MEZZION®

Shaping the Future of the Fontan Community

Non-Confidential Deck

DEC, 2025

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Interim Analysis: 임상시험 중 중간 분석

FUEL-2 : Blind 상태에서 전체 환자에 대한 SD (Standard Deviation) 수치 분석 (protocol)

- 목적 : if SD가 예상보다 높으면 (>4ml/kg/min), 임상시험 참여자 수를 늘릴 수 있음 (안전장치)

  → 회사의 의무사항이 아닌 선택사항

- 효과 :

  - 임상시험 (특히, CPET)이 잘 관리되어 진행되고 있는지 파악할 수 있음
  - effect size에 대한 예측치 제공

Interim Analysis

FUEL-1 study Results

	Udenafil	Placebo
LOCF	n=200	n=200
Difference, Week 26-BL		
Mean	-0.23	-0.89
SD	4.056	3.672
Median	-0.17 (-2.55, 1.70)	-0.85 (-3.13, 1.17)
No imputation	n=189	n=190
Difference, Week 26-BL		
Mean	-0.24	-0.94
SD	4.172	3.762
Median	-0.34 (-2.76, 1.92)	-1.05 (-3.23, 1.20)
Excluding Super Fontan	n=150	n=152
Difference, Week 26-BL		
Mean	0.23	-0.89
SD	4.17	3.74
>45% to <80%	n=141	n=140
Difference, Week 26-BL		
Mean	0.17	-1.09
SD	4.05	3.74

Interim Analysis

FUEL-2 study

Peak VO_2 & SD (Standard Deviation)

Interim Analysis	1st	2nd	3rd	4th	5th	6th
Difference: 26W-Base(ml/kg/min)						
Mean	-0.215	-0.118	-0.059	-0.054	-0.071	-0.197
Median	-0.3	-0.3	-0.3	-0.15	-0.2	-0.350
SD	2.481	2.509	2.701	2.594	2.538	2.490
Min	-10.1	-10.1	-10.1	-10.1	-10.1	-10.1
Max	5.9	7.3	7.7	7.7	7.7	7.7

Estimated Effect Size

Study/Assumption	Total mean change	Treatment mean change	SD Treatment change	Placebo mean change	Effect size
FUEL-1	-0.197	0.50	2.490	-0.89	1.39

