## **adjucence** Corporate Presentation Q2 2023

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### **Advicenne's value proposition**



- European organization
- Operating platform in France and the UK
- Rare diseases expertise
- Sibnayal® (ADV7103) dRTA commercial status with full European coverage through distribution agreements
- Phase III studies agreed upon with EMA in Cystinuria



- US footprint
- ADV7103 Orphan Drug Designation in dRTA
- Low clinical risk / Pediatric indication / formulation
- Significant US market potential in two orphan indications
- Potential extended IP protection beyond currently 2031
- Regulatory clarity for NDA
  - Agreed pathway for dRTA
  - Strategic clarity on pathway in first line cystinuria

### Sibnayal® / ADV7103

- Approved in EU and UK in April 2021 for the treatment of dRTA (distal Renal Tubular Acidosis) in pediatric (from one year of age) and adult patients
- Sibnayal<sup>®</sup> unique and patented prolonged-release formulation has been designed to deliver effective alkalizing therapy with twice-a-day oral administration
- Sibnayal<sup>®</sup> contains the active substances **potassium** citrate and **potassium hydrogen carbonate**





# ADV7103: a breakthrough alkalinizing asset for rare renal diseases

- **Patented** prolonged release **combination** of potassium citrate (CK) and potassium hydrogen carbonate (bicarbonate BK) enabling **twice-daily dosing**
- Only convenient chronic oral treatment (>6-year European follow-up data):
  - Sustained efficacy
  - Strong treatment compliance
  - Very good safety profile



✓ Centralized market approval in EU and the UK (Commercial name: Sibnayal <sup>®</sup> )
✓ Orphan Drug Designation in the US
✓ Phase III clinical development plan (ARENA-2) agreed with the FDA
<ul> <li>Phase III clinical plan (CORAL-1) agreed with the European Medicines Agency</li> </ul>
✓ Potential orphan drug designation in the US to be to be approved as a "Treatment of cystinuria, in addition to conventional first-line therapy"

<sup>(1)</sup> distal Renal Tubular Acidosis is a rare but serious chronic disease characterized by the increase of acid ions in the blood

### **ADV7103: intellectual property**

- **ADV7103** is protected by 3 family patents, including the patent that covers the combination of potassium citrate and potassium bicarbonate in a delayed-release formulation
- Initial patents expiration date : November 2031



- Since the approval of ADV7103 in EU and the UK, relevant patent terms have been extended through Supplementary Protection Certificate (SPC) by 5 years (until 2036) in France, Italy and Spain ; pending UK extension request
- 6-month pediatric exclusivity extension



## **ADV7103 manufacturing overview**

### SIBNAYAL® / ADV7103:

- Manufacturing fully outsourced to CDMOs
- French-based Lündbeck facility, for API sourcing bulk granules manufacturing
- Primary Packaging subcontracted to Ivers Lee (CH), and secondary packaging done by Lündbeck
- Lündbeck is cGMP EMA approved (latest inspection: July 2021); Ivers Lee is cGMP Swiss Medic and FDA approved
- All IP, filings and processes are the property of Advicenne
- Current contractual agreements until 2030 provides enough capacity to cover sales and revenue potential









### dRTA: a rare disease with life-long complications

- distal Renal Tubular Acidosis (dRTA) is a rare and chronic serious renal disorder characterized by the increase of acid ions in the blood leading to decreased bone mineral density
- 2 identified forms:
  - **Genetic** (or inherited) form (usually identified in infancy)
  - Acquired form
- An underdiagnosed and undertreated disease:
  - c.20,000 clearly identified cases in Europe and c.
     20,000 in the US
- Potential c.150,000 RTA treatable population in the US

- Failure to thrive
- Muscle weakness / paralysis
- Rickets / Osteomalacia / soft bones / Fractures
- Cardiac dysfunctions / arrythmia
- > Nephrocalcinosis
- Lithiasis
- Chronic Kidney Disease (CKD)



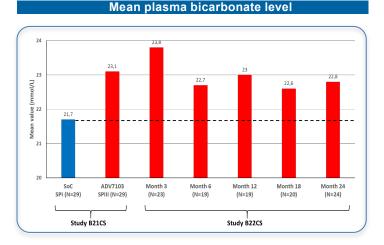




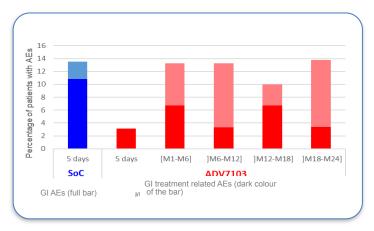
Sources: Lopez-Garcia et al 2019, Rodriguez-Soriano et al 1982, Domrongkitchaiporn et al. 2002a, Domrongkitchaiporn et al. 2002b, MacSherry et al. 1978, Caldas et al. 1992



