ArTara Therapeutics and Proteon Therapeutics Proposed Combination

September 24, 2019

CAUTIONARY STATEMENT - FORWARD LOOKING STATEMENTS

This presentation is being made in respect of a proposed transaction involving ArTara Therapeutics, Inc. ("ArTara") and Proteon Therapeutics, Inc. ("Proteon" or "we" or "our"). Certain statements contained in this presentation regarding matters that are not historical facts are forward-looking statements within the meaning of Section 21E of the Securities and Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995 (the "PSLRA"). These include statements regarding management's intentions, plans, beliefs, expectations or forecasts for the future, and, therefore, stockholders are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. We use words such as "anticipates," "believes," "plans," "expects," "projects," "future," "intends," "may," "will," "should," "could," "estimates," "predicts," "potential," "continue," "guidance," and similar expressions to identify these forward-looking statements that are intended to be covered by the safe-harbor provisions of the PSLRA. Such forward-looking statements are based on management expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the forward-looking statements due to a number of factors, including, but not limited to, risks relating to the completion of the proposed transaction, including the need for Proteon's and ArTara's stockholder approval and the satisfaction of certain closing conditions; the anticipated financing to be completed concurrently with the closing of the proposed transaction; the cash balance of the combined company following the closing of the proposed transaction and the financing, and expectations with respect thereto; the potential benefits of the proposed transaction; the business and prospects of the combined company following the proposed transaction; and the ability of Proteon to remain listed on the Nasdaq Global Market. Risks and uncertainties that may cause actual results to differ materially from those expressed or implied in any forward-looking statement include, but are not limited to: the closing of the proposed transaction; ArTara's plans to develop and commercialize its product candidates, including TARA-002, and Choline Chloride; the timing, costs and outcomes of ArTara's planned clinical trials; expectations regarding potential market size; the timing of the availability of data from ArTara's clinical trials; the timing of any planned investigational new drug application or new drug application; ArTara's plans to research, develop and commercialize its current and future product candidates; ArTara's ability to successfully collaborate with existing collaborators or enter into new collaborations, and to fulfill its obligations under any such collaboration agreements; the clinical utility, potential benefits and market acceptance of ArTara's product candidates; ArTara's commercialization, marketing and manufacturing capabilities and strategy; ArTara's ability to identify additional products or product candidates with significant commercial potential; developments and projections relating to ArTara's competitors and industry; the impact of government laws and regulations; ArTara's ability to protect its intellectual property position; and ArTara's estimates regarding future revenue, expenses, capital requirements, and the need for and timing of additional financing following the proposed transaction. These risks, as well as other risks associated with the proposed transaction, will be more fully discussed in the proxy statement/prospectus that will be included in the registration statement on Form S-4 that will be filed by Proteon with the U.S. Securities and Exchange Commission (the "SEC") in connection with the proposed transaction. Additional risks and uncertainties are identified and discussed in the "Risk Factors" section of Proteon's Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and other documents filed from time to time with the SEC. Forward-looking statements included in this presentation are based on information available to Proteon and ArTara as of the date of this presentation. Neither Proteon nor ArTara undertakes any obligation to update such forward- looking statements to reflect events or circumstances after the date of this presentation.

No Offer or Solicitation:

This presentation does not constitute an offer to sell, or the solicitation of an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. No public offer of securities shall be made except by means of a prospectus meeting the requirements of Section 10 of the Securities Act of 1933, as amended.

Additional Information About the Proposed Transaction and Where to Find it

This presentation is being made in respect of a proposed transaction involving ArTara and and Proteon, and Proteon intends to file a registration statement on Form S-4 with the SEC, which will contain a proxy statement/prospectus and other relevant materials, and plans to file with the SEC other documents regarding the proposed transaction. The final proxy statement/prospectus will be sent to the stockholders of Proteon in connection with the Proteon's special meeting of stockholders to be held to vote on matters relating to the proposed transaction. The proxy statement/prospectus will contain information about Proteon, ArTara, the proposed transaction, and related matters. **STOCKHOLDERS OF PROTEON ARE URGED TO READ THE PROXY STATEMENT/PROSPECTUS (INCLUDING ANY AMENDMENTS OR SUPPLEMENTS THERETO) AND OTHER DOCUMENTS FILED WITH THE SEC CAREFULLY IN THEIR ENTIRETY WHEN THEY BECOME AVAILABLE, AS THEY WILL CONTAIN IMPORTANT INFORMATION THAT STOCKHOLDERS OF PROTEON SHOULD CONSIDER BEFORE MAKING A DECISION ABOUT THE PROPOSED TRANSACTION AND RELATED MATTERS**. In addition to receiving the proxy statement/prospectus and proxy card by mail, Proteon stockholders will also be able to obtain the proxy statement/prospectus, as well as other filings containing information about Proteon, without charge, from the SEC's website at www.sec.gov or, without charge, by directing a written request to: Proteon Therapeutics, Inc., 200 West St. Waltham, MA 02451, Attention: Investor Relations.

Participants in the Solicitation

Proteon, ArTara and their respective executive officers, directors, certain members of management and certain employees may be deemed, under the SEC rules, to be participants in the solicitation of proxies from Proteon stockholders with respect to the matters relating to the proposed transaction. Information regarding Proteon's executive officers and directors is available in Proteon's proxy statement on Schedule 14A for its 2018 annual meeting of stockholders, filed with the SEC on April 26, 2018 and Proteon's Annual Report on Form 10-K and the amendment thereto for the year-ended December 31, 2018. These documents are available free of charge at the SEC's website at www.sec.gov or by going to Proteon's investor and media page on its corporate website at www.proteontherapeutics.com. Additional information regarding the persons who may, under the rules of the SEC, be deemed participants in the solicitation of proxies in connection with the proposed transaction, and a description of their direct and indirect interests in the proposed transaction, which may differ from the interests of Proteon's stockholders generally, will be set forth in the proxy statement/prospectus that Proteon intends to file with the SEC in connection with its stockholder vote on matters relating to the proposed transaction. Proteon stockholders will be able to obtain this information by reading the proxy statement/prospectus when it becomes available.

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MERGER - ARTARA THERAPEUTICS / PROTEON THERAPEUTICS

Definitive agreement for **all-stock merger announced on September 23, 2019**

Expected to be **completed in 4Q 2019**; new company applying to trade on Nasdaq under TARA

Requires each of Proteon and ArTara shareholder approval among other customary conditions

Concurrent financing **of $42.5 million led by healthcare dedicated investors** at the closing of the merger

Leadership: Jesse Shefferman, CEO of ArTara

Combined Company's Board expected to include **five nominees from ArTara, one from Proteon and Mr. Shefferman**

On a pro forma basis, **current Proteon holders will own approximately 10% of the combined company and ArTara investors and investors in the financing will own approximately 90% of the combined company**

EXPERIENCED LEADERSHIP – THE ARTARA TEAM

Jesse Shefferman
CEO

- Former Head of Business Development, member of the executive leadership team at Retrophin, Inc.
- Led the team that identified and executed a number of rare disease transactions including Cholbam, a rare hepatology product for monogenic bile acid synthesis disorders. Awarded and sold PRV for $245mm to Sanofi
- Previously at Vertex Pharma, responsible for BD and strategy for rare diseases and hepatology
- Prior 15-year career in healthcare investment banking and capital markets with Barclays Capital, Lehman Brothers, Citi and Credit Suisse First Boston
- Holds an MBA and certificate in Health Sector Management from Duke University's Fuqua School of Business and a BA in Accounting from Gordon College