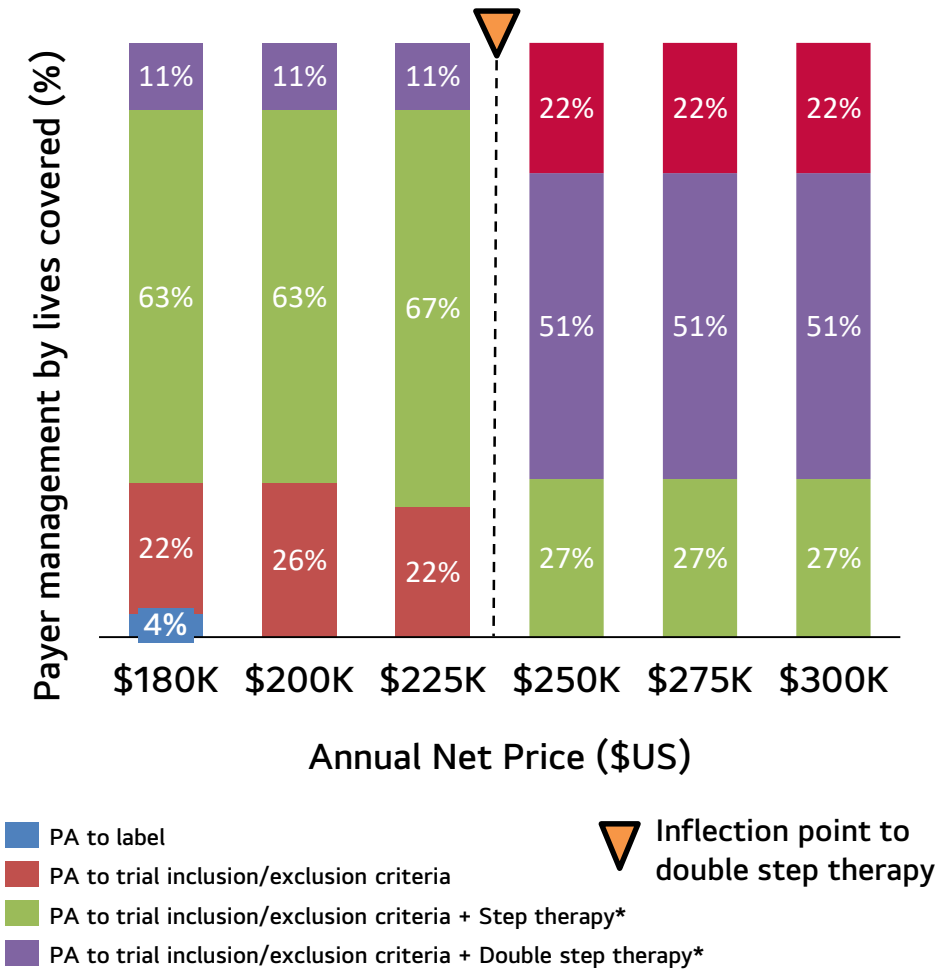
Market Research

Project Objectives

- Pressure test original price ranges (US, DE, FR, IT, ES, UK, JP, AUS) from 2023 forecast through analogue analysis that includes recent launches from rare pediatric conditions (e.g., Trikafta)
- Conduct US PMR with national and regional manage care organizations as well as PBMs to validate updated US price ranges / management practices (extrapolate ex-US)
- Update global forecast with new country-level launch dates, LOE as well as cost / NPV calculation functionality
- Integrate pricing assumptions from geographies (US, DE, FR, IT, ES, UK, JP, AUS) into Udenafil forecast and provide new sales ranges (base, high, low)
- Create executive-level presentation with key pricing research findings (analogues + PMR) for large shareholder meeting in December

IQVIA | Mezzion | Udenafil US Pricing Analysis Net Sales Forecast in SVHD | Final Report October 2025

Market Research



Payer Insights

- Formulary Inclusion: Most payers are expected to cover Udenafil regardless of price, given the high unmet need and absence of proven alternatives
  - One PBM indicated that Udenafil may not be added to the formulary if the annual net price exceeds $225K; however, coverage could still be granted under a medical exception
- Prior Authorization: Coverage will likely align with the trial's inclusion and exclusion criteria to ensure appropriate patient selection
  - PA requirements may be relaxed over time, influenced by emerging guidelines and KOL input
- Impact of Prevalence and Unmet Need: Given the low prevalence and high unmet need of SVHD, payers may not actively manage treatment(s) in the therapeutic area
  - Smaller plans will likely follow the management of larger plans

Abbreviations: PBM – pharmacy benefit manager; KOL – key opinion leader

Note: *Payers will rely on guidelines and KOL recommendations to determine whether step therapy is required and/or viable

Source: 2025 US Payer Research (n=5)

Market Research

1 Selected Analogues

trikafta

Fintepla (fenfluramine)

Epidiolex (cannabidiol)

WINREVAIR (sotatercept-csrk) for injection 45 mg, 60 mg

Evrysdi risdiplam

ADAKVEO crizanlizumab-tmca FOR IV INFUSION 10 mg/mL

Oxbryta (voxelotor)

Wakix pitolisant tablets

JYNARQUE (tolvaptan) tablets

2 Pricing analysis

- Reviewed drug regimen to determine number of standard units consumed/patient/year
- Estimated annual cost of therapy based on standard units required annually and cost of per unit of the drug
- Analysis in ex-US countries helped benchmark the ACOT with respect to US

3 Pricing Validation from PMR

- The estimated annual cost of therapy for Udenafil based on analogue analysis was estimated to be ~$180K in US
- For RoW, the cost was projected at 41% of the US value, reflecting regional pricing differences

These price ranges were pressure tested in the PMR to validate the launch price for Udenafil

Abbreviations: ACOT: annual cost of therapy; RoW: rest of the world; PMR – primary market research

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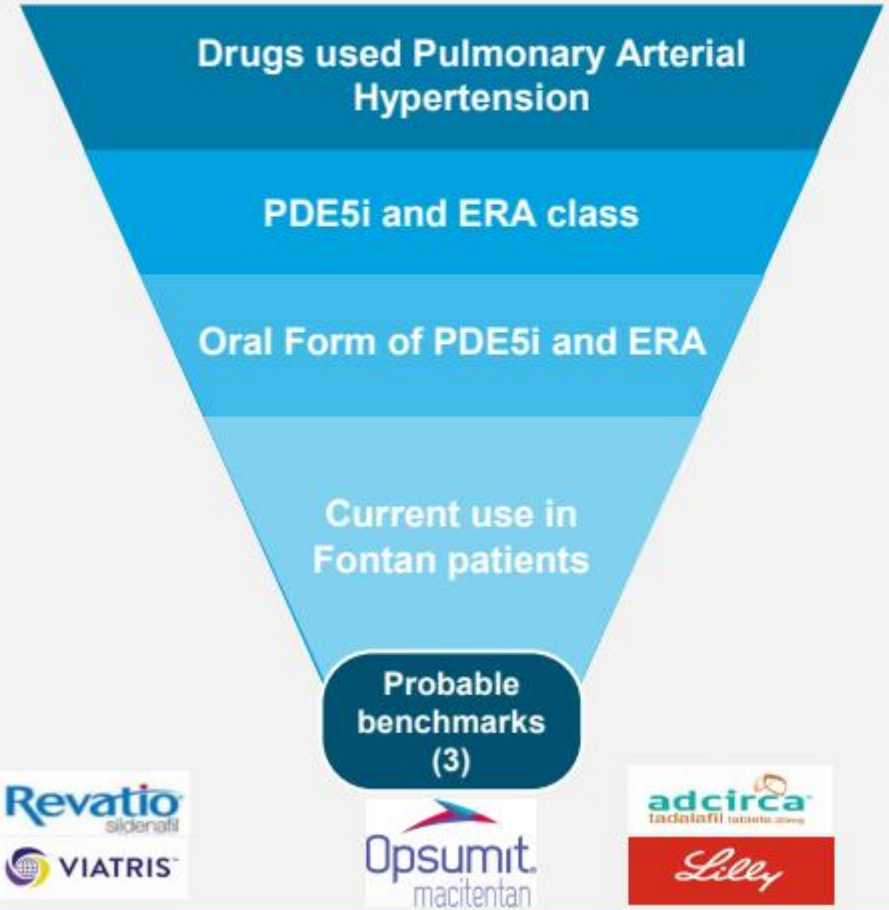
Market Research

