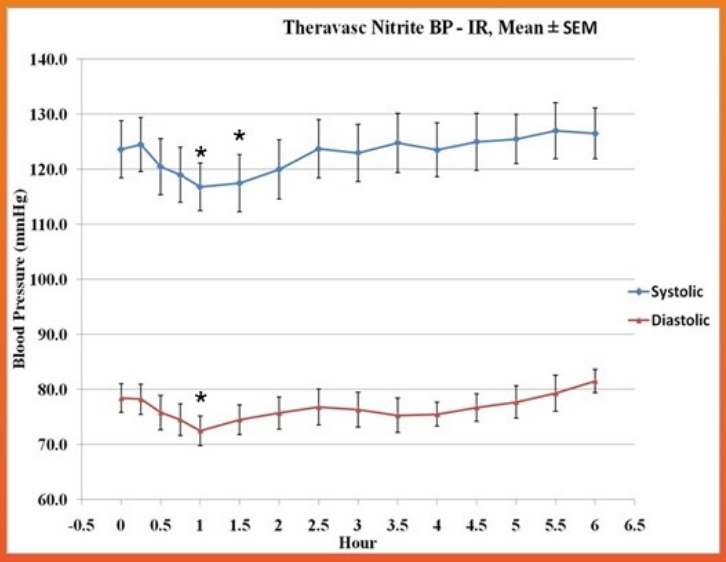
Sodium Nitrite Does not Increase Methemoglobin Levels



-Greenway et al Diabetes Technol Ther 2012

Nitrite is currently used to treat cyanide poisoning wherein the nitrite binds reversibly to globin preventing cyanide from binding irreversibly. This binding activity of nitrite to hemoglobin also leads to a major side effect, methemoglobinemia, which can cause headaches, dizziness and even comas when levels are increased significantly. Blood was collected every hour during the study to measure changes in percent methemoglobin. No increases in methemoglobin were observed with the 80-mg dose administered in this study.

Sodium Nitrite Causes an Asymptomatic, Transient Drop in Blood Pressure



-Greenway et al Diabetes Technol Ther 2012

Nitrite can also lead to vasodilation and a significant drop in blood pressure. To assess whether the 80-mg dose lead to a significant drop in blood pressure, blood pressure was measured regularly for 6 hours after administration of the sodium nitrite. Although, there was a significant drop in systolic blood pressure at 1.0 and 1.25 hours ($p<0.001$) and in the diastolic blood pressure at 1 hour ($p<0.003$), the drop was from 125/78 to 115/72 and was asymptomatic and returned to basal levels by 2h.

Phase I Study Conclusion

- 80 mg is safe and well tolerated
- 80 mg results in blood levels predicted to be therapeutic (4.1 observed μM vs 2.5 μM predicted)
- Change in blood pressure was asymptomatic and resolved quickly without treatment

Phase IIa PAD Study of Sodium Nitrite (SONIC Trial)

Placebo controlled, dose raging study to evaluate the safety, pharmacokinetics, and tolerability of multiple doses of oral sodium nitrite in patients with PAD.

- 40 and 80 mg doses, BID
- 10 week treatment period, followed by 1 week dose escalation
- Primary Objective: Safety and Tolerability
- Primary Endpoint: Flow Mediated Dilation (FMD)
- Secondary Objectives: Pharmacokinetics and evidence of functional improvement:
  - Quality of Life
  - 6 minute walk distance
  - Analysis of biomarkers

Phase IIa Enrollment

- 55 Subjects enrolled
- 10 Clinical Sites
  - University of Pennsylvania
  - Emory Medical School
  - Cleveland Clinic
  - University of Cincinnati
  - Medical College of Wisconsin
  - University of Colorado
  - The Ohio State University
  - Vanderbilt
  - University of Iowa
  - University Hospitals

Demographic Data

		Placebo n=18	40*mg n=19	80*mg n=18
Age at informed consent (years)		64.9 +/9 8.98	65.3 +/9 8.86	67.9 +/9 9.99
Gender	Male	13(72.2%)	15(78.9%)	13(72.2%)
	Female	5(27.8%)	4(21.1%)	5(27.7%)
Race/Ethnicity				
	Black or African American	5(27.8%)	6(31.6%)	8(44.4%)
	White	12(66.7%)	12(63.2%)	10(55.6%)
	Other	1(5.6%)	1(5.3%)	0(0.0%)
Weight(kg)		88.07 +/9 27.24	79.32 +/9 13.53	88.99 +/9 16.70
Height(cm)		173.18 +/9 13.29	172.01 +/9 9.87	172.18 +/9 9.95
Screening BMI (kg/m2)		29.32 +/9 8.31	26.71 +/9 2.99	30.01 +/9 5.03
ABI in index limb at screening		0.56 +/9 0.15	0.62 +/9 0.20	0.69 +/9 0.17
Diabetes Diagnosis		10(55.6%)	14(73.7%)	14(77.8%)
Hb A1c (% Hb) at screening		6.97 +/9 1.48	6.99 +/9 1.27	6.71 +/9 0.94