Julio Casoy, MD
Chief Medical Officer

- Dr. Casoy brings over 35 years of experience in both development and commercialization expertise to ArTara
- Dr. Casoy has built and led multidisciplinary teams for small molecules and biologics in therapeutic areas including neurology, psychiatry, women's health, and rheumatology
- He has been involved in several global, integrated drug development programs resulting in the approvals of more than twenty products
- Dr. Casoy has specific rare diseases experience, where he played a pivotal role in the research and development of several treatments for illnesses including Gaucher Disease, ALS and Duchenne Muscular Dystrophy
- Dr. Casoy has previously held senior leadership positions in Clinical Development at Wyeth, Shire, Sepracor/Sunovion, and Alkermes

Jackie Zummo, PhD, MPH, MBA
VP, Head of R&D Operations

- A 15-year career leading operations, medical affairs, and opinion leader relations at Wyeth/Pfizer, Sepracor/Sunovion, Alkermes and Vyera
- Led development of filings and interaction with regulatory bodies for several marketed products
- 10+ years leading Medical Affairs strategy, including HEOR data generation, for pipeline and commercial products
- 15 years communicating clinical and economic benefit to healthcare providers and payers

EXPERIENCED LEADERSHIP – THE ARTARA BOARD OF DIRECTORS

Scott Braunstein, MD
Chairman

- Dr. Braunstein is CEO of Marinus Pharmaceuticals and an Operating Partner at Aisling Capital
- Dr. Braunstein was previously COO at Pacira Pharmaceuticals
- Prior to Pacira, Dr. Braunstein spent 14 years as a Healthcare Analyst and Portfolio Manager at J.P. Morgan Asset Mgmt. and Everpoint Asset Mgmt.
- Dr. Braunstein serves as a Director of Esperion Therapeutics, Trevena, Inc., Marinus Pharmaceuticals, Inc., Ziopharm Oncology, Inc., and the Cornell Alumni Association for the College of Agriculture and Life Sciences
- Dr. Braunstein received his MD from the Albert Einstein College of Medicine and completed his residency in internal medicine at Cornell University-New York Hospital. He received his BS from Cornell University

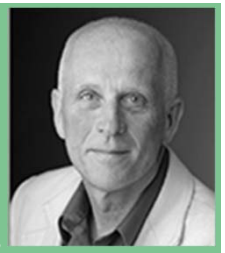
Luke Beshar, MBA
Director

- Luke Beshar was the CFO of NPS Pharmaceuticals until February 2015 when the company was sold to Shire plc
- At various points at NPS, Mr. Beshar was responsible for financial mgmt., investor relations, information technology, technical operations, supply chain mgmt., corporate development, alliance mgmt., project mgmt., contracts & outsourcing
- Prior to NPS, he served as Executive Vice President and CFO of Cambrex Corporation, a global life sciences company
- Mr. Beshar began his career with Arthur Andersen & Co. and is a CPA
- He obtained his BS in Accounting and Finance from Michigan State University and is a graduate of The Executive Program at the Darden Graduate School of Business at the University of Virginia
- Mr Beshar is also a Director of REGENXBIO and Trillium Therapeutics

Michael Solomon, PhD
Director

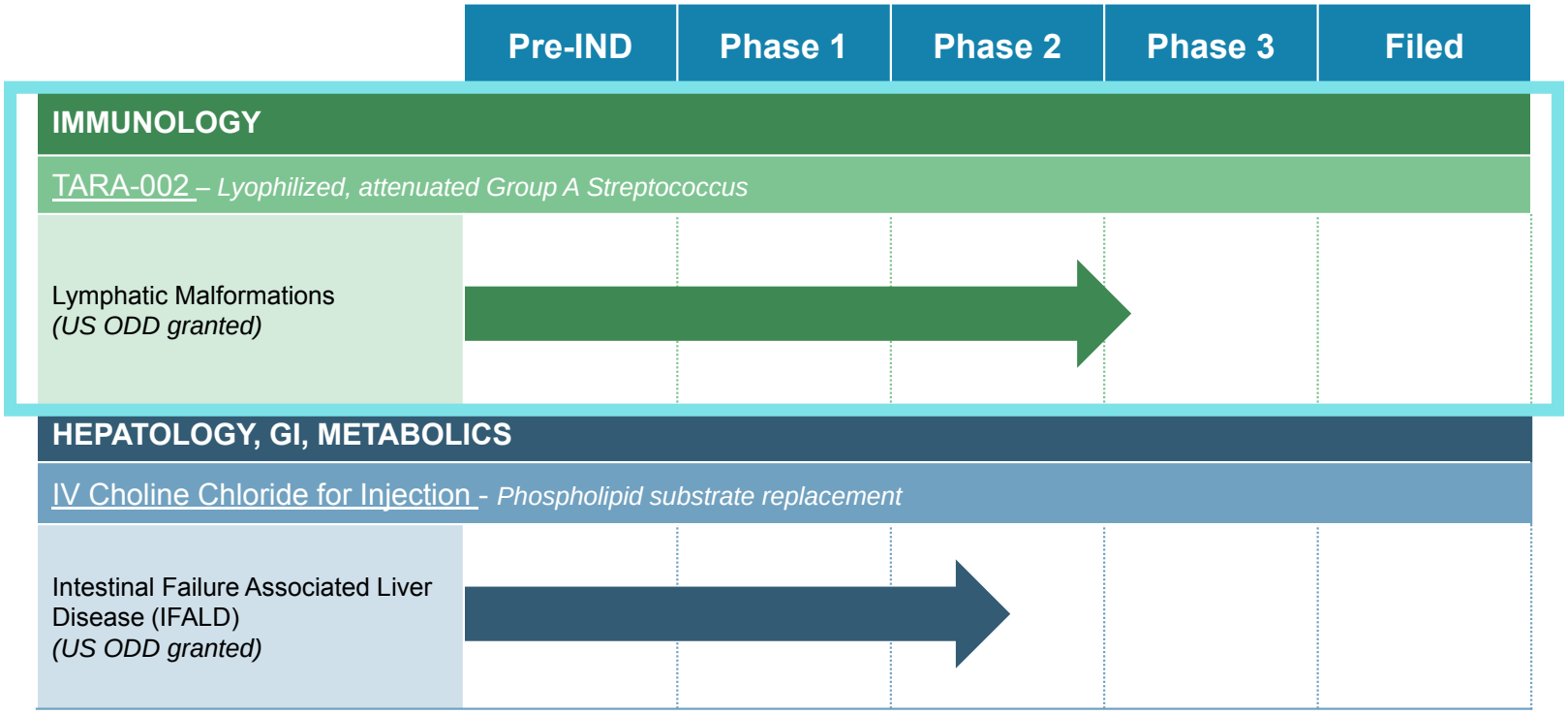
- Dr. Solomon is the CEO of Ribometrix, a platform company discovering small molecule drugs targeting functional 3D RNA structures
- Prior to Ribometrix, he held several leadership positions at companies founded by Third Rock Ventures where he was an Entrepreneur-in-Residence. These included COO at Decibel Therapeutics, COO at Ember Therapeutics, and Chief Business Officer at Link Medicine
- Dr. Solomon has held numerous senior scientific roles at growth biotech companies. He was founder and VP of Discovery at Epizyme Therapeutics and VP of Discovery at Hypnion, Inc. He started his career at Millennium Pharmaceuticals, where he was project leader for multiple programs
- He received his BS in Chemistry from the University of Massachusetts at Amherst. He earned his PhD. in Organic Chemistry at the University of Wisconsin and completed postdoctoral work in Synthetic Organic Chemistry at Scripps