Analogues used in 2023 exercise were based on a given set of criteria



Three more analogues were used to widen the scope of analysis as a part of 2025 update

Evrysdi®
risdiplam

trikafta®

Fintepla®
(fenfluramine)
2.2 mg/mL oral solution

Abbreviations: PDE5i - phosphodiesterase 5 inhibitors; ERA - endothelin receptor antagonists

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Market Research

Analogue	Manufacturer	Indication	Prevalence	Annual Price	Additional Details
trikafta	VERTEX	Cystic Fibrosis (CF)	~35K[1]	~$370K	2024 revenue reached over $10B driven by label expansion beating expectations[8]. Similar prevalence as SVHD
Epidiolex® (cannabidiol)	Jazz Pharmaceuticals	Seizures associated with LGS, DS, TSC and impaired hepatic function	LGS: ~48K[5] DS: ~20K[6]	~$19-38K	2024 revenue of ~$972M an increase of 15% from past year[13]. Similar prevalence as SVHD
Fintepla (fenfluramine)	ucb Pharma	Seizures associated with LGS and DS		~$238K	2024 revenue of ~$340M and expected to be a blockbuster[14]. Similar prevalence as SVHD
Evrysdi risdiplam	Genentech A Member of the Roche Group	Spinal Muscular Atrophy (SMA)	~10-25K	~$400K	2024 revenue of ~$2B and similar prevalence as SVHD
WINREVAIR (sotatercept-csrk) for injection 45 mg, 60 mg	MERCK	Pulmonary Arterial Hypertension (PAH)	~50K[2]	~$250K	Peak revenue expectation increased to $3B+ after strong sales[9]. However, not a pediatric indication
Oxbryta (voxelotor)	Pfizer	Sickle Cell Disease (SCD)	~100K[3]	~$100-150K	Pulled back from the market in 2024[10]
ADAKVEO® crizanlizumab-tmca FOR IV INFUSION 10 mg/mL	NOVARTIS			~$128K	EMA revoked approval after Phase 3 trial data[11]
Wakix pitolisant tablets	HARMONY BIOSCIENCES	Narcolepsy	~200K[4]	~$100-200K	2025 revenue expected to be ~$820-860M on track to achieve blockbuster status[12]
JYNARQUE® (tolvaptan) tablets	Otsuka	Autosomal Dominant Polycystic Kidney Disease (ADPKD)	140K[7]	~$110K	2024 revenue of $1.5B but lost exclusivity in 2025 and had a REMS program[15]

Source: 1: CDC_CF; 2: Ruopp_et_al_2022; 3: CDC_SCD; 4: Narcolepsy_Network; 5: LGS_Foundation; 6: StokeTheraputics; 7: Willey_et_al_2019; 8: Vertex; 9: PharmaPhorum; 10: FiercePharma; 11: PharmaPhorum 12: Harmony Biosciences; 13: Jazz_10K; 14: FiercePharma; 15: Lupin
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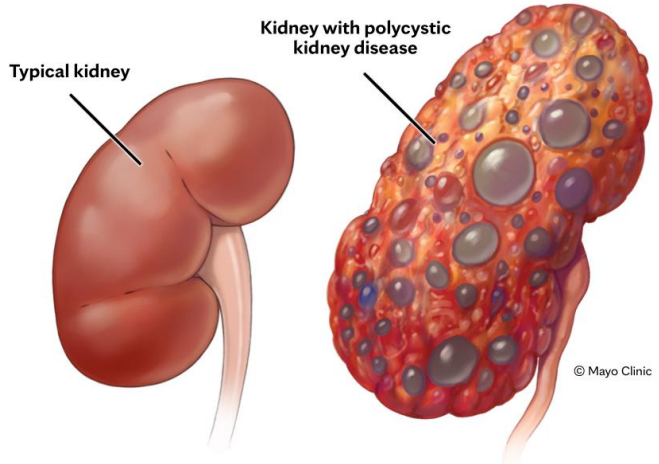
ADPKD

