
MEZZION
Discovering • Developing • Delivering Hope

Mezzion Pharmaceuticals

Shaping the future of single ventricle heart disease (SVHD)

Erik Emerson, EVP Commercial Operations

World Orphan Drug Conference – Barcelona Spain
November 2018

MEZZION

Safe Harbor Statement

- This presentation includes certain forward-looking statements as defined in Section 27A of the Securities Act of 1933 as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. While these forward-looking statements represent our current judgment on what the future holds, they are subject to risks and uncertainties that could cause actual results to differ materially. You are cautioned not to place undue reliance on these forward-looking statements, which reflect our opinions only as of the date of this presentation. Please keep in mind that we are not obligating ourselves to revise or publicly release the results of any revision to these forward-looking statements in light of new information or future events.

MEZZION

Mezzion Pharmaceuticals Inc.
Shaping the future of SVHD

- Mezzion Pharma Co., Ltd. is publicly-traded on Korea's KOSDAQ.
- Founded in 2002, Mezzion focuses on the development and commercialization of udenafil for the treatment of single ventricle heart disease in patients that have undergone Fontan palliative surgery.
- Mezzion Pharmaceuticals Inc., a US entity, established in 2018 with 2 operational offices in US.

MEZZION

Opportunity and Indication

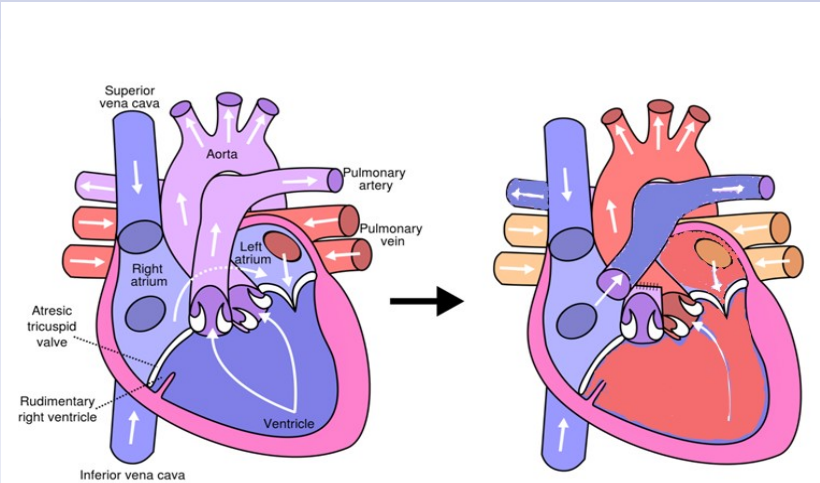
- Udenafil, a unique PDE-5 inhibitor, delivers a mechanism of action demonstrated to generate improved blood flow for patients with SVHD
- Single Ventricle Heart Disease (SVHD) is a congenital heart defect identified at birth and affects over 77,000 patients across the US
  - *There are currently no approved treatments for SVHD*
  - ~70% of patients are under the age of 18
- Mezzion, in partnership with the National Heart Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) and the Pediatric Heart Network (PHN) have completed enrollment in a 400 patient, phase 3 clinical trial (FUEL) measuring improvement of exercise capacity

Following the FUEL trial, Mezzion will seek FDA approval for use of udenafil to treat patients 12 and over with single ventricle physiology after Fontan surgery to improve aerobic capacity and exercise tolerance.

MEZZION

What is Fontan Procedure

- The Fontan Procedure (FP) is a surgical intervention performed in children born with functional single-ventricle hearts, a congenital heart defect, who are not candidates for a two-ventricle repair.
- FP consists of re-configuring the circulation to maximize the efficiency of a single ventricle
  - “Fontan circulation” is achieved when the single ventricle is able to pump blood returning from the lungs to the body
  - The blood returning from the body by passes the heart and travels to the lungs by direct blood vessel connections without the need of a right ventricle pumping chamber