Roger Garceau, MD
Director

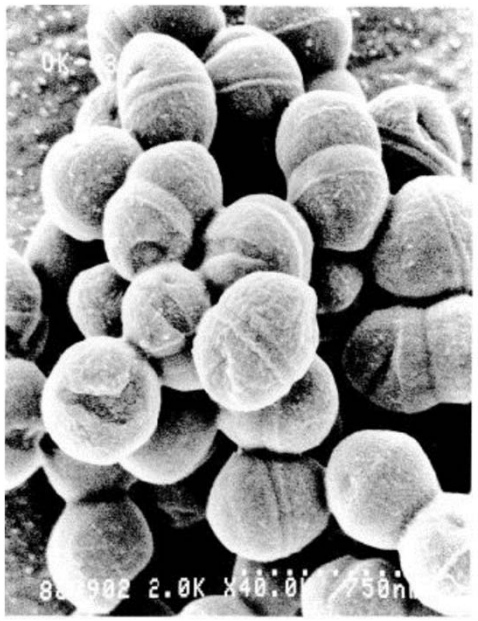


- Dr. Garceau has more than 30 years of global pharma experience in drugs and biologics for orphan and non-orphan indications
- Dr. Garceau served as Chief Medical Officer of NPS Pharmaceuticalsx` from 2008 to 2015, when NPS was acquired by Shire plc
- At NPS he led two orphan products through filing, Advisory Committees and registrations. Previously, he served in several leadership positions with NPS, Sanofi and Pharmacia Corporation
- Dr. Garceau has been a Director of Enterome SA since December 2016 and Entera Bio since March 2016
- Dr. Garceau is a board-certified pediatrician and is a Fellow of the American Academy of Pediatrics. He holds a BS in Biology from Fairfield University and an MD from the University of Massachusetts Medical School

PIPELINE - A GROWING RARE DISEASES PORTFOLIO



TARA-002 – STANDARD OF CARE IN JAPAN FOR LYMPHATIC MALFORMATIONS



- TARA-002 is derived from an originator therapy OK-432, also known as Picibanil, an attenuated strain of *Streptococcus pyogenes*
- Originally invented and commercialized in Japan, OK-432 is the standard of care for Lymphatic Malformations (LMs) and has been used as adjunctive therapy in several oncology indications in Japan and Taiwan for over 40 years(1)
- We have begun building modern manufacturing for TARA-002 and intend to demonstrate comparability of TARA-002 to OK-432 to support our regulatory efforts
- OK-432 was sporadically available in the US through the University of Iowa via a now-closed Expanded Access Program
- The University of Iowa led OK-432 Collaborative Study Group generated data from more than 600 US patients, including a randomized study of 117 patients. The study demonstrated strong results in resolving LMs that were confirmed appropriate for treatment via imaging(2)
- We have licensed all data for this study from the University of Iowa and intend to use it as a key component of our regulatory strategy

(1) Poldervaart M, et al. J Craniofac Surg. 2009;20:1159-1162.
(2) Smith M, et al. Laryngoscope. 2009;119:107-115.

OVERVIEW – LYMPHATIC MALFORMATIONS (LMs)

We are initially pursuing development of TARA-002 in Lymphatic Malformations

Lymphatic malformations are rare, non-malignant, lesions consisting of dilated, lymphatic fluid-filled sacs caused by abnormal development of the lymphatic endothelial system[(1)]

Development is congenital and usually observed *in utero* during the second trimester. They typically present as antero-lateral cervical masses

Standard of care outside Japan is surgical excision with high complication (33%) and recurrence (55%) rates[(2)]

Epidemiology: ~1 in 4000 live births in the United States[(3)]

Population is >90% pediatric: Majority of LMs present at birth (65-75%) or by age 3 (80-90%) during active lymphatic growth period[(4)]

(1) Brouillard P, et al. J Clin Invest. 2014;124:898-904.
(2) Ha J, et al. Curr Ped Rev. 2014;10:238-248.
(3) Boon, et al. Fitzpatrick's Derm in Gen Med. 2008:1651.
(4) Padia, R, et al. Laryngoscope investigative otolaryngology. 2019;4:170-173.

CLINICAL EXPERIENCE – RANDOMIZED CONTROLLED STUDY

Randomized, Controlled Study (N=117)[1]	
Age	6 mos – 18 yrs
Inclusion Criteria	LMs of the head and/or neck confirmed by MRI or CT ▪ Radiographically confirmed macrocystic LM or mixed macrocystic-microcystic LM with >50% macrocysts At least 6 mos since prior surgery for lymphangioma
Exclusion Criteria	Penicillin allergy, pregnancy and/or nursing, personal or family history of rheumatic heart disease, post-streptococcal glomerulonephritis, PANDA, history of significant cardiac, pulmonary, hepatic, renal, or hematologic disease
Treatment Groups	Immediate Treatment Group (ITG): Received OK-432 shortly after enrollment Delayed Treatment Group (DTG): Observed for 6 mos for spontaneous regression, then treated with OK-432 Open Label Group (OLG): nonrandomized, included infants <6 mos, adults >18 yrs, patients with LMs in sites other than the head, and patients treated on an emergent basis
Randomization	2:1 Randomization (per blocks of 6 enrollees) 2/3 in ITG and 1/3 in DTG (control group)
Duration of Treatment	1-4 injections 8 weeks apart
Dose	Max of 0.2mg/session (i.e. 2 Klinische Einheit)

Primary Endpoint: Response to treatment in the ITG compared to the spontaneous resolution rate observed in the DTG, 6 months after enrollment

Definition of Response

Response to therapy was measured radiographically (MRI or CT) by quantitating change in lesion size and graded as:

- Complete (90%–100%),
- Substantial (60%–89%),
- Intermediate (20%–59%),
- None (<20%)

Secondary Endpoints:

1) The proportion of ITG patients versus DTG patients who demonstrated a complete response (90%–100%) six months following enrollment