- Autosomal Dominant Polycystic Kidney Disease (ADPKD, 상염색체 우성 다낭성 신질환):
  - 선천성 희귀질환으로 신장에 수 많은 낭종(cysts)이 발생하여 말기 신장 이상으로 악화
  - 유전자 (PKD1, PKD2) 변형으로 인하여 발생
  - 만성신부전 및 혈액투석 환자의 상당수를 차지하고 있음
  - 미국에 약 14만명의 환자
  - 매년 신규 환자 5 ~6,000명 (미국)



- Market Landscape:
  - 치료법은 매우 제한적으로, 주요 치료는 질환 진행 억제보다는 증상 완화에 초점
  - Jynarque ® (tolvaptan)가 현재 FDA에서 승인된 유일한 치료제로 2024년 $1.5B 매출
  - 2030년대 초반에는 ADPKD 시장 규모가 약30억달러에 이를 것으로 예측 (시장 조사 기관)

ADPKD

- **Principal Investigator**: Dr. Fouad Chebib, Mayo Clinic, Florida, USA

- **Study Design**:

  In Vitro: Assess dose-response and measure biochemical markers (cAMP, cGMP)

  Ex Vivo: Evaluate Udenafil's impact on cyst formation in organ cultures

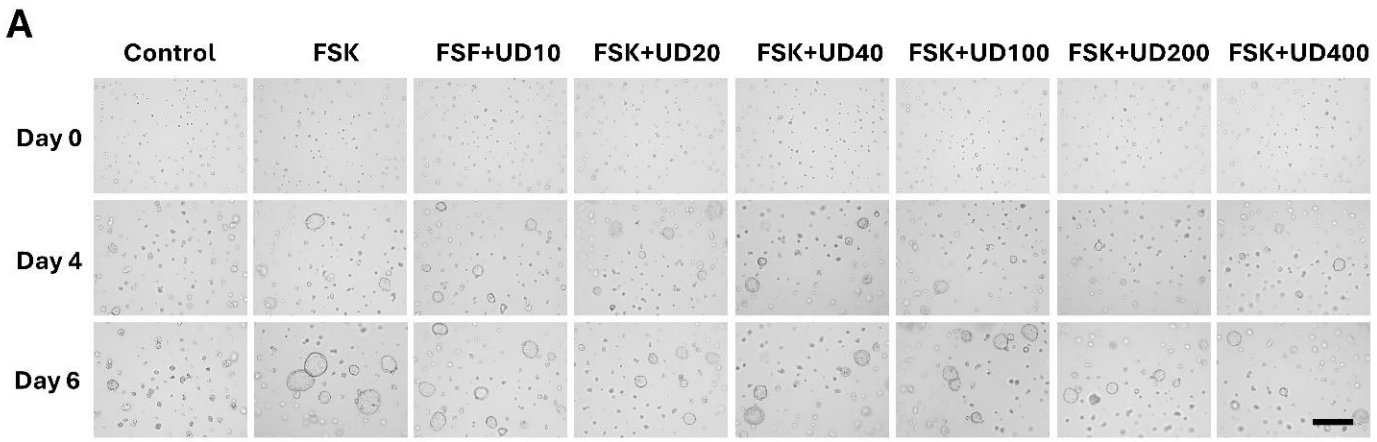
  In Vivo: Test efficacy and safety in Pkd1RC/RC mouse model; measure kidney function and conduct histopathological analyses

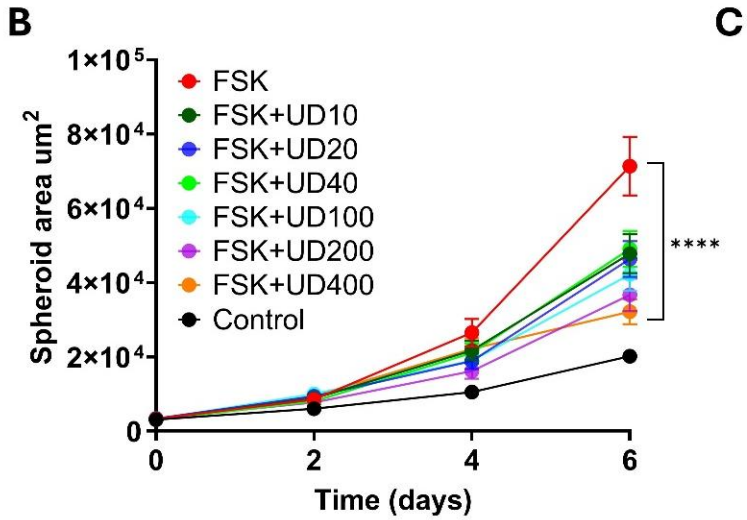
- **전임상시험을 통해서 다음과 같은 사실 확인 예정**
  - ➢ 효과적으로 cystogenesis를 줄여주는 udenafil 용량 확인
  - ➢ Cystogenesis 억제와 PDE5 inhibition의 상관관계 확인
  - ➢ PKD mouse models에서 kidney cyst 감소 및 신장기능 개선 사실 입증