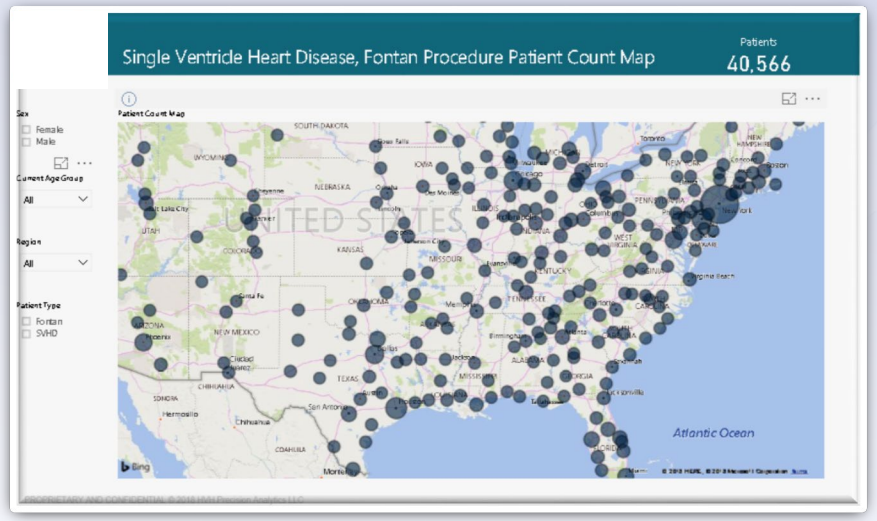
Hosein et al., 2007. Eur. J. Cardiothorac. Surg., 31, 344-353.; O no et al., 2006. Eur. J Cardiothorac. Surg., 30, 923-929.

- The goal of the FP is to separate the systemic and pulmonary circulations and to improve oxygen levels by redirecting venous blood directly to the lungs. In turn, this creates two separate circulations and thereby decreases the workload of the heart.

MEZZION

Epidemiology of SVHD

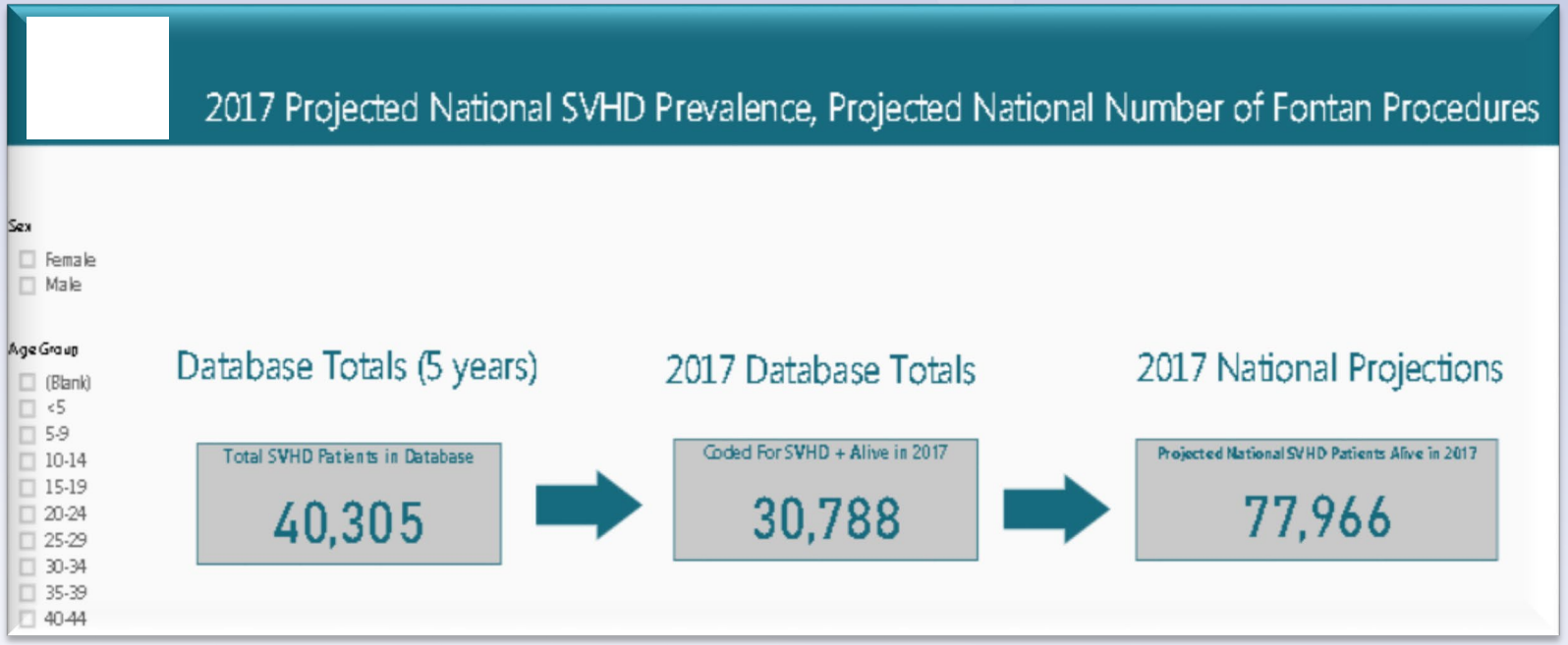
- Congenital defect in the heart identified by one operating ventricle
  - Consists of about 1% of the total congenital heart defects. ~5.3 of every 10,000 infants are born with the SVHD defect (~2,000 patients)
- Fontan operation: A series of operations (total of 3 operations) to recover the function of the heart as normal as possible in children with SVHD
  - The Fontan procedure is typically done from age 2~5
  - About 65% of patients with SVHD survive through Fontan operation
  - There are roughly 1,300 new Fontan patients every year