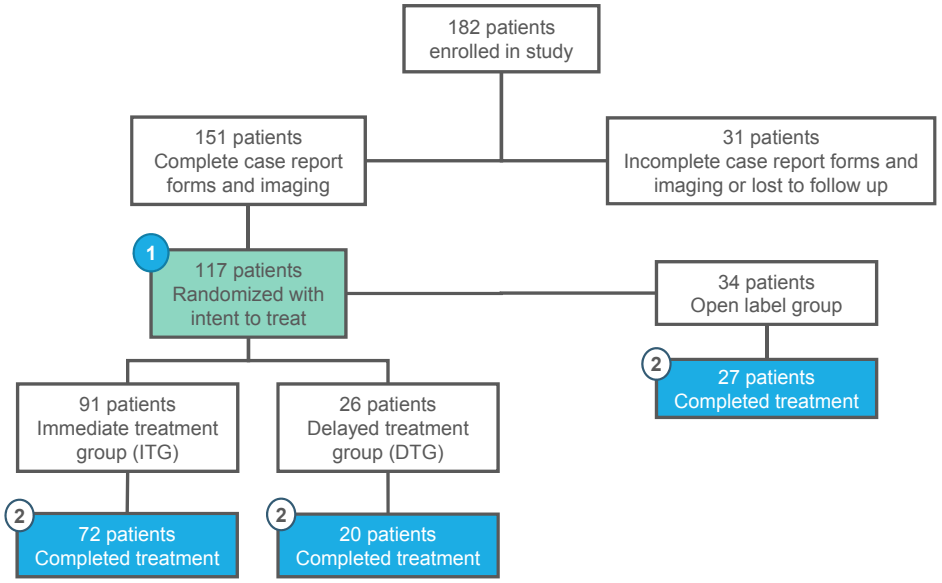
2) The proportion of randomized patients who demonstrated at least a substantial response (60%–100%) greater than 6 months following the last injection (i.e. persistence of response)

3) The proportion of patients in the OLG who demonstrated at least a substantial response (60%–100%) 6 months following enrollment and six months following the last injection (i.e. persistence of response).

(1) Smith M, et al. Laryngoscope. 2009;119:107-115.

CLINICAL EXPERIENCE – PATIENT DISPOSITION

Study Design & Highlights(1)



1 **Intent to Treat** (N=117): Randomized, completed visits to first 6 months

2 **Completers** (N=119): Completed all protocol visits, received up to 4 injections and evaluated 14 days after last injection, includes non-randomized Open Label Group

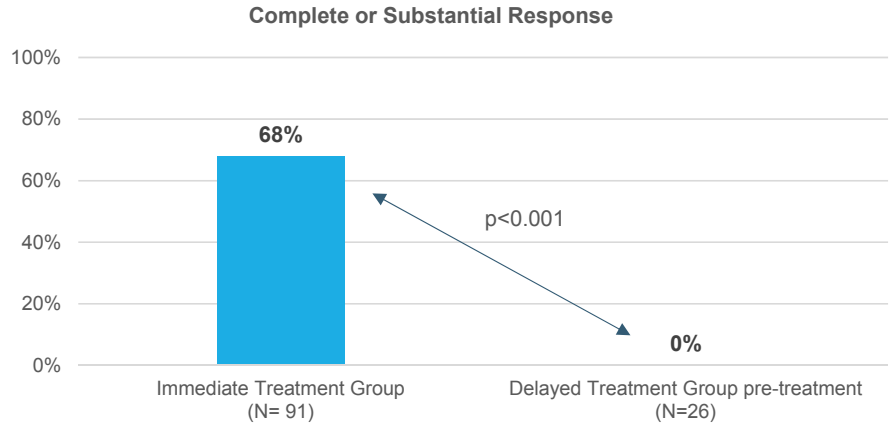
Patient Demographics

Group	Patients Enrolled (n=182)	Patients Randomized Completing Treatment (n=92)	Open-label Group Completing Treatment (n=27)
Sex (F:M)	92 : 90	42 : 50	15 : 12
Age Range (years)	0-73.1	0.5-15.5	0-73.1
Mean/median age (years)	5.8/1.7	3.5/2.1	13.4/1.1
Race Demographics			
Caucasian	133	74	20
African-American	15	8	2
Asian-Pacific Islander	14	4	4
Hispanic	10	6	1
Unknown	10		

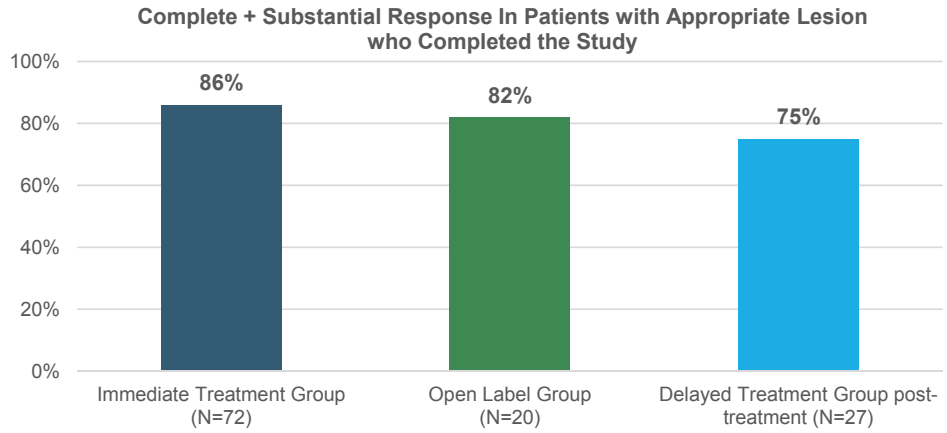
(1) Smith M, et al. Laryngoscope. 2009;119:107-115.

CLINICAL EXPERIENCE – COMPELLING EFFICACY IN LARGE, 8-YEAR STUDY

INTENT-TO-TREAT: Observations six months after enrollment[1]



COMPLETERS: Clinical Success‡ of OK-432 in Lymphatic Malformations[1]



68% Clinical Success in immediate treatment group 6 months after enrollment

- None of these patients required surgery
- During this same period, **NO** patients in the delayed treatment group experienced spontaneous regression of a LM (p<0.001)
- Treatment: 1-4 injections at 8-week intervals max of 0.2mg/session (2 KE)

Compelling results across cohorts; 27 US Sites, 1998-2004

n=119, 72 ITG, 20 DTG, 27 OL (outside inclusion criteria)

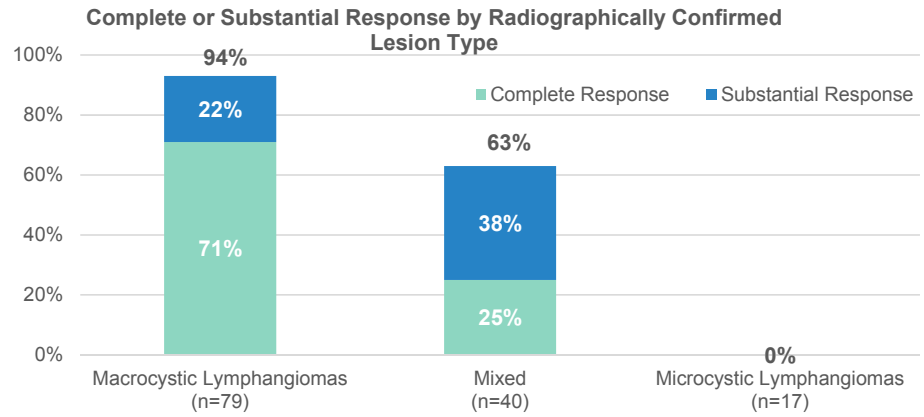
- Clinical Success:
  ITG 62/72 (86%), DTG 15/20 (75%), OC 22/27 (82%), All combined 99/119(86%)
- Duration of response: follow up 1.1 to 8.0 yrs, median 2.9 yrs, with 4% recurrence rate same site and 5% new lesion rate in different sites
  - Median duration of response not reached