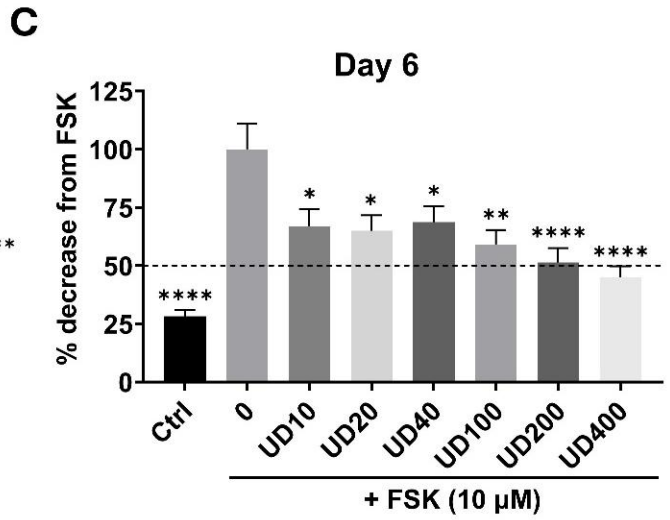
➔ **Udenafil의 PKD 치료 효과와 유효 용량 범위를 확인한 후 임상시험 진입**

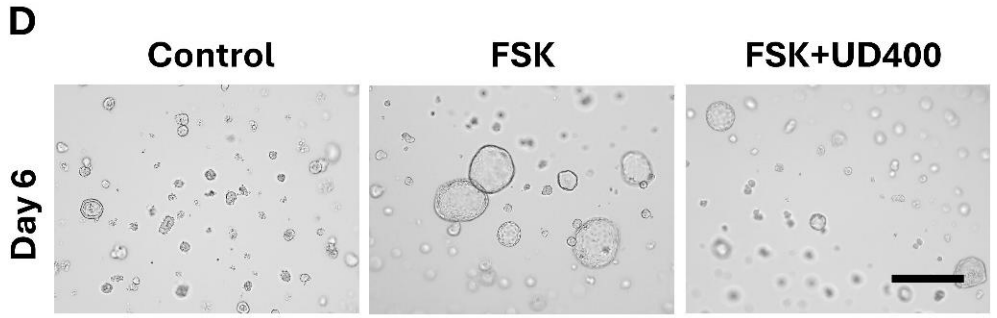
ADPKD (In Vitro)

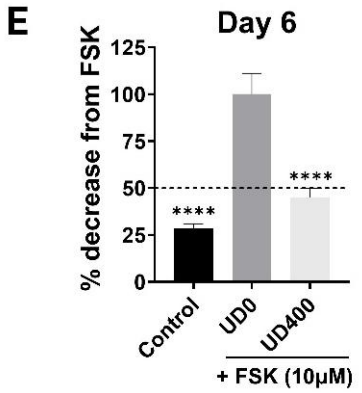
- 3D cystogenesis model에서, Udenafil이 투여 용량에 비례하여 spheroid (cyst) growth 억제