MEZZION

US prevalence of SVHD

Based on US ICD code analysis - ≥77,000 total patients



SVHD: High unmet medical need

- **Facts on SVHD Patients**
  - Limited ability to augment pulmonary blood flow due to a lack of a sub-pulmonary ventricle.
  - Aerobic exercise capability decreases significantly during their adolescence
  - The risk of hospitalization and cardiac death rise significantly in the second and especially in the third decade of life.
  - Non-cardiac complications such as protein losing enteropathy, plastic bronchitis and liver failure occur with increasing frequency beginning in the second decade of life.

- **No approved treatments are available at this point**
  - There are no FDA approved medications specifically indicated for the treatment of single ventricle heart disease or SVHD patients who have undergone Fontan palliation.

MEZZION

SVHD: Impacting Fontan patient outcomes

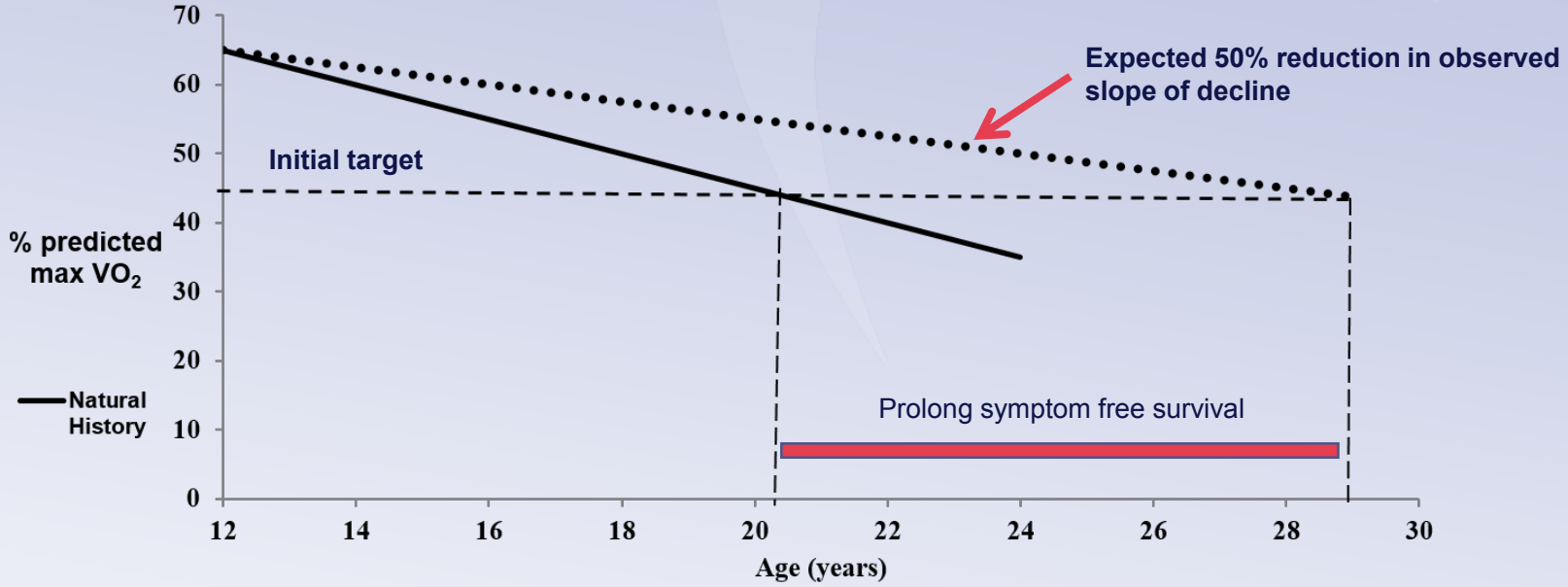


Figure. Projected decline in percent predicted max. VO_2 vs. age in years. Comparison of baseline projected rate of decline in percent predicted max. VO_2 (solid line) compared to a 50% reduction in the slope (dotted line). Note that there is an approximately 8 year difference between the two conditions for reaching 45% of predicted max. VO_2 (horizontal dotted line).