(1) Smith M, et al. Laryngoscope. 2009;119:107-115. ‡Clinical Success was defined as complete or substantial response

CLINICAL EXPERIENCE – COMPELLING EFFICACY IN LARGE, 8-YEAR STUDY

Significant benefit in appropriate lesion types

Clinical Success‡ of OK-432 in Lymphatic Malformations(1)



94% clinical success in patients with macrocystic lesion types

136 patients provided conclusive data

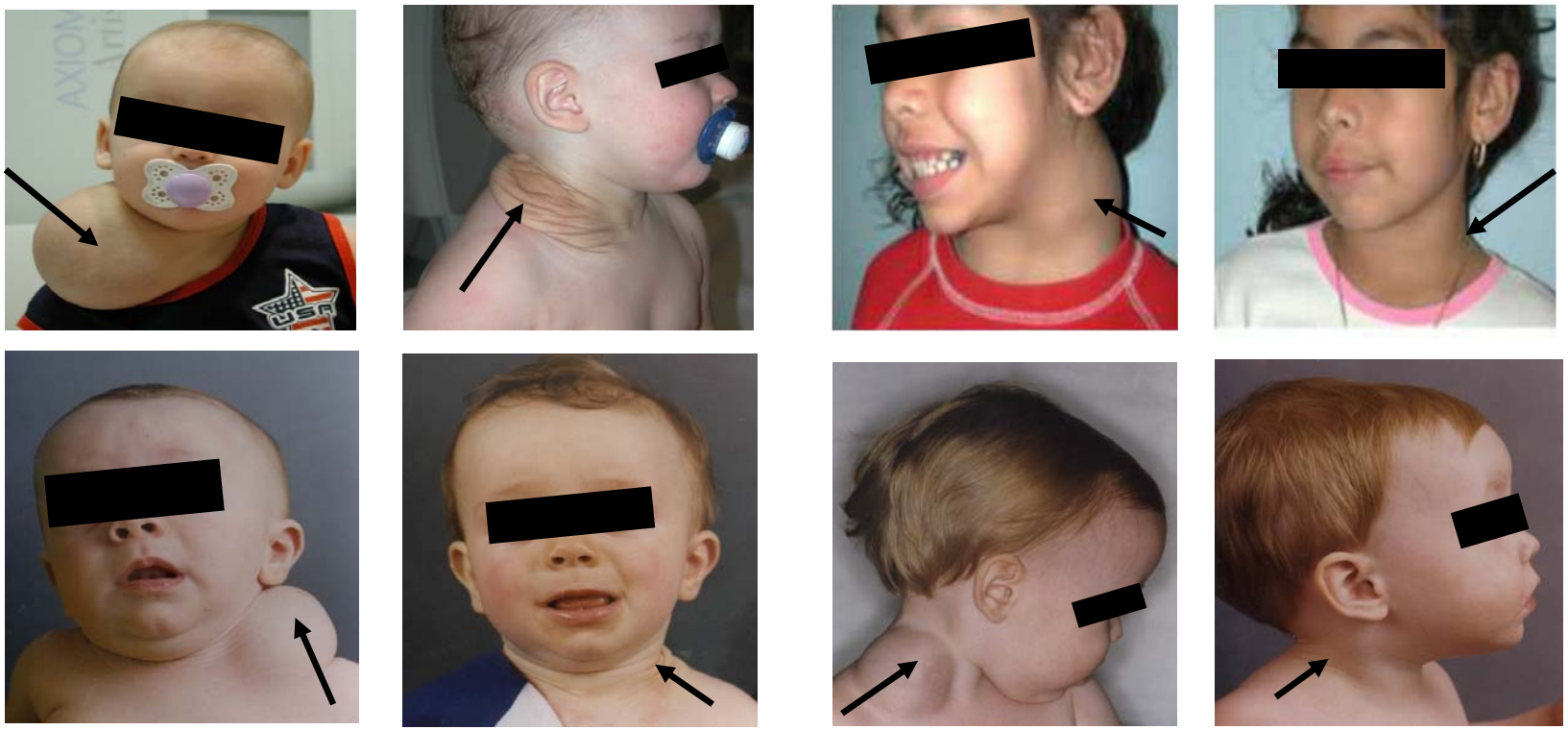
- Patients with radiographically confirmed appropriate lesions had the greatest chance for clinical success
- In those patients with mixed lesions, clinical success was still achieved

(1) Smith M, et al. Laryngoscope. 2009;119:107-115

‡ Clinical Success was defined as complete or substantial response

OK-432 IN LMs – OUR ACADEMIC COLLABORATOR'S RESULTS

Effective, reliable treatment for LMs



(1) Smith M, et al. Laryngoscope. 2009;119:107-115.

CLINICAL EXPERIENCE – COMPELLING SAFETY WITH UP TO 8-YEAR FOLLOW-UP

Long-term safety data in 99 patients

Safety Profile

- Most common AEs with treatment were local injection site reactions, fever, fatigue, decreased appetite, with resolution within a few days
- SAEs **related** to OK-432: re-hospitalization for infection (n=3) and severe edema (n=3), airway obstruction necessitating tracheostomy tube placement (n=4), and submental intra-cystic hemorrhage necessitating surgical excision (n=1)
- Minor AEs **related** to OK-432: temporary brachial plexus compression (n=1), myalgia, infections treated with oral antibiotics, intra-cystic hemorrhage, and dehydration
- Two SAEs **not related** to OK-432: death due to tracheotomy tube obstruction and vision loss following proptosis

(1) Smith M, et al. Laryngoscope. 2009;119:107-115.

IOWA EXPERIENCE – CONCLUSION

Efficacy and Response:

- 94% of patients with macrocystic LMs and 63% of patients with mixed LMs had clinical benefit
- No patients in the delayed treatment group experienced spontaneous resolution prior to treatment with OK-432
- 75% of patients in the delayed treatment group, with appropriate lesion type, received a clinical benefit after treatment with OK-432