- No differences between treatment groups
- Most subjects were diabetic
- ABI was relatively low (0.56-0.69) suggesting subjects exhibited fairly severe PAD

Subject Withdrawals

- No differences in subject withdraws between treatment groups
- Hypotension, headaches and dizziness led to withdraws in the 80 mg treatment group

SUMMARY OF SUBJECT DISPOSITION

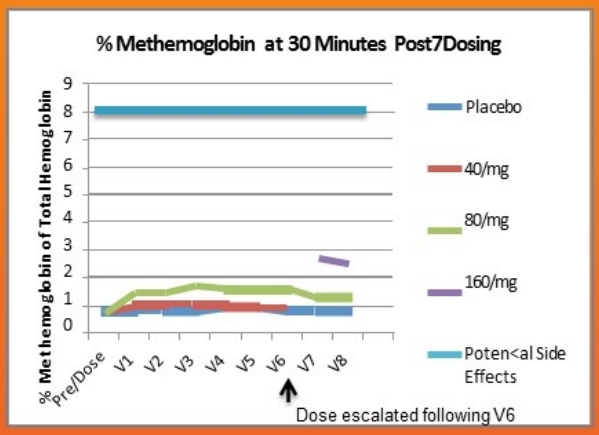
	Placebo n=18	40 mg n=19	80 mg n=18
Subjects who completed the study	15(83.3%)	17(89.5%)	15(83.3%)
Subjects who withdrew prior to completion	3(16.7%)	2(10.5%)	3(16.7%)
Reasons for withdrawal:			
Adverse Event	0(0.0%)	1(5.3%)	2(11.1%)
Met withdrawalJnew hypotension	1(5.6%)	0(0.0%)	1(5.6%)
Subject RequestJlack of energy	0(0.0%)	1(5.3%)	0(0.0%)
Subject requestJ refused to continue	1(5.6%)	0(0.0%)	0(0.0%)
Subject requestJno benefit	1(5.6%)	0(0.0%)	0(0.0%)

Safety Data: Adverse Events

- 2 SAEs Reported, both in Placebo group
- 50%, 63% and 78% of subjects reported at least one AE in the placebo, 40 and 80 mg groups, respectively
- Headaches and dizziness were the adverse events likely related to treatment, with 44% reported by patients in the 80 mg group

	Placebo	40 mg	80 mg
Blood and lymphatic system disorders	0	0	1(5.6%)
Cardiac disorders	0	2(10.5%)	0
Eye disorders	0	0	2(11.1%)
GI disorders	4(22.2%)	2(10.5%)	3(16.7%)
General disorders	0	2(10.5%)	1(5.6%)
Infections and intestations	1(5.6%)	2(10.5%)	1(5.6%)
Injury, poisoning and procedural complications	0	3(15.8%)	0
Investigations	3(16.7%)	1(5.3%)	3(16.7%)
Musculoskelatal and connective tissue disorders	2(11.1%)	3(15.8%)	2(11.1%)
Neoplasms benign, malignant and unspecified	0	0	1(5.6%)
Nervous system disorders (not incl. headaches/dizziness)	1(5.6%)	2(10.5%)	2(11.1%)
Headaches and dizziness	0	4(21.0%)	8(44.4%)
Renal and urinary disorders	0	2(10.5%)	0
Respiratory, thoracic and mediastinal disorders	2(11.1%)	0	1(5.6%)
Skin and subcutaneous tissue disorders	1(5.6%)	0	1(5.6%)
Vascular disorders	1(5.6%)	0	3(16.7%)

Safety Data: Methemoglobin and ECG



	Visit 1	Visit 5	Visit 8
Heart Rate (beats/minute)			
Placebo	72.1 +/: 13.9	71.7 +/: 15.1	73.0 +/: 12.2
40:mg	71.4 +/: 12.7	72.2 +/: 14.8	
80:mg	62.7 +/:10.7	65.5 +/: 11.9	74.3 +/: 16.9
160:mg			64.7+/: 10.0
QTcB interval (msec)			
Placebo	433.2 +/: 33.0	430.9 +/: 24.0	438.6 +/: 35.3
40:mg	415.9 +/: 49.0	430.1 +/: 34.8	
80:mg	422.3 +/: 34.0	411.6 +/: 49.7	423.2 +/: 40.3
160:mg			427.7 +/: 31.9
QTcF interval (msec)			
Placebo	421.2 +/: 31.4	419.7 +/: 22.5	425.4 +/: 33.9
40:mg	404.8 +/: 44.9	417.7 +/: 24.0	
80:mg	419.9 +/: 30.5	406.2 +/: 46.2	409.5 +/: 34.3
160:mg			422.8 +/: 27.9

