Novel Therapies Targeting Kidney Disease

September 2024

GUARD THERAPEUTICS

GUARD THERAPEUTICS – IN SHORT

- Recently started Phase 2b *POINTER* study with candidate drug RMC-035 – results expected year-end 2025
  - Granted **FDA Fast Track Designation** (kidney protection in open-heart surgery)
  - Eligible for **Breakthrough Designation Therapy**
- Clinical PoC established on hard kidney endpoints in placebo-controlled Phase 2a study enrolling 177 patients
- Lead indication >USD 1 bn opportunity – first-to-market potential & no approved therapies
- Massive opportunity & unique positioning in kidney disease with preclinical GTX peptide
  - Clinically validated target, robust efficacy in numerous disease models
- Listed on Nasdaq First North Growth Market in Stockholm [GUARD]

FDA, food and drug administration; PoC, proof-of-concept

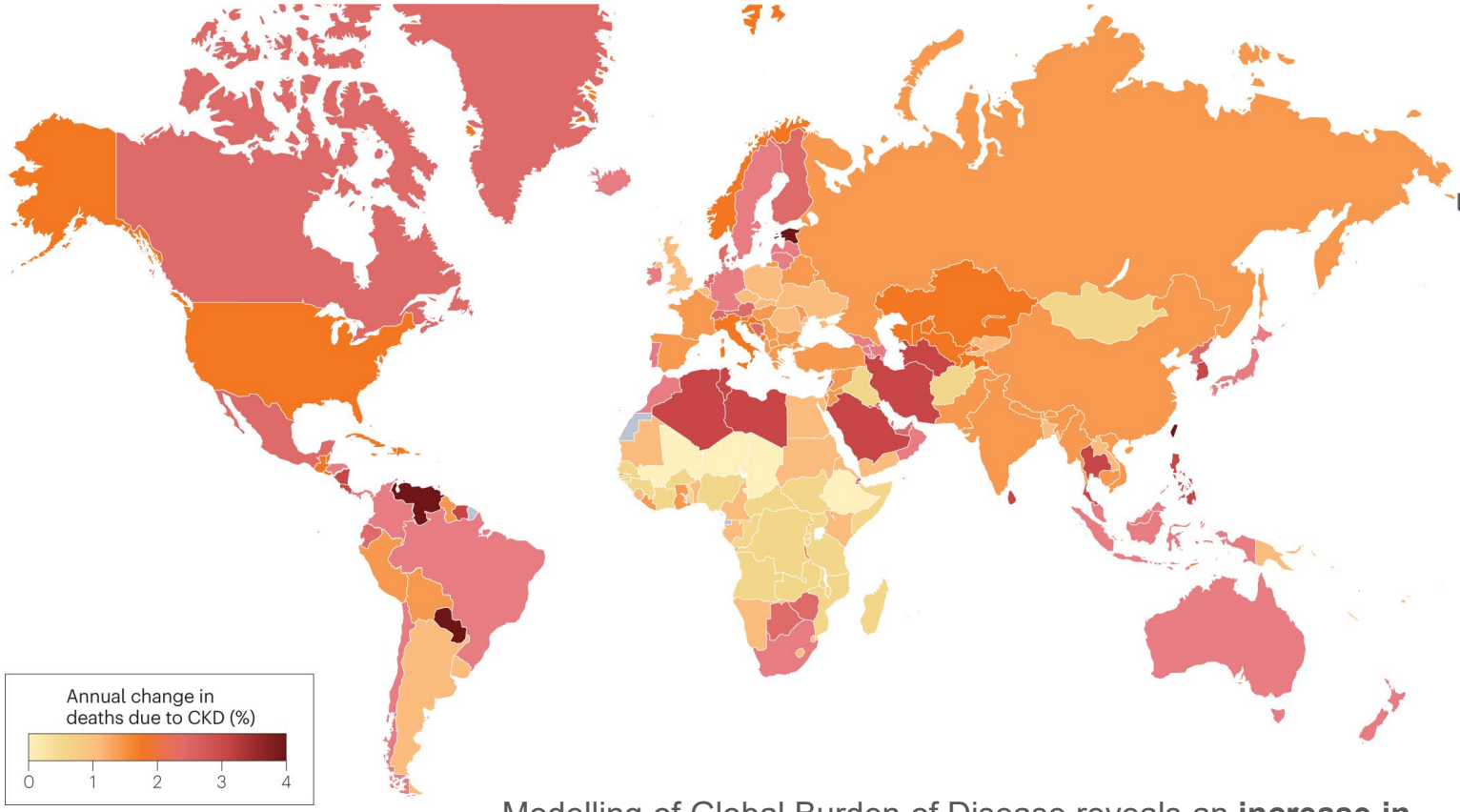
EXPERIENCED MANAGEMENT TEAM WITH PROVEN STRONG TRACK RECORD IN DRUG DEVELOPMENT

NAME / POSITION	EXPERIENCE		NAME / POSITION	EXPERIENCE	