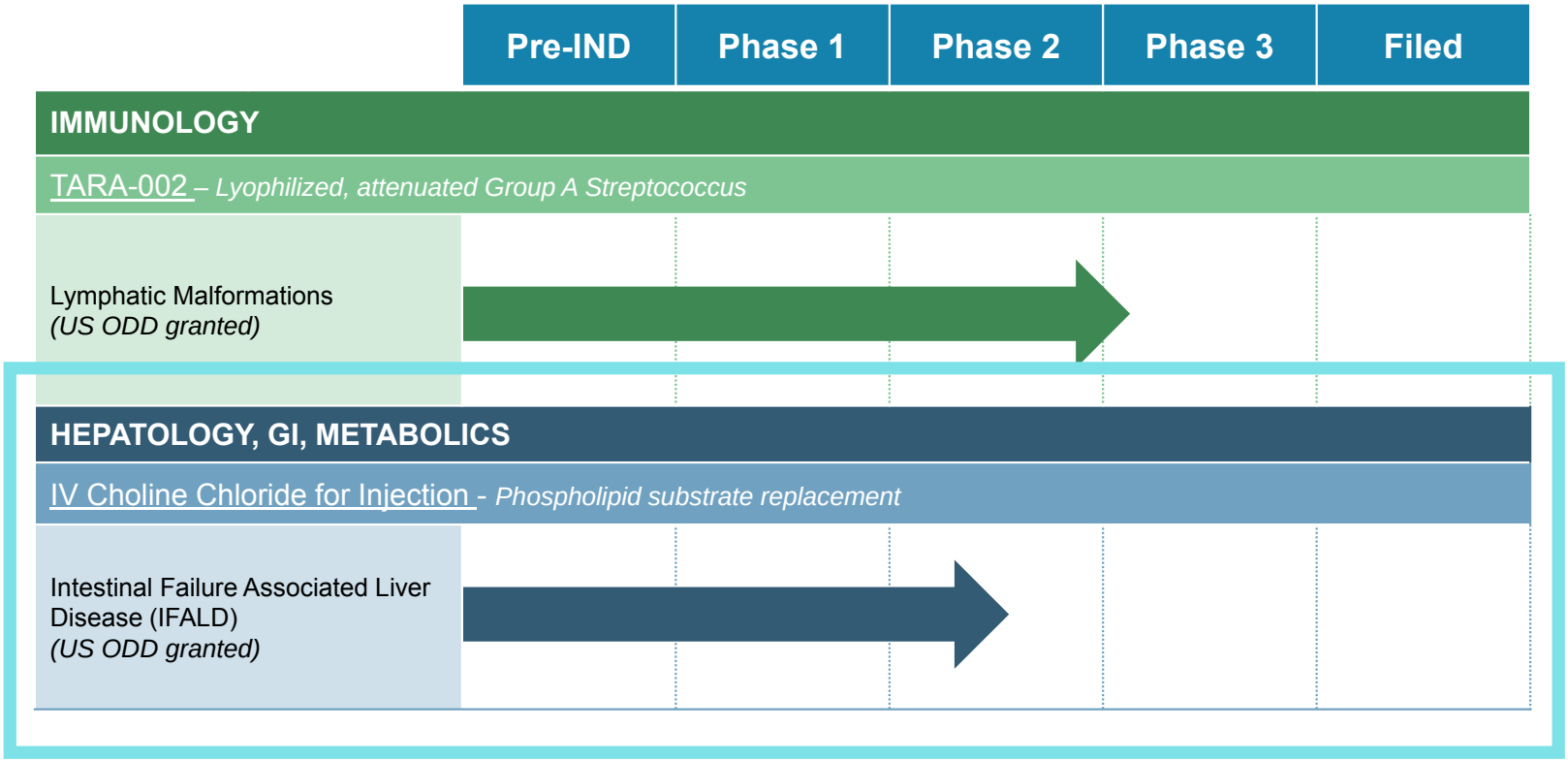
Duration of Response:

- The response to OK-432 immunotherapy was durable in 91% of patients who demonstrated a complete or substantial response to therapy over a median follow-up period of 2.9 years (range 1.1–8.0 years)

Safety of OK-432 immunotherapy:

- No serious hematologic, renal, hepatic, or cardiac adverse side effects were noted upon analysis of pre-treatment, concurrent, and post treatment

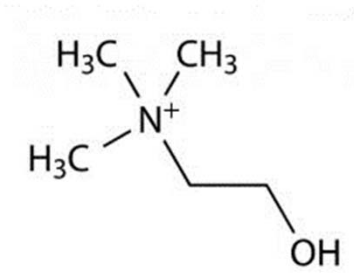
PIPELINE - A GROWING RARE DISEASES PORTFOLIO



CHOLINE – A KEY FACTOR IN IFALD

Choline plays a critical role in several metabolic processes but is not included in any Parenteral Nutrition (PN) mix

- First recognized as an essential nutrient in the early 1990's. Ubiquitous in the normal diet in eggs, meat, nuts, and vegetables[1]
- Methyl donor in many key metabolic reactions, similar to B-vitamins and folate[2]
- Vital for cell structure membranes (phospholipids), triglyceride transport via VLDL synthesis, cholesterol transport in bile, intracellular messaging, brain development and function (acetylcholine)[3,4]
- The only way to reliably replace choline stores is through exogenous consumption – salvage or secondary pathways are insufficient and subject to mutations[5]
- Choline is not included in PN products in sufficient amounts; recognized by ASPEN in 2012 as needed but unavailable as a commercial PN product[6]



(1) Buchman A, et al. Gastroent. 2009;137:S119-S12.
(2) Stegnik et al. Science. 1972;178:514-516.
(3) Chawla R, et al. Am J Clin Nutr. 1986 42:577-584.
(4) Zeisel S, et al. Neurology. 1980 30:1226-1229.
(5) Fischer L, et al. Am J Clin Nutr. 2007; 85;1275-1285.
(6) Vanek V, et al. Nutr Clin Pract. 2012;27:440-491.

FDA-ACCEPTED DEFINITION – INTESTINAL FAILURE ASSOCIATED LIVER DISEASE (IFALD)[1]

A Contemporary Definition of a Long-Observed Disease

1. **Requires long-term PN:** has chronic (6 months or greater) intestinal failure; and
2. **Cholestasis:** elevated alkaline phosphatase and/or elevated bilirubin, or histology
3. **Steatosis:** imaging techniques or biopsy
4. **May also have**: other signs of liver injury (elevated LFTs / fibrosis / cirrhosis / end stage liver disease [ESLD])

1) Per ArTara FDA interaction in end-of-phase-2 meeting 11/21/2018 with confirmatory written minutes dated 12/3/2018

CHOLINE SUBSTRATE REPLACEMENT IFALD STUDIES – SIGNIFICANT CLINICAL HISTORY

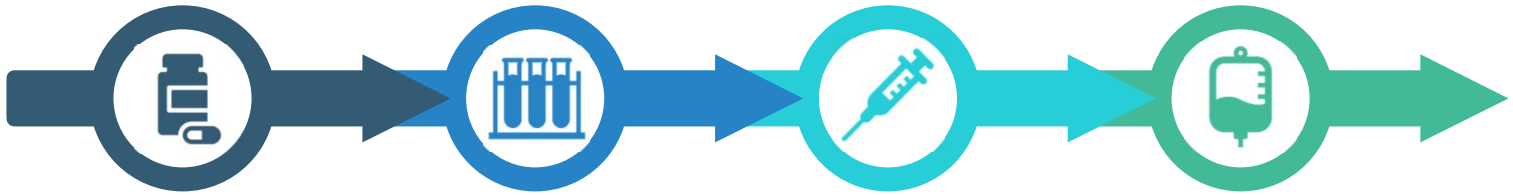
A significant body of supportive evidence across 4 studies

1992 - Oral Lecithin Study[1]
n=15 PN patients

Lecithin does not achieve physiologic levels, reduced steatosis, moderate ALP improvement

1994 - IV PK Study[2]
n=4 PN patients

1st continuous exposure to IV choline, established safety and 2g dose



1995 - IV Pilot Study[3]
n=4 PN patients

IV Choline replacement reversed steatosis, improved other measures of hepatobiliary injury

2001 - IV Phase 2 RCT[4]
n=15 PN patients

2g dose confirmed, reversal of steatosis, improvement in cholestasis (reduction of Alkaline Phosphatase)

1) Buchman A, et al. Gastroenterology. 1992;102:1363-1370.
2) Buchman A, et al. Clin Pharmacol Ther. 1994;55:277-283.
3) Buchman A, et al. Hepatol. 1995;22:1399-1403.
4) Buchman A, et al. JPEN. 2001;5:260-268.