- *The projected rate of decline in aerobic capacity for the PHN Fontan Study Cohort.*
- *The risk of serious complications will rise considerably once past the age of twenty.*

MEZZION

Fontan Udenafil Exercise Longitudinal Assessment (FUEL) – Phase 3 Pivotal Study

- The FUEL trial is being run in conjunction with:
  - NHLBI (National Heart Lung and Blood Institute)
  - PHN (Pediatric Heart Network)*
- The FUEL trial is comprised of 30 sites, including US, Canada and South Korea

Pediatric Heart Network

MEZZION
Discovering • Developing • Delivering Hope

NIH National Heart, Lung, and Blood Institute

**PHN (Pediatric Heart Network): established in 2001 by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). It was created to help doctors and nurses design and carry out clinical research so that children with heart disease can receive high-quality, evidence-based care.*

MEZZION

FUEL – Phase 3 Pivotal Study, fully enrolled

- **Study Design (randomized, double-blind, placebo controlled)**
  - Total number of subjects : 400
  - Duration of Drug Administration : 6 months
  - Study Sites : 30 hospitals
  - Age : 12 to below 19 who have undergone Fontan surgery
  - Dosing : Udenafil (87.5mg) BID (twice a day for 6 months)
  - **Completed randomization in June 2018!!**
  - **Last Patient, Last Visit – December 2018!!**

- **Study Endpoints**
  1. Primary Outcome
     - Improvement in the aerobic capacity (Max VO_2*)
  2. Secondary Outcome
     1) Improvement in the Myocardial Performance Index (MPI)
     2) Change in log-transformed Reactive Hyperemia Index derived from the EndoPAT device.
     3) Change in serum BNP* level (Biomarker for heart failure)

** Max VO_2: Maximum Oxygen Consumption, BNP : Brain-type natriuretic peptide*

MEZZION

Additional FUEL Program Trials

- FUEL – OLE (Open-label)
  - Total number of subjects : 300
  - Duration of Drug Administration: 24 months (recently increased from 12 months)
  - Sites, Age and Dosing consistent with FUEL trial
    - Primary Outcome
      - Long term Safety
- Fontan-associated Liver Disease (FALD) Study
  - Study Design
    - Total number of subjects: 100 (from OLE Study)
    - Dosing : MZ101 BID
  - Primary Endpoint
    - Liver stiffness as measured by Shear Wave Ultrasound Elastography or Magnetic Resonance Ultrasound

MEZZION

Fontan-Associated Liver Disease (FALD)

- FALD is liver disease in a Fontan patient not resulting from any other pathophysiology.
- FALD is one of the most common late complications after Fontan palliation and present in all Fontan subjects.
- FALD results in progressive hepatic fibrosis leading to cirrhosis and liver failure.
- FALD is not well-understood but it is postulated that persistent elevated, non-phasic systemic venous pressure causes chronic hepatic venous hypertension and congestion.
- The progression of hepatic congestion and fibrosis correlates with liver stiffness and liver stiffness can be measured using noninvasive ultrasound and magnetic resonance ultrasonography.

MEZZION

Fontan-Associated Liver Disease (FALD) & Treatment with udenafil

- There are currently no approved therapies for the treatment of FALD
  - Mezzion is conducting a clinical study to assess the effect of daily treatment with udenafil on liver stiffness in FALD subjects over time.
- Increasing liver stiffness is a marker of worsening FALD
  - It is hypothesized that decreasing liver congestion may attenuate fibrotic progression and delay or prevent liver failure
- Udenafil, a long-acting phosphodiesterase type 5 inhibitor is expected to cause relaxation and decongestion of the pulmonary and systemic venous vasculature resulting in a decrease in liver stiffness over time.
  - A positive outcome on liver stiffness will likely increase the use of udenafil significantly by prescribing doctors.

MEZZION

The FALD Clinical Study

The FALD study is the first study designed to determine scope of hepatic stiffness in Fontan patients by non-invasive ultrasound and magnetic resonance imaging elastography and evaluate the efficacy of udenafil in reducing liver stiffness.

Study Sites:

- Conducted at 16 Pediatric Heart Network Centers throughout the US.

Subject Population:

- Approximately 100 Fontan subjects who are also participating in the current long-term open label safety study (the FUEL-OLE Study) in which udenafil is dosed daily for 12 months.