 **TOBIAS L. AGERVALD** MD, PhD, CEO	**+10** years in industry	astellas	 **KARIN BOTHA** MSc, CFO	**+20** years in industry	NOVARTIS, SmithKline Beecham, GlaxoSmithKline
 **MICHAEL REUSCH** MD, CMO	**+30** years in industry	Fujisawa, astellas	 **PETER GILMOUR** MSc, PhD, CSO/Head of Preclinical	**+20** years in industry	AstraZeneca, astellas
 **TORBJÖRN LARSSON** BSc, Head of CMC	**+30** years in industry	Medivir, aprea therapeutics, Pharmacia &Upjohn	 **SARA THURESSON** MSc, Head of Clinical Operations	**+15** years in industry	oncopeptides, WILSON THERAPEUTICS, IQVIA, Medivir

VISION

Be a globally recognized leader in nephrology, **pioneering** transformative therapies for kidney disease, and **eliminating** the need for dialysis or kidney transplantation

CHRONIC KIDNEY DISEASE (CKD) – AN INCREASING GLOBAL HEALTH BURDEN REDUCING LIFE SPAN



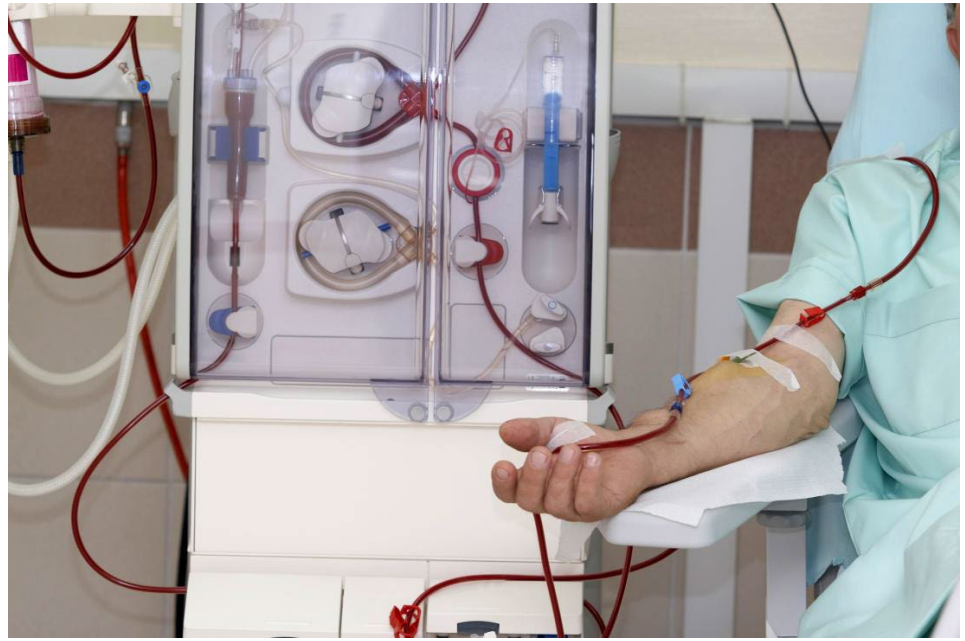
Modelling of Global Burden of Disease reveals an **increase in predicted deaths due to CKD between 1990 and 2040** (deaths per 100,000)

Years of life lost (YLL) due to CKD are predicted to **continue to increase and surpass diabetes** as a cause of YLL by 2040