- Only a slight increase observed in methemoglobin levels, a major concern with nitrite therapy, at 80 mg BID but well below that which causes concerns clinically.
- No cardiovascular concerns were noted
  - no QTc changes > 60 msec, which would be considered serious were observed
  - No QTc changes > 30 msec, which would be considered questionable

Safety Data: Pulse Rate and Blood Pressure

- There was no clinically significant change in the resting heart rate or blood pressure in any of the groups.
- The maximum change in orthostatic pulse and blood pressure was seen early after initial drug administration of the 80 mg group and dissipated over the course of study.

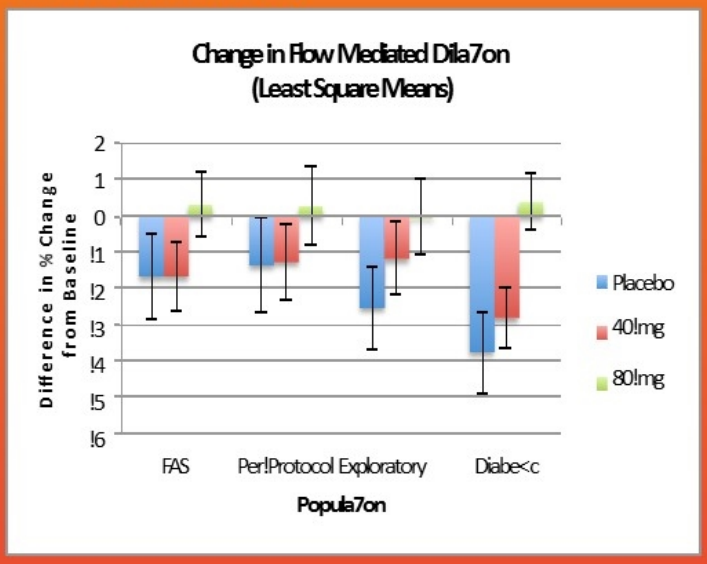
		Screening	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
Supine (Mean)										
Pulse	Placebo	73.6	74.4	73.0	71.0	74.8	74.6	73.1	73.1	75.6
	403mg	71.4	74.1	74.1	74.7	71.7	72.7	70.4	73.1	70.2
	803mg	63.9	65.6	65.1	66.7	64.6	68.7	65.5	64.3	68.3
Blood Pressure	Placebo	141.3/77.9	141.4/78.3	139.9/78.4	138.4/77.4	137.8/75.4	140.3/76.9	145.4/79.5	139.8/77.8	136.1/75.1
	403mg	136.8/75.8	129.7/72.3	128.0/70.5	129.8/72.5	128.4/71.1	124.1/72.0	127.3/73.7	126.7/71.3	130.0/72.2
	803mg	132.4/69.4	129.8/68.4	122.8/66.7	127.1/66.7	125.1/65.2	124.6/68.9	123.1/66.2	118.4/64.4	120.7/66.9
Standing (Mean)										
Pulse	Placebo		78.1	77.8	74.9	78.1	78.5	76.0	76.1	77.4
	403mg		75.8	78.6	76.7	75.6	76.6	73.9	76.3	74.3
	803mg		72.6	72.3	72.9	72.6	72.5	67.6	70.4	72.6
Blood Pressure	Placebo		141.6/81.7	144.3/81.2	139.9/79.4	139.9/80.3	137.7/79.4	143.3/78.4	141.3/78.7	138.2/75.0
	403mg		129.5/73.1	128.3/72.6	129.4/73.1	124.9/71.0	124.3/71.6	127.6/73.2	122.2/73.2	123.1/68.7
	803mg		125.4/70.2	123.1/71.9	124.8/69.2	123.7/68.8	119.5/71.9	124.8/70.0	123.3/67.1	117.7/67.9
Orthostatic Changes										
Pulse	Placebo		3.7	4.8	3.9	3.3	3.9	2.9	3.0	1.8
	403mg		1.8	4.5	2.0	3.9	3.8	3.5	3.2	4.1
	803mg		6.9	7.3	6.2	7.9	3.8	2.1	6.1	4.3
Systolic BP	Placebo		0.2	4.3	1.6	2.1	32.6	32.1	1.5	2.2
	403mg		30.3	0.3	30.4	33.4	0.3	0.3	34.5	36.9
	803mg		34.4	0.3	32.3	31.4	35.2	1.6	4.8	33.0
Diastolic BP	Placebo		3.3	2.8	1.9	4.9	2.5	31.1	0.9	30.1
	403mg		0.8	2.1	0.6	30.1	30.4	30.5	1.9	33.5
	803mg		1.8	5.2	2.5	3.5	3.0	3.8	2.7	1.0