MULTI-CENTER PHASE 2a STUDY – PROOF OF CONCEPT

Randomized, Controlled Study Design & Objective

IV CHOLINE REPLACEMENT PROOF OF CONCEPT STUDY[1]	
Study Design	Randomized Double-blind Ph2 Trial
Subjects	15 (9 per protocol)
Age	>16 years old
PN Requirement	Greater than 80% of all nutrient requirements supplied by PN
Randomization	1:1 Usual PN or PN + 2g IV choline/Day
Duration of Treatment	24 Weeks
Visits	Weeks 2,4,6,12,16, 20, 24
Follow up	Week 34
Dose	2g Choline Chloride QD in PN solution

- The IV Choline Chloride replacement proof-of-concept, randomized study did not have pre-specified endpoints
- The primary objective of the original study was to determine if IV Choline Chloride substrate replacement would reverse hepatic steatosis and improve liver function in patients receiving long-term parenteral nutrition (PN)

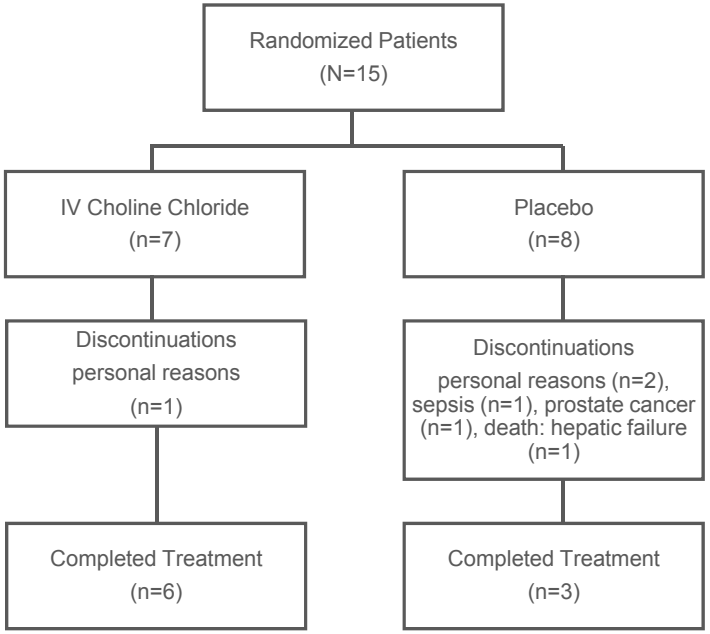
1) Buchman A, et al. JPEN. 2001;5:260-268.

MULTI-CENTER PHASE 2a STUDY – PATIENT DISPOSITION

Patient Demographics[1]

Safety Population *Mean, (SD)*	Choline Chloride group (n=7)	Placebo group (n=8)
Age, (years)	33.6 (9.8)	38.8 (15.9)
Gender (M/F)	4/3	6/2
Body weight (kg)	58.1 (6.4)	68.23 (17.3)
Ideal body weight (kg)	63.6 (2.9)	65.51 (14.0)
Duration of TPN (years)	12.3 (6.1)	11.3 (7.3)
Underlying disease		
Short bowel syndrome	1	2
Crohn's Disease	4	3
Mesenteric Vein Thrombosis	0	2
Pseudo-obstruction	2	1
Other medical history	3	6
Plasma Free Choline Level (nmol/mL)	3.7 (1.1)	5.3 (1.7)
mITT Population[1]	Choline Chloride group (n=7)	Placebo group (n=7)
CT-Converted MRI-PDFF (%)	14.98 (3.7)	21.64 (7.5)
Alkaline Phosphatase (IU/L)	239.3 (118.9)	148.1 (100.2)

Study Design & Highlights



1) Buchman A, et al. JPEN. 2001;5:260-268. [1]A placebo subject was excluded from all analyses due to likely IV contrast-induced imaging abnormalities, confirmed by independent radiologist.

PHASE 2a REANALYSIS – UPDATED METHODS AND FORMATS

ArTara's strategy: Utilize raw CRFs to replicate a modern study with statistical plan and modern analyses

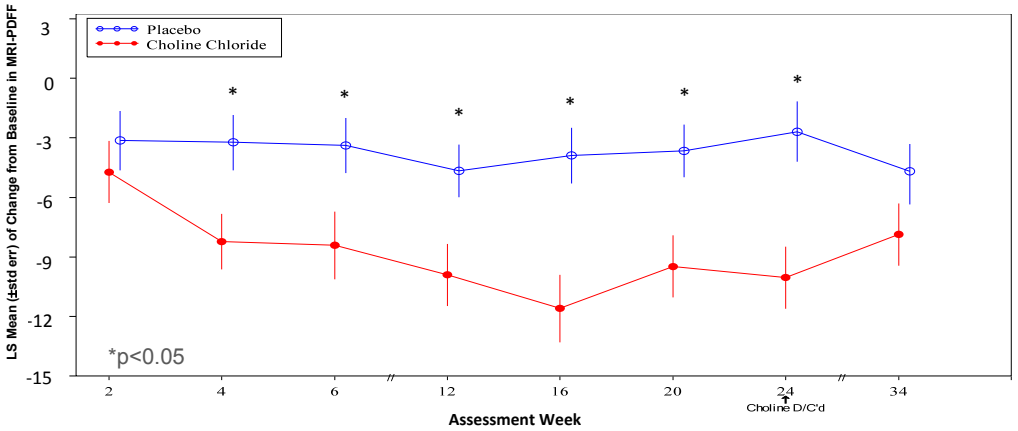
Format, Variable, or Method	Original	New	Rationale
Database	Patient and research charts (paper), miscellaneous tables and spreadsheets	Electronic Common Technical Document format	Required for FDA and EMA submissions and review
Confounding Patients	Included septic, hospitalized placebo patient with confounding imaging	Excluded via third party radiology confirmation	Patient would have been discontinued due to protocol violation
Steatosis (liver fat quantification)	Unenhanced CT scan calibrated to a standardized quantity (Hounsfield Units)	MRI-Proton Density Fat Fraction	New imaging gold standard, large validation database, improved sensitivity, reliability across machines
Cholestasis	Heterogeneity of ALP baselines	Subgroup with abnormal ALP (>ULN; >1.5x ULN)	Contemporary definition of IFALD (steatosis + cholestasis)
Statistical Model	Intent-to-treat, observed cases, Wilcoxon Rank-Sum Test	MMRM with baseline as a covariate, and treatment group, visit, and their interaction as fixed effects	Current standard for clinical trials analysis

ALP=alkaline phosphatase; ULN=upper limit of normal; MMRM=mixed model for repeated measures

PHASE 2 REANALYSES – IMPROVEMENT IN STEATOSIS

Clinically meaningful improvement in steatosis

STEATOSIS: Conversion[ł] to MRI-PDFF[(1)ł]