Francis et al, Nature Reviews Nephrology 2024

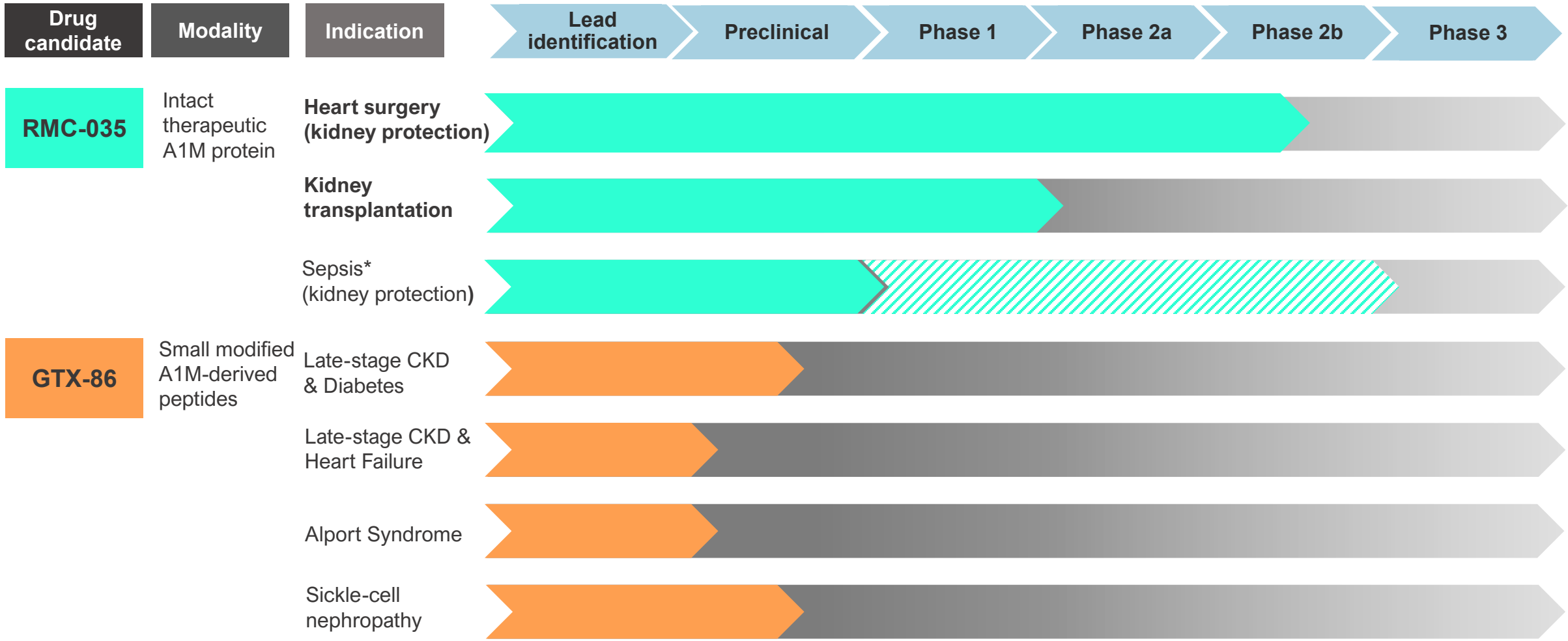
END-STAGE RENAL DISEASE (ESRD) – A DEVASTATING CONDITION WITH POOR OUTCOMES & SOARING HEALTHCARE COSTS

- Requires life-long dialysis treatment (or kidney transplantation)
- Annual mortality unacceptably high (15-20%)
  - Prognosis worse than many types of metastatic cancer
- High morbidity, poor quality of life
- Cost of patient management very high
  - Medicaid annual spend on ESRD treatment >**USD 50 bn**
  - ~7% of total Medicaid budget, although ESRD beneficiaries only account for ~1% of Medicaid population



P Stenvinkel and TE Larsson, Am J Kidney Dis, 2013 Aug;62(2):339-51; Francis et al, Nature Reviews Nephrology 2024; July 2024 Data Book: Health Care Spending and the Medicare Program – MedPAC

GUARD THERAPEUTICS PIPELINE



*Opportunity to initiate pivotal Phase 3 study in sepsis following results in ongoing Phase 2b study (*POINTER*) in open-heart surgery

A1M, alpha-1-microglobulin; CKD, chronic kidney disease

A1M ANALOGS TARGET COMMON & UNIVERSAL PATHWAYS OF ACUTE & CHRONIC KIDNEY DISEASE

Neutralize oxidative stress

- **Reductase activity**
  - Reduction of 5-6 free radicals per A1M molecule
- **Free radical trapping**
  - Covalent trapping of 3-4 radicals per A1M molecule