Dose escalated following V6

Biological Activity Data: FMD

- Flow Mediated Dilation is a ideal imaging modality to assess endothelial cell dysfunction
- Brian Annex has shown that FMD is severely compromised in diabetic patients
- Since the mechanism of action of nitrite is to improve endothelial cell function, FMD was used to assess biological activity

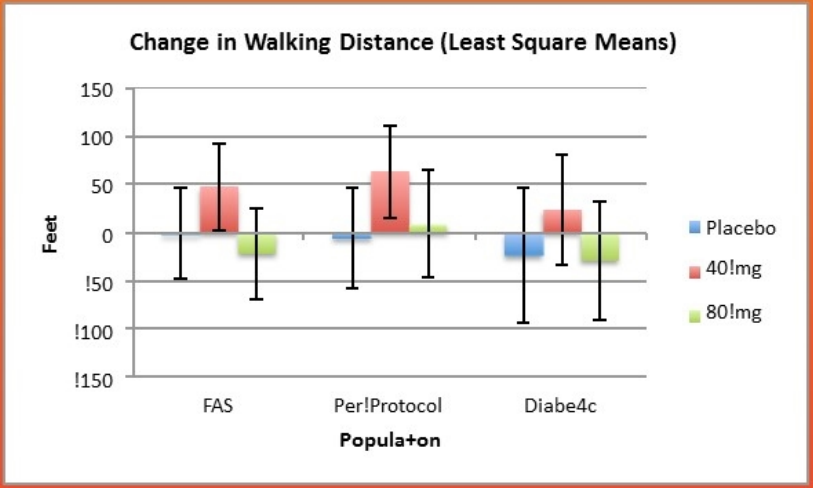
- In the intent-to-treat population there was no significant difference in FMD at baseline among the groups.
- The difference in FMD from baseline was assessed at 10 weeks and a non-significant trend was noted for worsening of FMD in the placebo and 40 mg bid group whereas maintenance of baseline FMD was observed in the 80 mg bid group.
- In the diabetic cohort, the change in FMD in those receiving the 80 mg bid dose was significantly greater than those receiving placebo and 40 mg bid dose ($P < 0.01$).



Biological Activity Data: 6 Minute Walk

- The main complaint associated with PAD, in the inability to walk even short distances without pain.
- The 6 minute walk test measures the distance a subject can walk up and down a corridor in 6 minutes.
- This test was conducted to determine the number of subjects needed to power the next trial.

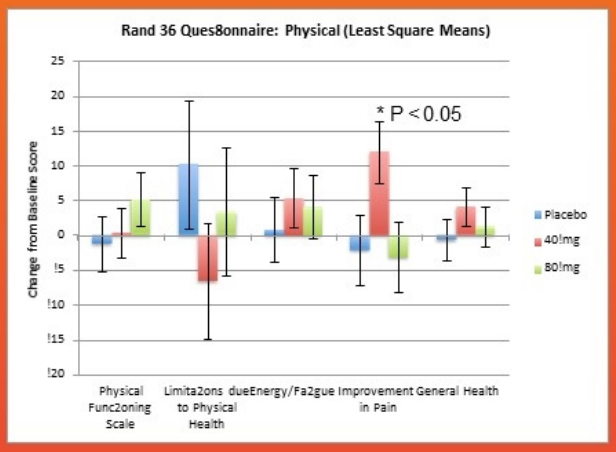
- The 40 mg bid dose group showed a numeric improvement in the 6 minute walk test over time compared to placebo but this was not statistically significant.
- The mean improvement in the Per-Protocol group was 57 feet and the median improvement was 99 feet.



Biological Activity Data: Quality of Life (QoL)

- Limitations due to pain in the affected leg leads to poor quality of life.
- A RAND 36 Quality of Life Questionnaire and Walking Impairment Questionnaire were used to assess improvements in QoL.
- This test was conducted to determine the number of subjects needed to power the next trial.

There was a significant improvement in the pain domain for physical component of SF 36 questionnaire (P<0.05) among patients randomized to 40 mg group compared with placebo.