# ADV7103 for treatment of dRTA: Compelling clinical efficacy



#### Gastro-intestinal adverse events

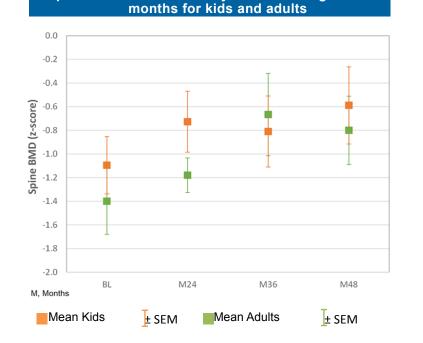


#### B21CS and B22CS are European clinical studies part of the ARENA-1 clinical program

Sources: Bertholet-Thomas et al. Efficacy and safety of an innovative prolonged-release combination drug in patients with distal renal tubular acidosis: an open-label comparative trial versus standard of care treatments. Paediatric Nephrol. 2021 Jan;36(1):83-91; Safety, efficacy, and acceptability of ADV7103 during 24 months of treatment: an open-label study in paediatric and adult patients with distal renal tubular acidosis. Paediatric Nephrol. 2021 Jul;36(1):1765-1774.



### ADV7103: increasing clinical efficacy over time



Spine bone mineral density z-score change over 48

#### Analysis of covariance of z-score

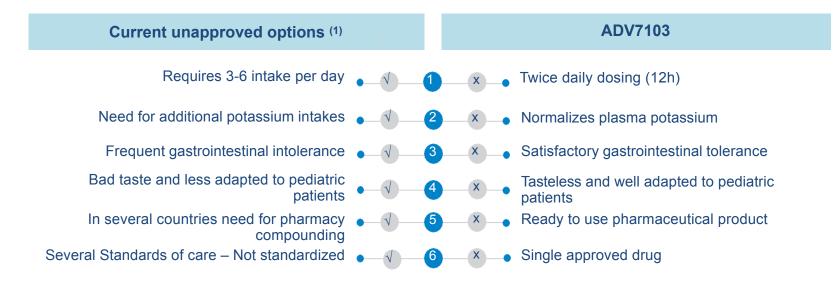
### Statistical significance overall spine (ANCOVA)

- Significant increase of z-score in spine BMD compared to baseline (ANCOVA) for both kids and adults (24 patients)
- At month 24: LS mean difference estimate [95% CI] of 0.22 [-0.01, 0.44] units (p=0.0573)
- At month 36: LS mean difference estimate
   [95% CI] of 0.31 [0.08, 0.54] units (p=0.0103\*)
- At month 48: LS mean difference estimate [95% CI] of 0.36 [0.13, 0.60] units (p=0.0038\*)



Sources: Bertholet-Thomas et al. Efficacy and safety of an innovative prolonged-release combination drug in patients with distal renal tubular acidosis: an open-label comparative trial versus standard of care treatments. Paediatric Nephrol. 2021 Jan;36(1):83-91. ; Safety, efficacy, and acceptability of ADV7103 during 24 months of treatment: an open-label study in paediatric and adult patients with distal renal tubular acidosis. Paediatric Nephrol. 2021 Jul;36(1):1765-1774.

# ADV7103 for treatment of dRTA: Changing the treatment landscape



#### ADV7103: compelling treatment opportunity for patients with dRTA

(1) Mainly intake of high doses of alkalinizing agents, no approved SoC in the EU and the US before Sibnayal®



# ADV7103 approved for the treatment of dRTA in the EU and the UK...



Approved since **Q2 2021** for the treatment of dRTA for pediatric (from 1 year old) and adult patients, MA covers both **primary** (genetic) and **secondary** dRTA forms