Neutralize free heme

- **Heme binding & degradation**
  - Two specific heme-binding sites (binds heme in a 2:1 molar ratio)

Protect mitochondria

- **Mitochondrial binding/stabilization**
  - Binding to Cytochrome C (Complex I)

Oxidative injury, hematuria (heme toxicity) & mitochondrial dysfunction are hallmarks of acute & chronic kidney disease

Bergwik et al, Front Physiol 2021

A1M, alpha-1-microglobulin

Therapeutic approach:

“Leverage endogenous A1M defense system”

A1M, alpha-1-microglobulin

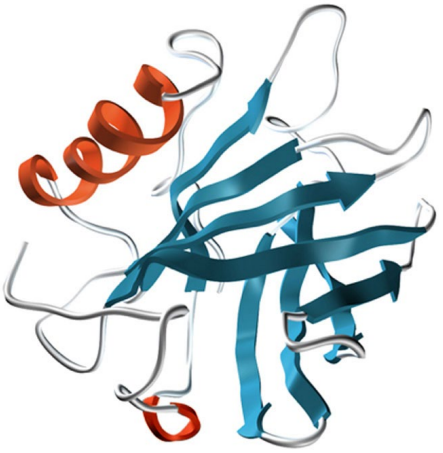
SYNERGY #1 – A1M TARGET HAS BROAD UTILITY IN KIDNEY DISEASE WITH PROVEN CLINICAL EFFICACY

Evolutionary conserved mechanism
– aligned with acute & chronic kidney disease mechanisms

Robust efficacy in numerous preclinical disease models
– provides translational confidence

Preferential biodistribution to the kidneys
– relevant exposure in target organ

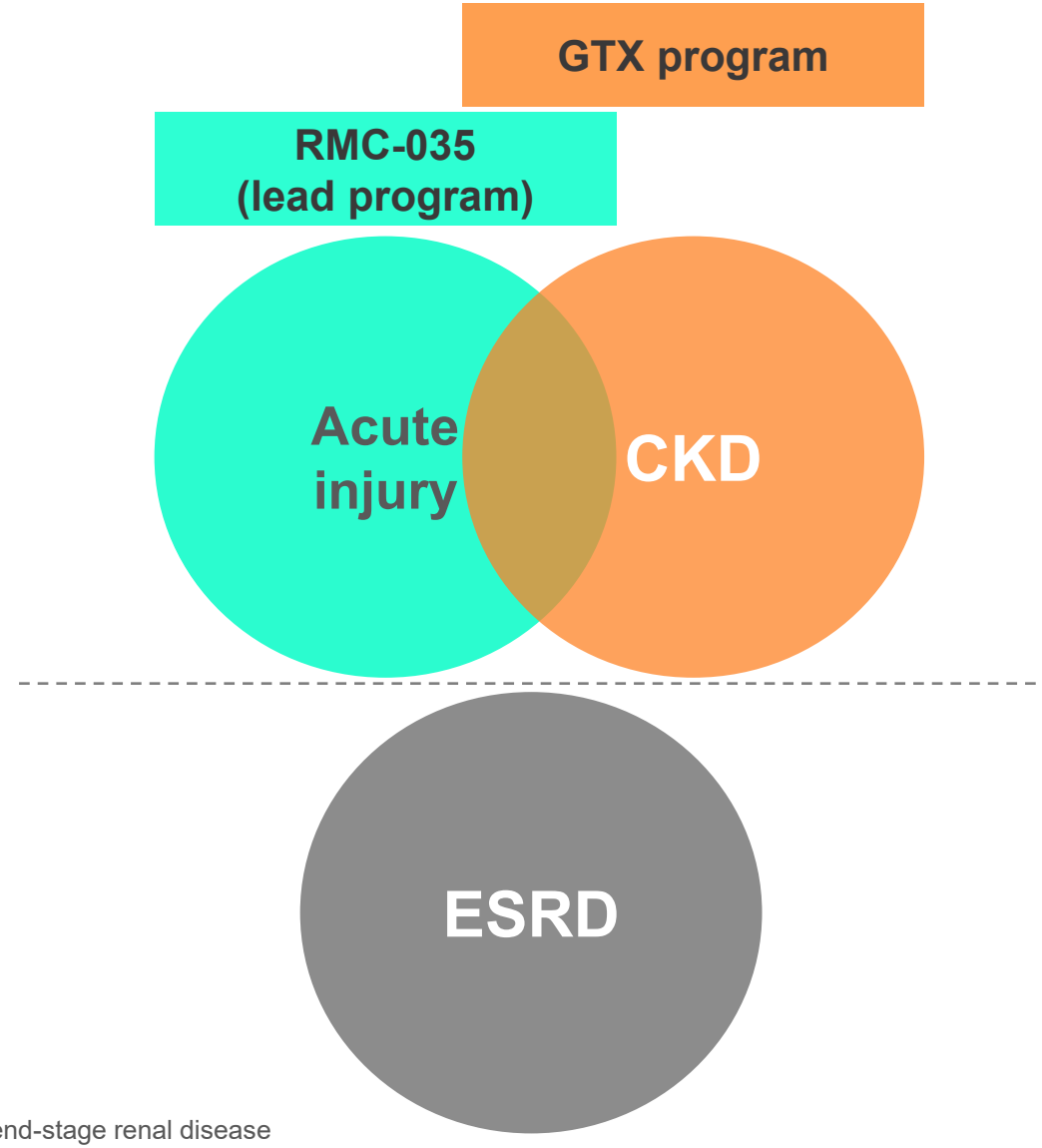
Clinically validated mechanism in Phase 2 study (n=177)
– established proof-of-concept for kidney protection in heart surgery