Study Conclusions

- No clinical safety concerns
- Clear evidence of biological activity
- Indication of clinical outcome for treating PAD patients

but

- Dose dependent increases in headaches and dizziness may have contributed to subjects in the 80 mg group performing worse in the 6 minute walk test and their assessment of quality of life.

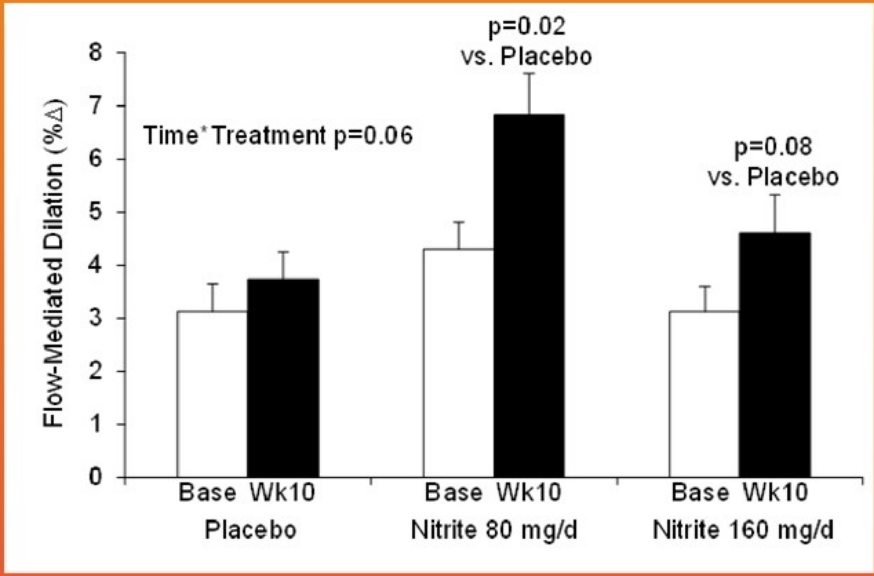
- Sustained release formulation should provide clinical benefits while reducing headaches and dizziness, which track the high C_{max} of the rapid release formulation

Phase IIa: Sodium Nitrite Effects on Aging

Doug Seals Ph.D., Univ. of Colorado

- Has shown that vascular function declines with age beginning at 50 years old
- Received R21 grant
- Following SONIC protocol, except:
  - Healthy subjects aged 50-85
  - Replaced 6 minute walk with time to exhaustion on treadmill
  - Had a number of secondary endpoints
- Received an RO1 grant to study 40 mg sodium nitrite sustained release vs placebo in 34 subjects per group

Sodium Nitrite Improves Flow Mediated Dilation in Healthy Subjects

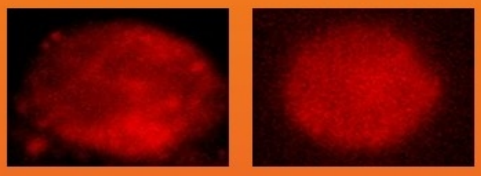


Brachial artery flow-mediated dilation (FMD) was improved with 10 weeks sodium nitrite supplementation (80 mg/day bar middle bars, 160 mg/day right most bars) compared with placebo (left most bars). Values are means ± SE. * P ≤ 0.10 Placebo vs Low Dose (80 mg/day).