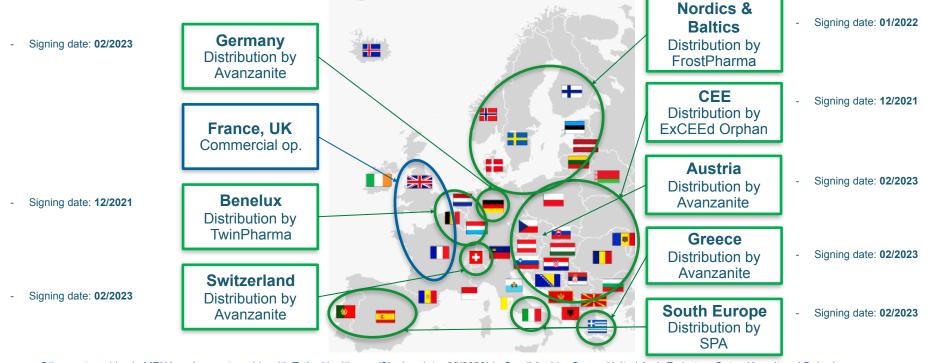
### Successful ARENA-1 program (B21 and B22 studies)

- B21: multi-center, open label, non-inferiority study versus standard therapy with 32 patients, demonstrated long-term control of metabolic acidosis with very good safety and tolerability profiles
- B22: open label, efficacy and safety long term follow up trial with 27 patients followed up to 72 months. 24-month data published. EOS report signed and 72-month data to be published shortly
- > No safety or pharmaco-vigilance event since European commercial launch

On-going pricing discussions following completion of the commercial European coverage



## ...and supported by a rejuvenated platform for its distribution



Other partnerships in MENA region: partnership with Taïba Healthcare (Signing date: 06/2022) in Saudi Arabia, Oman, United Arab Emirates, Qatar, Kuwait and Bahrain

Sibnayal mainly sold through hospital channels

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### **Development status of ADV7103 for dRTA in the US**



ODD status in December 2022 for the treatment of genetic dRTA

Current ARENA-2 program (B23 and B24 studies) agreed with FDA and ready to be launched:

- B23: phase III pivotal safety and efficacy registration trial, 32-patient, multi-center, double-blind, randomized study comparing ADV7103 vs. placebo, 6-day efficacy trial, blood pH as primary endpoint
- B24: long-term safety evaluation (2 years)



# **Cystinuria: a rare and well documented genetic disease**

- **Cystinuria** is a rare genetic disease characterized by a build-up of undissolved cystine in the kidneys and bladder, leading to the formation of cystine crystals and/or stones which may block the urinary tract
- Cystine stones are challenging and often require expensive, invasive surgical removal
- Cystinuria often leads to chronic kidney disease (CKD), nephrectomy, kidney atrophy, recurrent urinary tract infections and hypertension
- Estimated prevalence of c.40,000 cases in Europe/UK, c.30,000 cases in the US
- US ICD-10 code for easier diagnosis and reimbursement processes



# FY 2022 financial statements

### **Consolidated P&L IFRS**

<b>CONSOLIDATED INCOME STATEMENT</b> (in thousands of euros)	December 31, 2022	December 31, 2021
Revenues Income from partnerships Other operating income	2 341 56 611	2 670 19 1 078
Total revenue and other income	3 008	3 766
Cost of goods sold Research and development expenses Sales and marketing expenses Overhead and general expenses	-1 117 -7 077 -1 066 -3 807	-973 -8 964 -1 569 -4 703
Operating Income	-10 059	-12 444
Net financing costs Other financial expenses Other financial income	-1 373 -3 1	139 -148 14
Income before taxes	-11 434	-12 438
Income taxes	-37	11
Consolidated net profit / loss	-11 470	-12 427
<ul> <li>Attributable to shareholders of Advicenne SA</li> <li>Attributable to non-controlling interests</li> </ul>	-11 470 -	-12 427 -
Earnings per share (€/share) Diluted earnings per share (€/share)	- 1,16 - 1,16	- 1,34 - 1,34

2022 IFRS revenue (Gross sales net of rebates / tax):
2.3 m€ in 2022 vs 2.7 m€ in 2021

- Income from partnerships: royalties from Ozalin's sales by Primex Pharmaceuticals
- Other operating income: RTC (0.6 m€ for 2022, decreasing by 0.5 m€ comp. to 2021) :
  - since MA for Sibnayal®, mainly centers' closing costs, support documentation, reports and archiving
  - no new clinical development in Europe in 2022
- Operational expenses: 13.1 m€ vs 16.2 m€ in 2021 (-19%)
  - **CoGS:** steady ~30% of product sales
  - R&D expenses: decrease by 1.9 m€ (-21%)
    - 3.0 m€ in the US, steady vs LY
  - Sales & marketing expenses (-32%): adapted to promotional needs (Likozam & Levidcen), Sibnayal® w/o promotion in post-ATU status; no sales force since early 2021
  - Overhead & general expenses: 3.8 m€ (-0.9 m€ vs 2021): strict control of expenses by management, reorganization (savings around 0.8 m€ on a full year basis)
- Financial result: -1.4 m€ vs 0 m€ in 2021 (cf. dedicated slide)