3-D structure of A1M

A1M, alpha-1-microglobulin; CKD, chronic kidney disease

SYNERGY #2 – PIPELINE TARGETS BOTH ACUTE & CHRONIC KIDNEY DISEASE TO REDUCE RISK OF ESRD



CKD, chronic kidney disease; ESRD, end-stage renal disease

Clinical results & late phase program

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PHASE 2 CLINICAL RESULTS DEMONSTRATE KIDNEY PROTECTION WITH RMC-035 IN HEART SURGERY

- Double-blind placebo-controlled Phase 2a study (*AKITA*) in open-heart surgery
  - N=177 patients at increased risk for kidney injury (1:1 randomization drug:placebo)

Key results:

- Statistically significant & clinically meaningful improvement of kidney function (Day 90)
  - 4.3 mL/min/1.73m^2 (full population)
  - 7.9 mL/min/1.73m^2 (pre-defined subgroup of patients with CKD)
- Reduced proportion of patients with severe loss of kidney function
  - 59% relative risk reduction for composite endpoint MAKE (death, dialysis, ≥ 25% eGFR loss)
  - MAKE is the anticipated primary endpoint in Phase 3

Results support progression to late phase development

Study ROS-05 Clinical Study Report; Thielmann et al., eClinical Medicine 2024

eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; MAKE, major adverse kidney events

PHASE 2b (*POINTER*) – RESULTS EXPECTED YEAR-END 2025

- Global study (US IND study), recruitment in Europe & Canada
- Sample size ~160 patients
  - 30% required to have CKD
- Two dose arms (60 & 30 mg) & Placebo (2:2:3 randomization)
- Data Monitoring Committee will review safety based on data from 1/3 & 2/3 of patients
- All regulatory & ethics approvals obtained
- **First patient enrolled in Q3 2024**
- Expected recruitment time ~1 year, 3 months follow-up