Reduction in Flow Mediated Dilation is Associated with Reduced Oxidative Stress

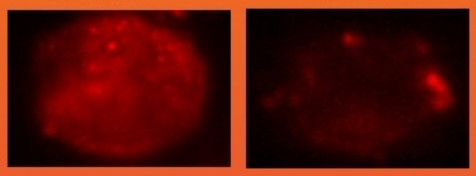
Placebo

Baseline | Week 10



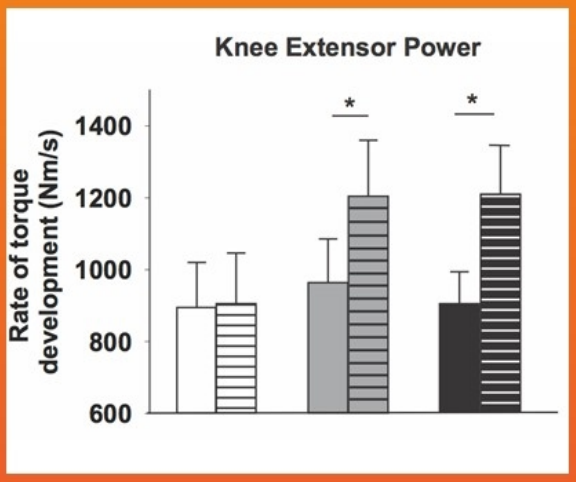
Nitrite 80 mg/d

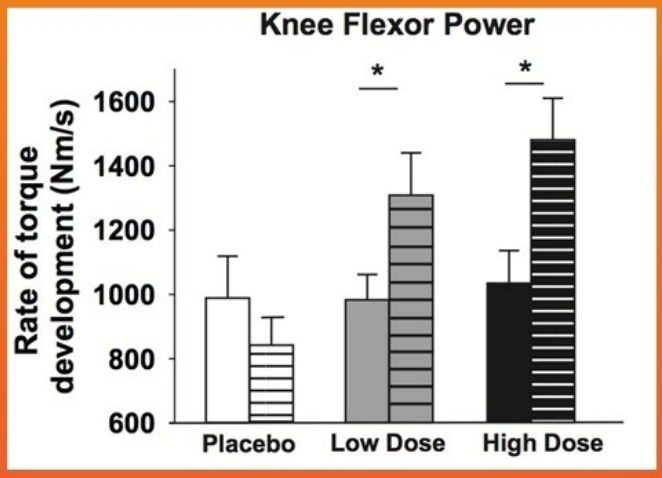
Baseline | Week 10



The improvement in brachial FMD with sodium nitrite supplementation was associated with a *reduction in nitrotyrosine staining, a cellular marker of oxidative stress* (representative images for 80 mg/d shown).

Sodium Nitrite Improves Motor Function





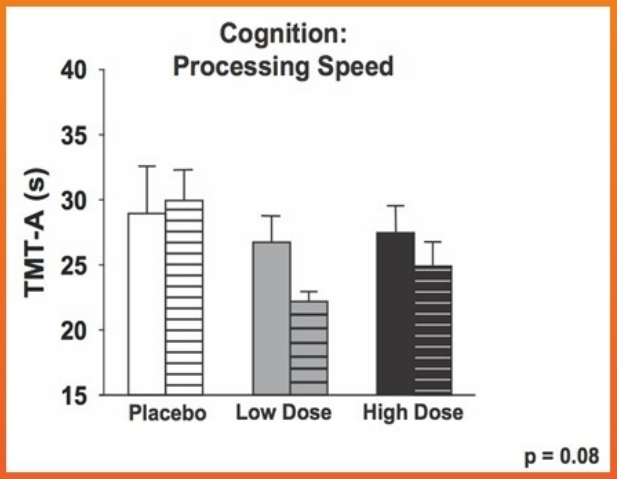
Knee extension and flexion rate of torque development (RTD), an index of lower body power and force generation, is improved sodium nitrite compared with placebo. Solid bars represent baseline RTD and striped bars are RTD following 10 weeks sodium nitrite (gray bars = low dose 80 mg/day; black bars = high dose 160 mg/day) compared with placebo (white bars).

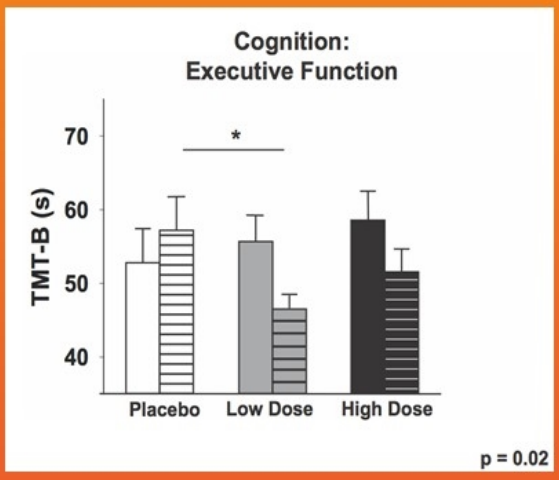
Sodium Nitrite Improves Secondary Indicators of Motor Function

		Improve from Baseline (%)		
Subdomain	**Functional Measure**	**Placebo**	**Nitrite 80 mg/d**	**Nitrite 160 mg/d**
Balance	↓ Rapid step errors	-4.7%	+31.7%	+31.8%
Endurance Time	Balke treadmill	-0.2%	+10.0%	+3.4%
	Heel-rise	+3.5%	+30.1 %	+23.5%
Strength	Grip strength	-2.1%	+6.0%	+3.7%

Improvements observed expressed as % change from baseline in secondary motor function outcomes following 10-week supplementation of sodium nitrite in healthy middle-aged and older adults.

Sodium Nitrite Improves Cognitive Function





Time to complete the Trail Making Test part A (TMT-A) and part B (TMT-B)\ an index of processing speed and executive functioning, respectively, is improved sodium nitrite compared with placebo. Solid bars represent baseline and striped bars are TMT times following 10 weeks sodium nitrite (Low dose 80 mg/day, High dose 160 mg/day) compared with placebo.