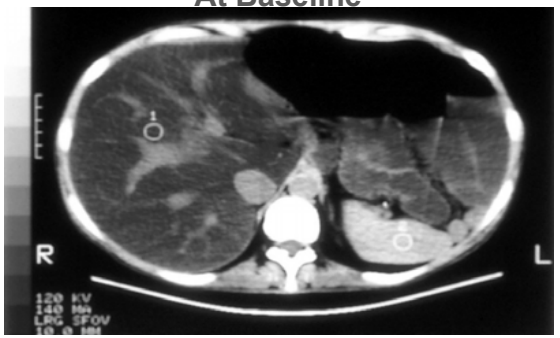
CT converted to MRI-PDFF:
[ł]MRI-PDFF (%) = -0.572 x Liver CT(HU) + 37.264[(2)]

- Conversion to the imaging gold standard of MRI-PDFF maintained effect observed in original trial report
- A placebo subject was excluded from all analyses due to likely IV contrast-induced imaging abnormalities, confirmed by independent radiologist
- Relative change of MRI-PDFF; drug-placebo differences from Weeks 4-24 were large (range 31%-54%) and clinically meaningful **per 30% agreed definition with FDA**

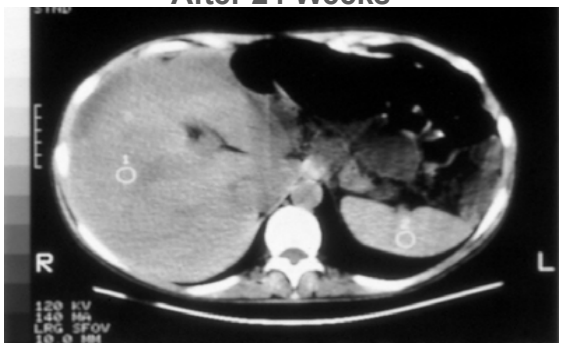
[ł]Mixed model for repeated measurement (MMRM) method used for imputation

Clinically Meaningful Improvement in Steatosis

At Baseline



After 24 Weeks

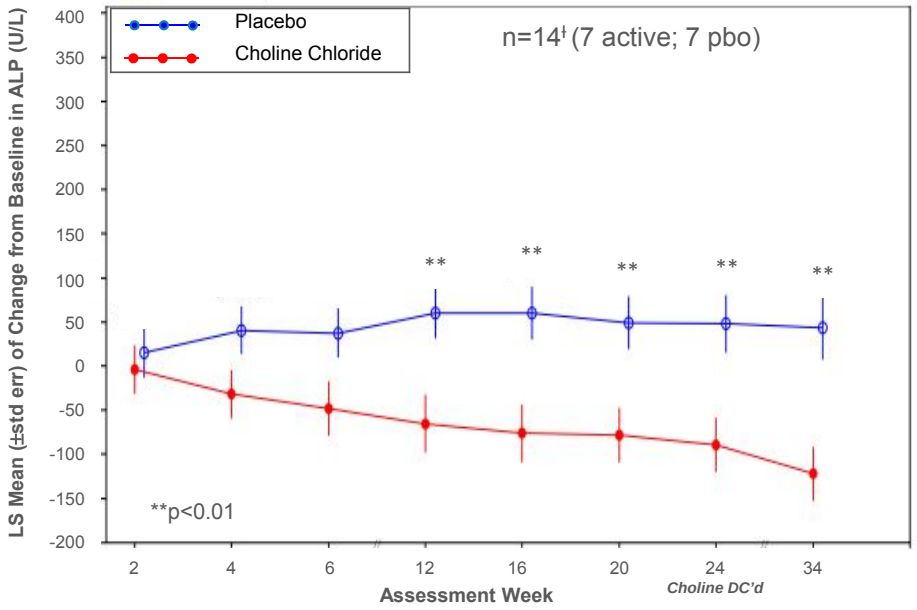


(1) ArTara Therapeutics. Data on file. 2018.
(2) Kramer H, et al. AJR Am J Roentgenol. 2017;208:92–100.

PHASE 2 DATA – IMPROVEMENT IN CHOLESTASIS

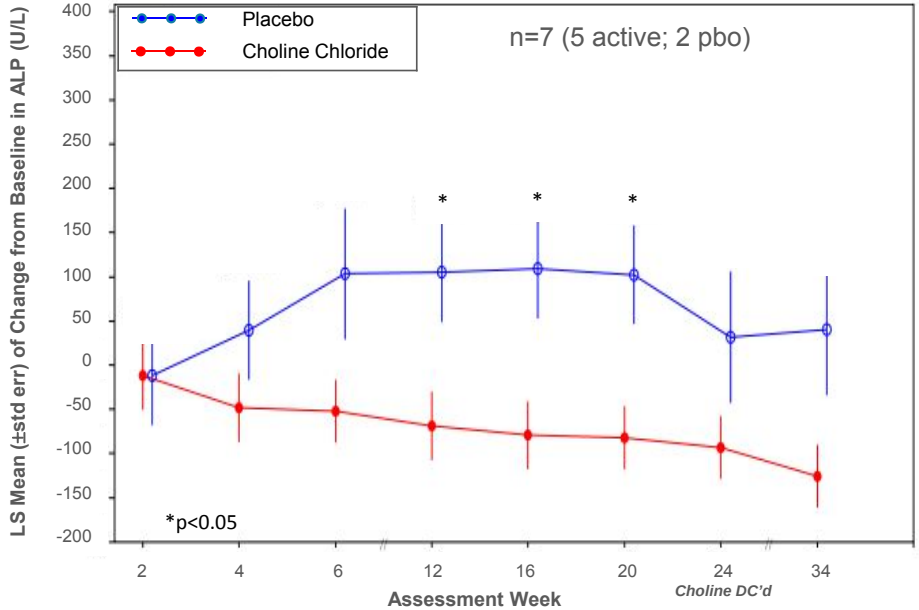
Sustained improvement throughout study in IFALD-defining pathology

CHOLESTASIS IMPROVEMENT: ALL PATIENTS‡



Placebo, n	6	7	6	6	5	5	4	3
Choline, n	6	6	5	4	4	5	5	5

CHOLESTASIS IMPROVEMENT: 1.5x ULN ITT POPULATION‡



Placebo, n	2	2	1	2	2	2	1	1
Choline, n	5	4	4	5	4	4	5	5

- Pronounced treatment effect as measured by reduction in alkaline phosphatase (ALP) levels
- Subgroup analyses of ALP >1.5x ULN demonstrated clinically meaningful (20-30%) improvement **per agreed definition with FDA of 20%**

ǂA placebo subject was excluded from all analyses due to likely IV contrast-induced imaging abnormalities, confirmed by independent radiologist
‡Mixed model for repeated measurement (MMRM) method used for imputation

SAFETY – SUMMARY OF SAFETY EXPERIENCE

IV Choline Chloride had a good safety profile and was well tolerated

- A total of five serious adverse events (SAEs) were reported in four subjects
  - Choline Chloride group: hospitalization for dehydration and fever (n=1)
  - Placebo group: catheter sepsis (n=2), hepatic failure resulting in death (n=1), and peroneal pain due to recurrent desmoid tumor (n=1)

- None of the AEs were deemed related to study drug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