Aims:

- Define the range of liver stiffness in those who have had the surgical creation of a total cavopulmonary connection – Fontan subjects
- Determine the impact of udenafil treatment on liver stiffness in a large cross-section of adolescents who have undergone the Fontan surgical procedure.
- Determine the relationship between clinical outcomes and liver stiffness.
- Assess the association between biomarkers of both heart failure and liver fibrosis and liver stiffness

Efficacy Endpoint:

- Reduction in liver stiffness after 12 months of udenafil therapy as measured by ultrasound and magnetic resonance imaging elastography.

Timeline:

- Data expected in 2020.

MEZZION

Early Access Program (EAP)

- What is EAP?
  - EAPs offer ethical, compliant, and controlled mechanisms of access to investigational drugs outside of the clinical trial space and before NDA approval and commercial launch of the drug to patients with life-threatening diseases having no treatment options available.

- Benefits?
  - Compassionate use by making drug available during NDA pendency
  - Immediate market access of drug upon FDA approval
  - Development of positive relationships with key opinion leaders (KOL) during NDA pendency
  - Data captured from the implementation of EAP supports global commercialization strategies

- Mezzion is in the process of implementing an EAP for the Fontan patients with protocol provided to FDA

MEZZION

Why PDE-5 and why udenafil

- Udenafil is long-acting selective inhibitor of cyclic guanosine monophophase (cGMP)- specific phosposphodiesterese type 5.
- Udenafil has an excellent safety profile with less incidence and severity of the class side effects (headache and facial flushing) of other PDE5i's and less incidence of vision side effects and leg and back pain in the adult male population.
- Early studies in SVHD subjects indicate that udenafil is well tolerated in the adolescent population of males and females.
- Early studies with udenafil signal its potential for lowering pulmonary vascular resistance, an essential element to improving aerobic capacity which could translate into several additional years of symptom free survival

MEZZION

Exclusivity of udenafil

- U.S. exclusive marketing rights to be granted by the FDA upon approval of udenafil
  - Run concurrently with Mezzion's U.S. patents.
  - Exclusive marketing rights prevent submission or effective approval of ANDAs or 505(b)(2) applications:
    - 7 year orphan drug (ODE), 5 year NCE and 3 year data exclusivity in US (in parallel)
  - U.S. Patent No. 8,796,286 - Method of Use Patent for use of udenafil to reduce hepatic fibrosis - expires on October 27, 2029
  - Patents applied for globally covering (a) oral compositions of matter for udenafil and (b) methods of use of udenafil for treatment of SVHD (~ June 30, 2035 expiration)
  - USPTO Method of use patent issued November 2018, for treating adolescent Fontan patients with udenafil to improve exercise capacity or increase the likelihood of improving exercise capacity (~June 30, 2035 expiration)

**ED : Erectile Dysfuntion, BPH : Benign Prostate Hyperplasia*

MEZZION

Market Opportunity

- First FDA approved treatment for SVHD market of >77,000 patients of which a high mortality rate exists and >75% have fontan physiology
- Strong clinical rationale and safety history
- Significant opportunity to impact patient quality of life in a disease >70% pediatric
- Extensive Key Opinion Leader engagement and passion to improve patient outcomes
- Pricing potential consistent with pediatric rare diseases of similar patient size
- Reminiscent of early Pulmonary Arterial Hypertension market
- Orphan, NCE and Other exclusivity and strong IP position through ~2035

MEZZION

Ex-US opportunity

- Exclusivity
  - Evolving patent position
- Pricing
  - Consistent in key countries with US opportunity
- Regulatory
  - EMEA orphan designation granted
    - Population of more than 500 million (including UK) with the guaranteed market exclusivity of 12 years (10 years for the orphan status and +2 years for being a pediatric drug) when approved.
    - Market Approval is possible without additional clinical trials, which enables the market entry after the approval in US.
  - Discussions with Japanese PMDA initiated
    - In Japan, we are planning to file an application for the Orphan drug designation which will give us a market exclusivity of 10 years.

MEZZION

Key Milestones

1. 4th Quarter 2018
    1. Brand name filed with FDA and global trademark rights sought
    2. Last Patient, Last Visit in FUEL trial
    3. EAP program protocol approved
2. 1st Half 2019
    1. Top Line Data
    2. EAP Program Launch
    3. Brand name acceptance
    4. NDA Filing
3. 2nd Half 2019
    1. Approval and Launch

MEZZION

Thank you

Mezzion Pharma Co., ltd.