Results from Doug Seals Aging Study

- Demonstration of bioactivity through improvement in FMD
  - No improvement noted in interim time point (4 weeks); demonstrates chronic vs acute mechanism of action
- Demonstration of clinical benefit:
  - Significant improvement in motor function
  - Improvement in cognitive function
- Reduction in oxidative stress

➢ In many parameters the 40 mg BID (80 mg/day) dose was superior to the higher dose, similar to the findings in the SONIC study.

Human Clinical Trials with Sodium Nitrite have been Initiated

- University of Colorado Study on Normal Aging
  - 64 subjects, 60-79 yo,
  - Randomized 1:1 (placebo:40 mg TV1001sr)
  - 12 weeks, BID treatment
  - Endpoints
    - Vascular function improvement
    - Motor function improvement
    - Sensation improvement
    - Cognitive improvement
    - Changes in fMRI assessments of global and regional brain structure and task induced neural activation patterns during motor and cognitive tasks
- Diabetic Neuropathy Trial (Completed)

Diabetic Neuropathic Pain Study using Sustained Release Nitrite

- Rationale
  - In SONIC study, subjects reported a significant reduction in pain.
  - In a study carried out at NIH with topical nitrite and sickle cell patients with foot ulcers, subjects reported significantly less pain. (ADD REFERENCE)
  - Improving blood flow to the damaged neurons and reducing inflammation will likely lead to improved neuronal function and reduced pain.
  - Most current therapies are Class 5 narcotics, Sustained Release Nitrite represents a non-addictive, cost effective method for treating pain.

- Pain Phase IIa Clinical Study
  - Conducted at the Ohio Pain Clinic by Dr. Amol Soin
  - Placebo vs 40 and 80 Sustained Release Nitrite, double blind
    - 90 days BID
  - Primary Endpoints – Safety, PK
    - Reduction in blood pressure drop, headaches and dizziness
    - Demonstration of sustained release profile
  - Secondary Endpoints – Biological Activity
    - Pain questionnaires
    - Quantitative sensory pain scoring

Demographic Data

	Placebo	40 mg group	80 mg group
Number	9	7	8
Age, years (SD)	60.0 (13.1)	63.1 (11.8)	50.2 (9.8)
Sex, male	5 (55.6%)	4 (57.1%)	3 (37.5%)
Race, white	100%	100%	100%
Ethnicity, white	100%	100%	100%
Smoking Status			
Former	6 (66.7%)	3 (42.9%)	3 (37.5%)
Current	0	1 (14.3%)	0
Peripheral Vascular Disease	0	1 (14.3%)	0
Cardiovascular Disease	6 (66.7%)	6 (85.8%)	3 (37.5%)
HbA1c at screening (SD)	7.7 (1.4)	7.7 (1.2)	8.5 (2.4)

- No differences between treatment groups

Safety Data: Adverse Events

	Mean of:	
	Total AEs	Total SAEs
Combined Placebo	29	2
40 mg TV1001	23	5
80 mg TV1001	23	2
F(2,23)	.10	.13
p	.905	.880

- No differences in reported AEs or SAEs.
- All reported SAEs were not deemed to be treatment related.
- **No reports of headaches or dizziness at either dose.**

Preliminary Pharmacokinetic Data with Sustained Release Nitrite

Note: Due to problems with sample prep, many samples were lost to analysis and data was therefore imputed. Pharmacokinetic analysis will need to be repeated.

Effects of Sustained Release Nitrite on Neuropathic Pain Symptom Inventory

Summary of Reported Treatment Effects on Pain						
NPSI		V1	V2 Change from V1	V3 Change from V1	% Change of V3 to V1	JAN101 Fold Improvement Over Placebo
Total Score	Placebo	47.4	C8.44	C4.00	8.4%	
	40 mg	34.7	C4.71	C4.43	12.7%	1.51
	80 mg	56.0	C1.88	C10.00	22.0%	2.62

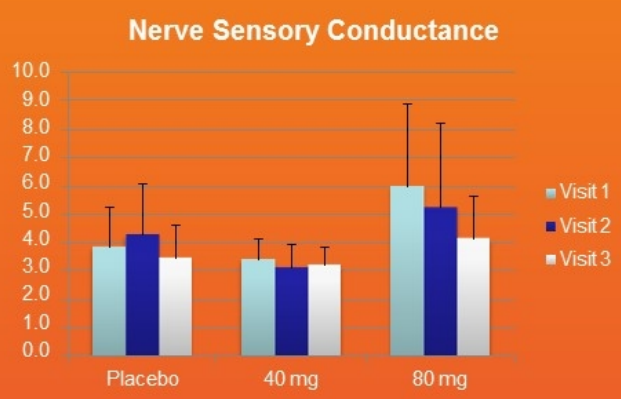
Effects of Sustained Release Nitrite on Brief Pain Inventory