IND, investigational new drug; CKD, chronic kidney disease

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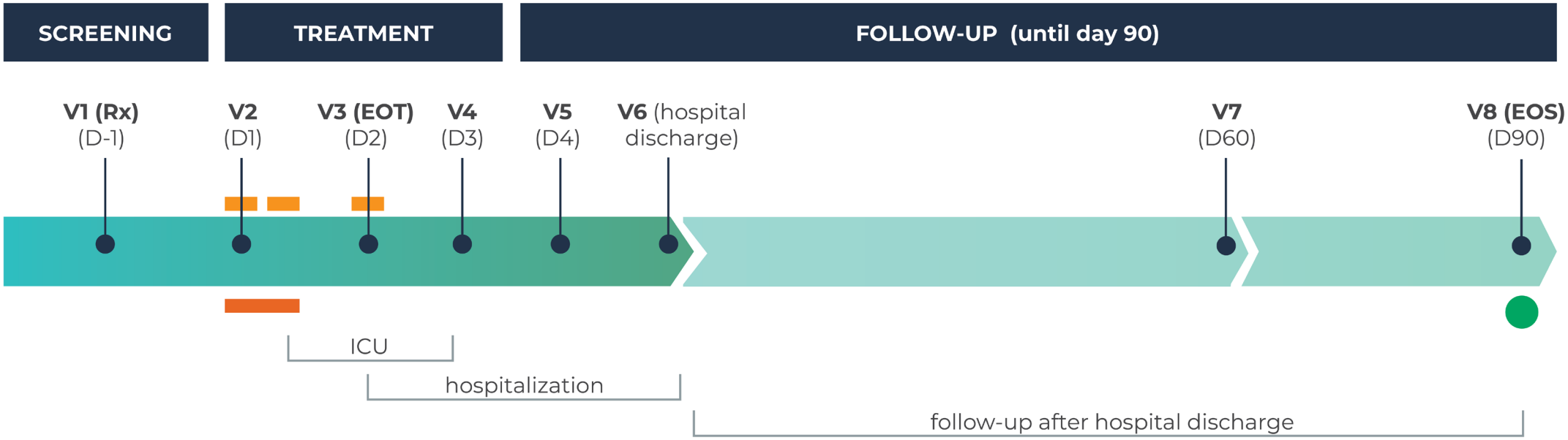
OVERVIEW OF PHASE 2b *POINTER* STUDY



Rx = randomization
EOT = end-of-treatment
EOS = end-of-study

- study visit
- administration of study drug
- cardiac surgery
- primary endpoint evaluation

Key endpoints:

Primary: change of renal function (eGFR) from baseline to Day 90

Secondary: MAKE90

ICU, intensive care unit; eGFR, estimated glomerular filtration rate; MAKE, major adverse kidney events

CLEAR PATH FOR RMC-035 TOWARDS MARKET APPROVAL

- **Fast Track Designation** granted by the US FDA
  - Indication eligible for **Breakthrough Therapy Designation**
- **Phase 2b POINTER results** expected year-end 2025
- **Single pivotal Phase 3 study** sufficient to support market approval
  - Primary endpoint is MAKE at Day 90 after surgery (~600 patients)
  - Potential for accelerated approval based on interim analysis of eGFR (~300 patients)

MAKE, major adverse kidney outcomes; eGFR, estimated glomerular filtration rate;

GTX peptides

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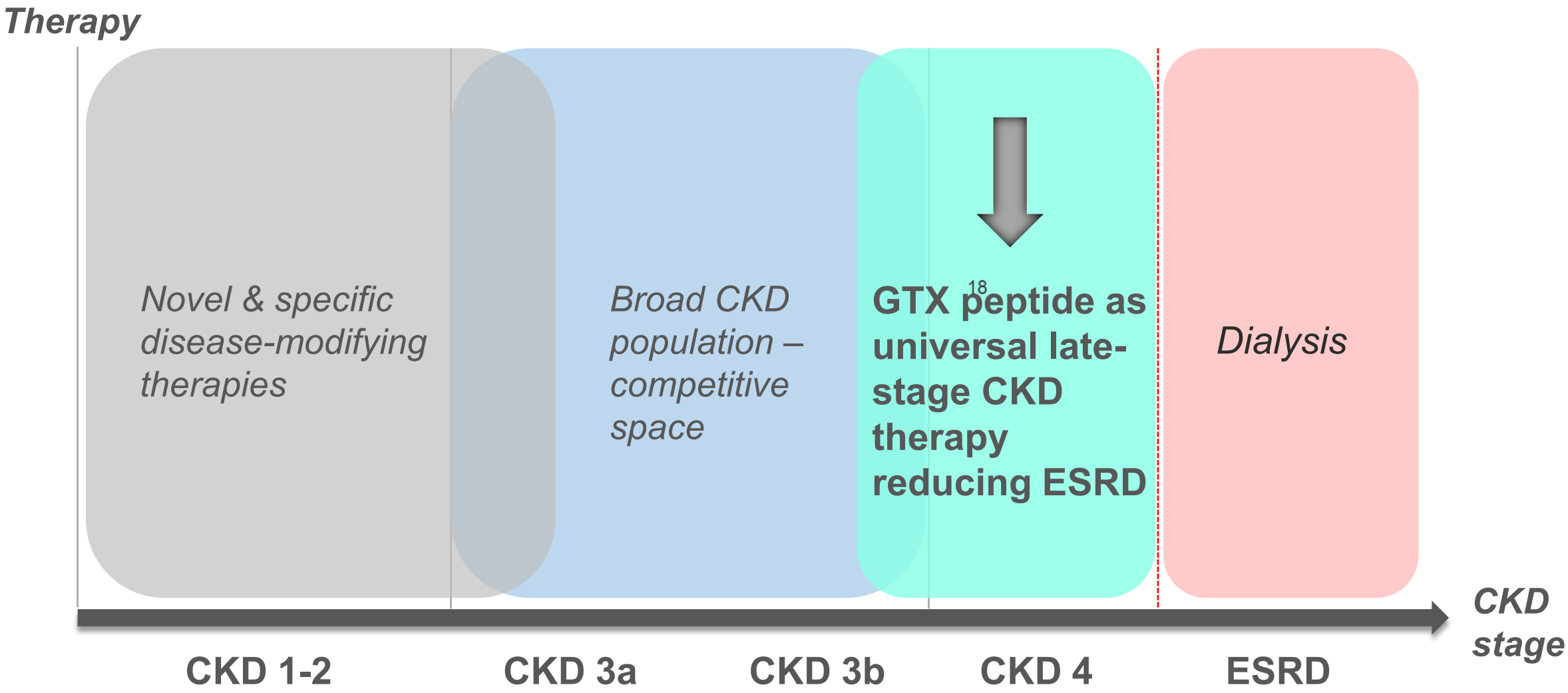
GTX PEPTIDES – OPPORTUNITY IN LATE-STAGE CKD