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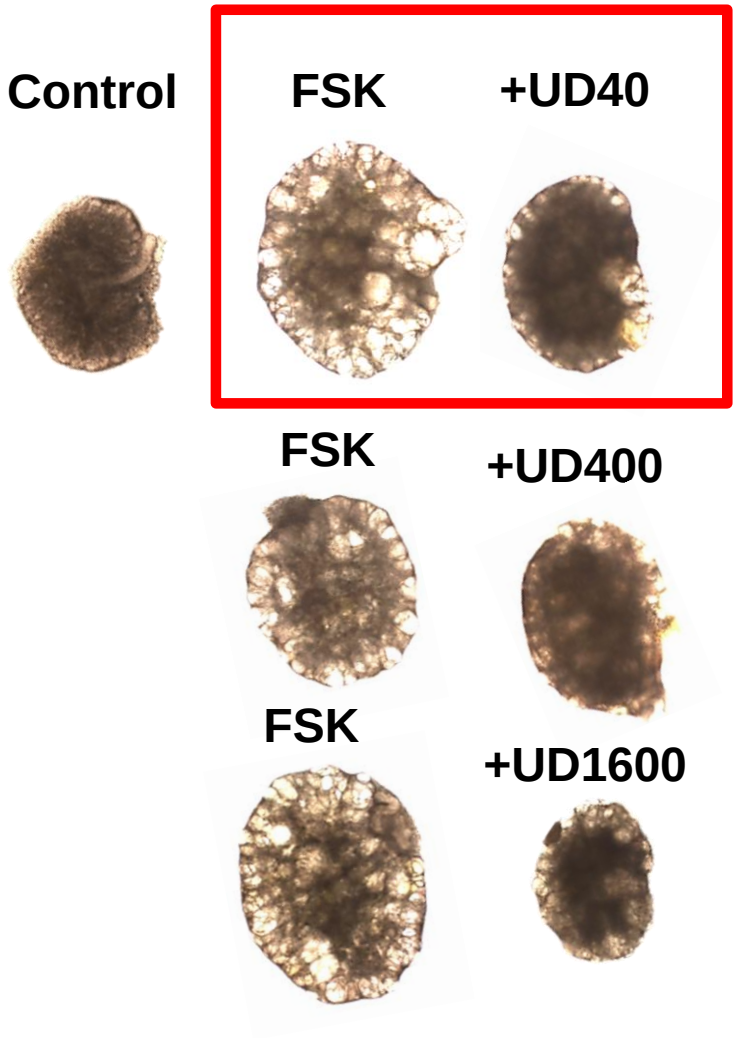
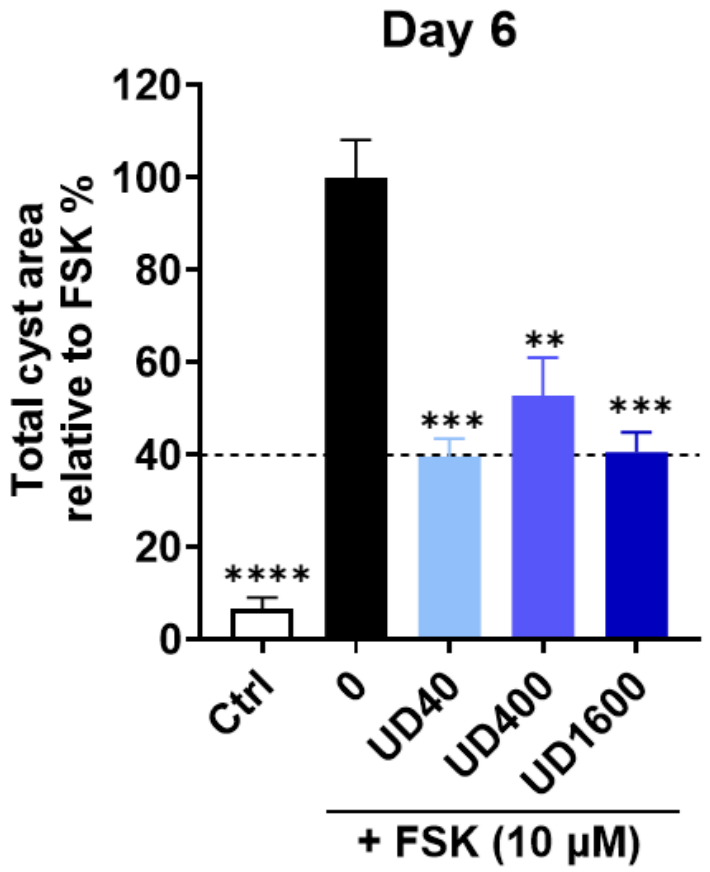
ADPKD (Ex Vivo)