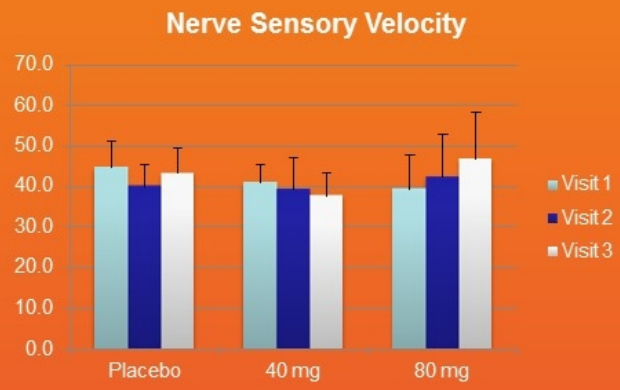
Summary of Reported Treatment Effects on Pain						
Brief Pain Inventory		V1	V2 Change from V1	V3 Change from V1	% Change of V3 to V1	JAN101 Fold Improvement Over Placebo
Severity Score	Placebo	5.1	D0.96	D0.24	5.9%	
	40 mg	4.3	D1.06	D0.48	11.6%	1.97
	80 mg	5.9	D0.54	D0.84	13.6%	2.34
Interference Score	Placebo	5.0	D0.57	D0.73	14.0%	
	40 mg	4.4	D1.11	D0.20	4.5%	D3.11
	80 mg	6.4	0.62	0.77	10.94%	D1.28

Effects of Sustained Release Nitrite on McGill Pain Index

Summary of Reported Treatment Effects on Pain						
McGill Pain Index		V1	V2 Change from V1	V3 Change from V1	% Change of V3 to V1	JAN101 Fold Improvement Over Placebo
Total Score	Placebo	5.1	B1.4	B1.5	29.4%	
	40 mg	3.9	B0.7	B1.4	35.9%	1.22
	80 mg	4.8	0.8	B0.2	4.2%	B7.00
Continuous Pain	Placebo	5.0	B1.9	B1.8	36.0%	
	40 mg	3.7	B0.2	B1.7	48.6%	1.35
	80 mg	4.4	1.2	B0.1	2.3%	B15.7
Intermittent Pain	Placebo	6.0	B1.6	B1.9	31.7%	
	40 mg	4.6	B1.1	B1.8	39.1%	1.23
	80 mg	5.9	0.7	B0.6	10.2%	B3.11

Effects of Sustained Release Nitrite on Nerve Conductance and Velocity





Nerve Sensory Testing. The mean and standard deviations for Nerve Sensory Conductance and Nerve Sensory Velocity are shown for Visit 1 (baseline), Visit 2 and Visit 3 (end of the study) for the placebo group (n=9), 40 mg BID JAN101 treatment group (n=7) and 80 mg BID treatment group (n=8).

Phase II Diabetic Neuropathy Study Results with Sustained Release Nitrite

- No reports of headaches or dizziness.
- C_{max} = ~0.8 uM, time to C_{max} ~ 3 hours.
- 40 mg and 80 mg doses caused reduction in pain (when compared to placebo) in most questionnaires:
  - Brief Pain Inventory (Severity): 1.97X (40 mg), 2.34X (80 mg)
  - Neuropathic Pain Symptom inventory: 1.51X (40 mg), 2.62X (80 mg)
  - McGill Pain Index (main subsections): 1.22-1.35X (40 mg)

Clinical Trials Summary

Trial	PAD	Aging	Diabetic Neuropathy
Formulation	Sodium Nitrite	Sodium Nitrite	Sustained Release Nitrite
N	55	30	26
Side Effects	Headaches	Headaches	None
FMD	Improved	Improved	Not Measured
NCV	Not Measured	Not Measured	Improved (80 mg)
Pain	Reduced (40 mg)	Not Measured	Reduced
Physical Functioning	Improved (NS)	Improved	Not Measured

Overall Data Summary

- Patients with cardiovascular disease involving PAD and Diabetes are deficit in circulating nitrite;
- Preclinical studies have shown that nitrite stimulates angiogenesis specifically in ischemic tissue, while also reducing oxidative stress and inhibiting inflammation;
- Human studies have demonstrated bioactivity of oral sodium nitrite and also significant reduction in pain in two different patient populations;
- The sustained release formulation maintains the same benefits as the immediate release while reducing headaches and dizziness; and
- Numerous method of use and composition patents have been issued in the US, Europe, Australia, Japan, China and Israel.