- GTX peptides enable **subcutaneous delivery & chronic treatment**
- Opportunity to improve patient outcomes regardless of underlying etiology
  - Efficacy shown in >10 disease models, supporting therapeutic concept
- **Late-stage CKD is an underserved patient group**
  - Highest risk for progression to ESRD
  - Often excluded from participation in clinical trials
  - Available CKD therapies frequently discontinued or contraindicated in this patient group
  - Not in scope for novel & specific disease-modifying therapies

Preventing ESRD in patients with late-stage CKD offers strong value proposition for patients, physicians & payors

CKD, chronic kidney disease; ESRD, end-stage renal disease

GTX PEPTIDES IN LATE-STAGE CKD OFFER A UNIQUE COMMERCIAL POSITIONING & STRONG VALUE PROPOSITION



CKD, chronic kidney disease; ESRD, end-stage renal disease; CKD classification based on Kidney Disease Improving Global Outcomes

SOLID IP POSITION

RMC-035

- Composition of matter until 2037
- Approved in all major regions (US, EU, China, Japan)

GTX

- Composition of matter until 2044
  - Currently in PCT phase
- Potential exclusivity beyond 2044 based on Orphan Drug Designation

IP, intellectual property; PCT, patent cooperation treaty

RECENT PHARMA DEALS SPOTLIGHT NEPHROLOGY AS HIGH-GROWTH THERAPEUTIC AREA

Vertex Pharmaceuticals Acquisition of Alpine Immune Sciences (2024)
Deal value **$4.9 billion**, driven by mid-stage drug candidate povetacicept targeting IgAN. Largest acquisition in biopharma 2024.

Biogen Acquisition of Human Immunology Biosciences (2024)
Deal value **$1.15 billion**, single asset (feltzartamab), Phase 2 data in IgAN, primary membranous nephropathy & antibody-mediated rejection

Asahi Kasei Acquisition of Calliditas (2024)
Deal value **$1.1 billion,** lead asset Tarpeyo (budesonide) for the treatment of IgAN.

Novartis' Acquisition of Chinook Therapeutics (2023)
Deal value **$3.5 billion**. This deal was primarily motivated by Chinook's strong pipeline in kidney disease, especially its two late-stage assets, atrasentan and zigakibart, both of which are being developed to treat IgAN.

AstraZeneca Acquisition of CinCor Pharma (2022)
Deal value **$1.8 billion**. Deal included baxdrostat, an aldosterone synthase inhibitor, for the treatment of uncontrolled hypertension and cardio-renal syndrome.

CSL's Acquisition of Vifor Phama (2021)
Deal value **$12.3 billion**, largely driven by product portfolio in the nephrology space.

Vifor Pharma Acquisition of Sanifit Therapeutics (2021)
Deal value **$205 million** upfront, with potential milestone payments. Lead asset focused on treatment for calciphylaxis, a rare and serious condition associated with CKD. This acquisition expanded Vifor's portfolio in nephrology.