- 신장 조직에서, Udenafil이 cyst 생성 억제





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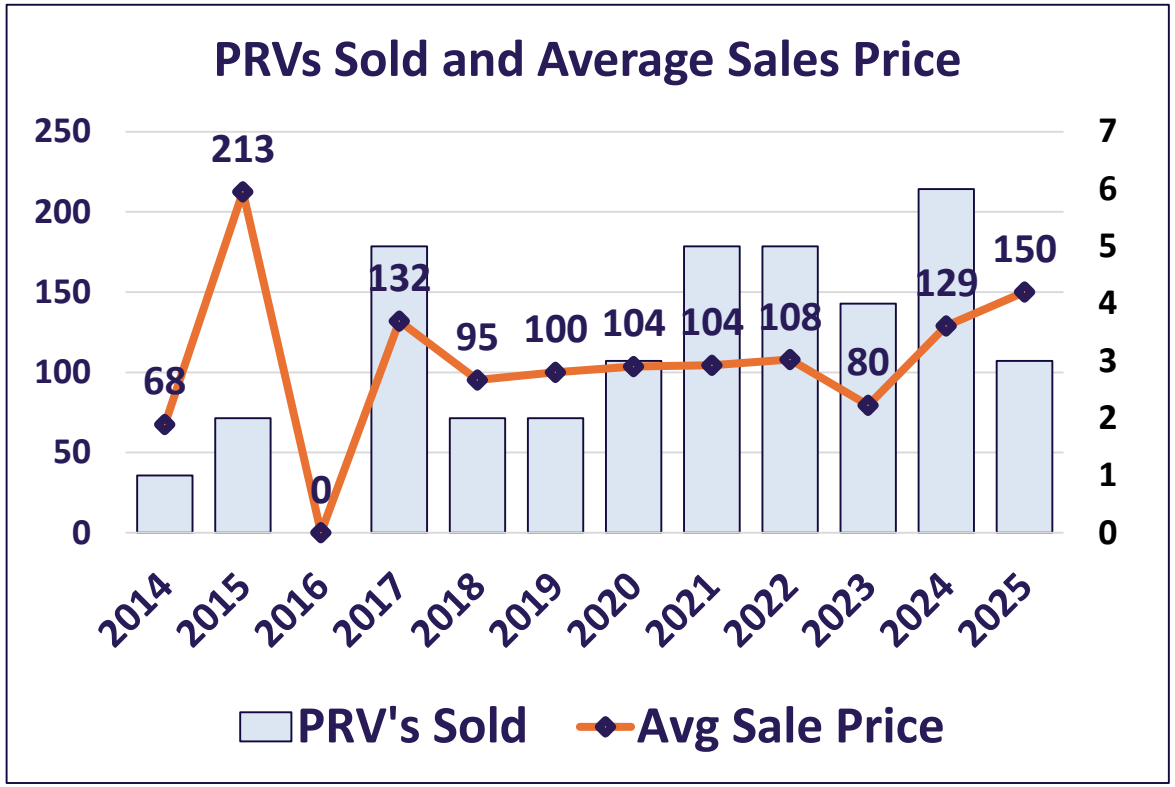
PRV(Priority Review Voucher)



***Source**: IQVIA 2025 based on publicly disclosed sales and prices*

Historical PRV sale values highlight meaningful incentive potential with latest PRVs selling for $150 each

- **Why it matters:** PRV is a meaningful incentive in rare pediatric disease; for Mezzion it represents potential strategic upside reinforcing the importance of Fontan as a high unmet medical need
- **Status:** The House unanimously passed the *Give Kids a Chance Act* on Dec 1, 2025, which would reauthorize the rare pediatric PRV program; it is awaiting Senate action
- **What we're doing:** Active work with Rare Disease Company Coalition (RDCC) + direct congressional engagement + support letters to help secure reauthorization

CNPV(Commissioners National Priority Voucher)

Mezzion advocacy on Capital Hill to advance FDA accelerants like CNPV and PRV and protect rare pediatric incentives like the orphan drug tax credit

- **What is the CNPV:** FDA pilot designed to shorten review from ~10–12 months to ~1–2 months for national priorities
- **FDA momentum:** 15 total vouchers have been awarded since launching this Summer across multiple therapeutic areas

  - 1st approval of antibiotic in 2 months (12/10)

- **Our status / actions:** Submission filed; active advocacy highlighting Fontan high unmet need and first-approved-therapy potential
- **Value:** If awarded, could meaningfully accelerate FDA review and time-to-launch

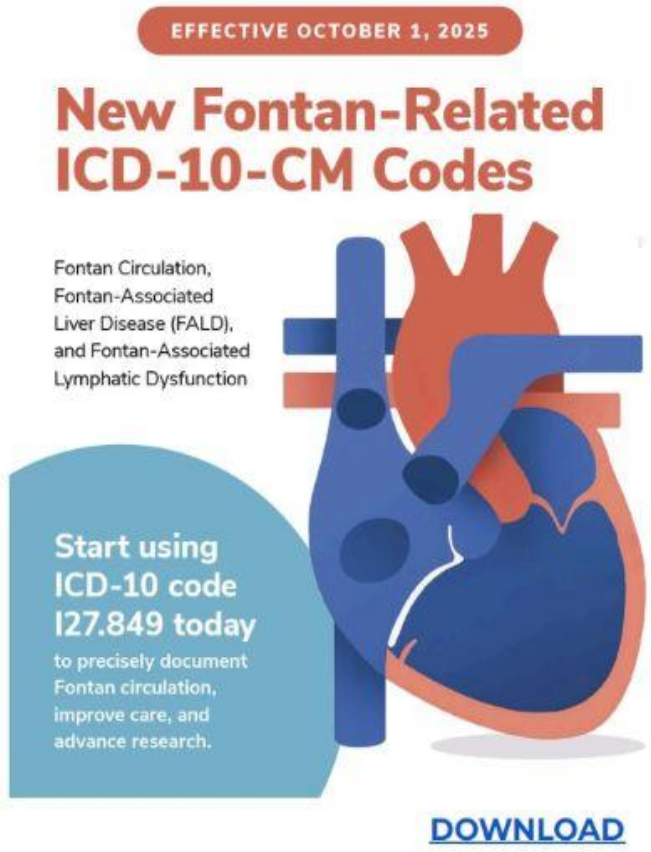
ICD-10(International Classification of Diseases) Code