### **Consolidated balance sheet IFRS**

<b>ASSETS</b>	December 31,	December 31,
(in thousands of euros)	2022	2021
Intangible assets	135	167
Property, Plant and Equipment	1 908	1 836
Other financial assets	133	263
Non-current assets	2 176	2 265
Inventory	982	717
Accounts receivable	1 088	802
Tax credit 1	602	1 126
Financial asset	2	-
Other current assets 2	1 087	1 286
Cash and cash equivalents 3	8 322	12 685
Current assets	12 083	16 616
Total assets	14 259	18 881

1. RTC: 0.6 m€ for 2022, reimbursement by French administration to be received end of 2023

2. Other current assets: mainly tax & social receivables

- 3. Cash position as at Dec. 31, 2022: 8.3 m€ vs 12.7 m€ end 2021:
- 5 m€ from EIB 2<sup>nd</sup> tranche drawdown in December 2022
- Payment terms strictly managed Delay in the US study costs

LIABILITIES and CAPITAL	December 31,	December 31,
(in thousands of euros)	2022	2021
Capital stock	1 991	1 990
Capital-related premiums	1 490	24 469
Reserves	-2 627	-13 723
Net income	-11 470	-12 427
Total equity capital	-10 616	309
Provisions	64	96
Long-term debt	(4) 17 218	12 371
Non-current liabilities	17 282	12 467
Financial liabilities	4 1 536	165
Accounts payable	5 1 390	2 929
Other current liabilities	6 4 668	3 012
Current liabilities	7 593	6 105
Total Liabilities	14 259	18 881

4. Financial debt: 18.8 m€ at the end of 2022 vs12.5 m€ end of 2021:

5 m€ from EIB 2<sup>nd</sup> tranche drawdown in December 2022 •

increase in interests (royalties) mainly on the 1st tranche of the EIB loan •

5. Accounts payable: decrease by 1.5 m€ related costs reduction and tough control of expenses

#### 6. Other current liabilities

Rebates on sales: 2.8 m€



### **Cashflow Statement IFRS**

CASH FLOW (in thousands of euros)	December 31, 2022	December 31, 2021
Net result (loss)	-11 470	-12 427
Amortisation, depreciation and provisions	334	426
Share-based payments	480	347
Other calculated income and expenses	24	3
Net financial costs	1 146	-139
Sale of PPE and intangible assets	52	9
Self-financing capacity	-9 434	-11 782
Changes in inventory	-265	18
Changes in trade and other receivables	435	296
Changes in trade and other payables	118	-1 057
Cash flow from operations	-9 147	-12 525
Acquisition of PPE and intangible assets	-115	-297
Acquisition of financial assets	-	-
Sale of financial assets	113	-98
Cash flow from investing activities	-2	-395
Capital increase (net)	23	9 088
Own shares held in treasury	-17	-56
Net borrowings and refundable advances	5 000	45
Repayment of borrowings and refundable advances	-222	-225
Cash flow from financing activities	4 783	8 853
Changes in value of local currencies	2	-18
Change in cash	-4 363	-4 085
Opening cash position	12 685	16 771
Closing cash position	8 322	12 685

#### **Operations**

- Cash flows used in operating activities significantly improved at -9.1 m€ in 2022 vs -12.5 m€ in 2021, thanks to the growth of product sales and control of expenses
- WCR favorably impacted by the payables decrease

#### Investments

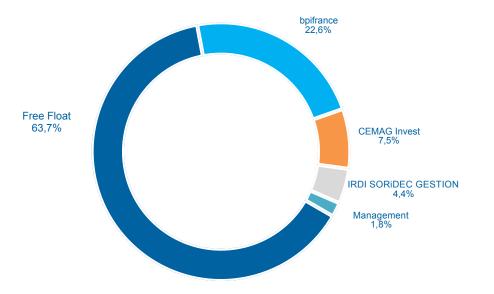
- mainly in manufacturing project
- regroupment of 3 sites (Nîmes, Grenoble & Paris rue de la Paix) in a unique one called "FSH"

#### Financing

- 5 m€ from EIB 2<sup>nd</sup> tranche drawdown in December 2022
- capital increase by 9.4 m€ in June 2021



### **Shareholding structure**<sup>1</sup>



1: On a fully diluted basis as of December 31st, 2022

Source: Company information



## advicenne

Contact: Didier Laurens - CEO dlaurens@advicenne.com