NovoNordisk Acquisition of Corvidia Therapeutics (2020)
Deal value **$2.1 billion,** goal to strengthen its cardiovascular & renal disease pipeline. Corvidia was developing therapies for CKD patients, including ziltivekimab, a drug for CKD patients with cardiovascular risk.

GLOBAL MARKET OPPORTUNITY SUPPORTS BLOCKBUSTER POTENTIAL IN SEVERAL INDICATIONS

RMC-035

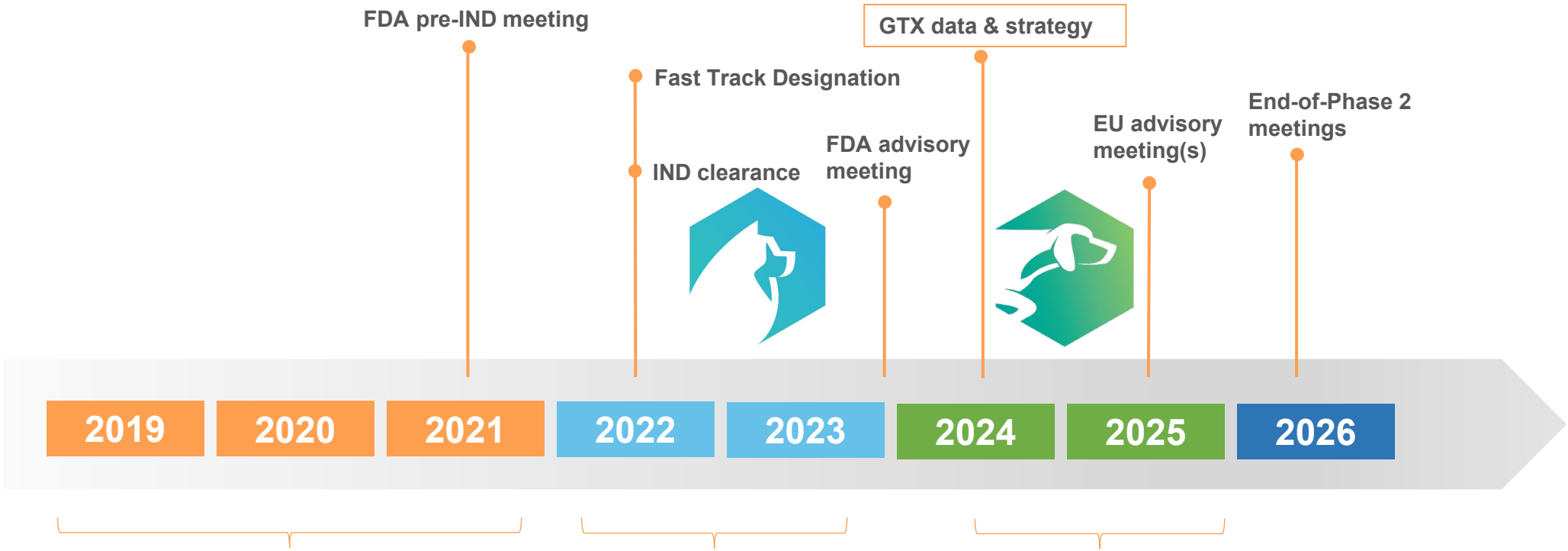
- Open-heart surgery: **>USD 1 bn**
- Total opportunity (including kidney transplantation & sepsis): **>USD 3 bn**

GTX

- Late-stage CKD: **>USD 5 bn**
- Orphan CKD: **>USD 3 bn**

CKD, chronic kidney disease

KEY MILESTONES & DELIVERY ACCORDING TO PLAN



Clinical Phase 1 program

- ✓ ROS-01 (single dose, healthy subjects)
- ✓ ROS-02 (multiple doses, healthy subjects)
- ✓ ROS-03 (renal impairment study)
- ✓ ROS-04 (safety/PK study in heart surgery)

Phase 2a *AKITA* study

- ✓ ROS-05 (proof-of-concept, heart surgery)

Phase 1b study

- ✓ ROS-06, kidney transplant

Phase 2b *POINTER* study

ROS-07 (dose-finding)

- ✓ First patient dosed

Phase 3 (*DOG NAME*) study

First clinical study with GTX peptide

Q & A

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