ICD code의 개정 및 시행

- ICD: 비용 및 보험 청구 그리고 환자군 추적에 사용

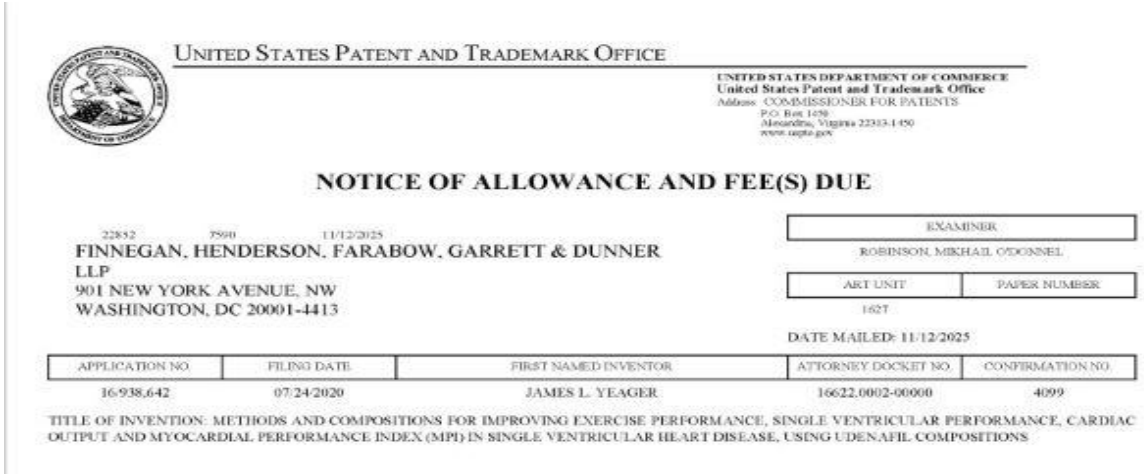
- 2025. 10. 01., 새로운 ICD-10 코드 시행
  - 폰탄 순환계 질환 최초 포함
  - 폰탄 질환과 관련한 다양한 의료 서비스/연구의 필요성이 인정됨
  - 폰탄 질환에 대한 추적 관리, 의료 서비스 제공, 보험 청구 지원
  - 상업화시, 가격 결정에 긍정적 영향

- 폰탄 ICD-10 등록 현황 (10.01 ~ 10.31, 1개월 현황)
  - 약 1,700 환자
  - 약 1,400 providers (의사, 병원 등)



IP

- ‘유데나필의 폰탄 환자 대상 운동 능력 개선 용도에 대한 핵심 특허 출원’에 대해 허가 통지



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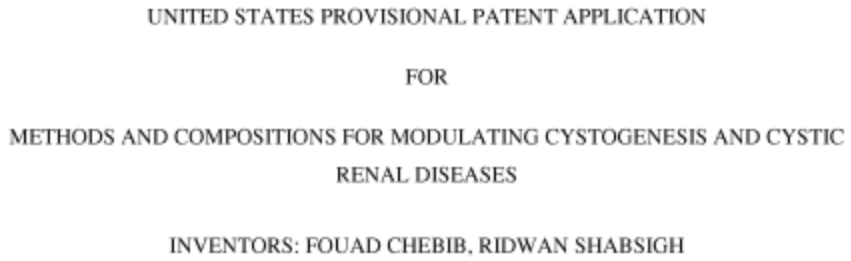
16/938,642	07/24/2020	JAMES L. YEAGER	16622.0002-00000	4099

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR IMPROVING EXERCISE PERFORMANCE, SINGLE VENTRICULAR PERFORMANCE, CARDIAC OUTPUT AND MYOCARDIAL PERFORMANCE INDEX (MPI) IN SINGLE VENTRICULAR HEART DISEASE, USING UDENAFIL COMPOSITIONS

- PKD 특허 출원



UNITED STATES PROVISIONAL PATENT APPLICATION

FOR

METHODS AND COMPOSITIONS FOR MODULATING CYSTOGENESIS AND CYSTIC RENAL DISEASES

INVENTORS: FOUAD CHEBIB, RIDWAN SHABSIGH

MEZZION