

Break-out session 2

# New CVRM: near-term opportunities

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Interactive event for investors and analysts. This webinar is being recorded.  
[https://astrazeneca.zoom.us/webinar/register/WN\\_3rpTdMKRnCkrhf2\\_ksHYA](https://astrazeneca.zoom.us/webinar/register/WN_3rpTdMKRnCkrhf2_ksHYA)



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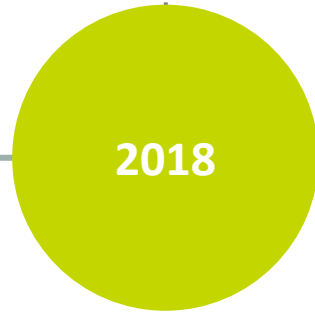


Farxiga

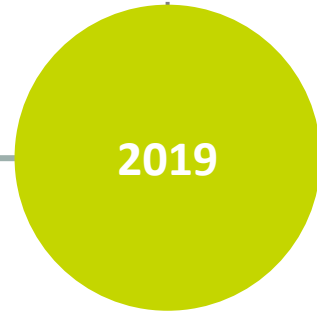
# Broad development programme beyond T2D<sup>1</sup>

**Farxiga**  
Building a new standard of care in cardiorenal disease

**DECLARE Phase III (T2D)**  
Positive cardiorenal benefit

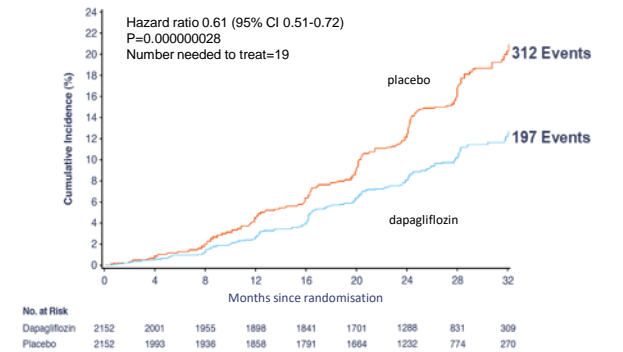
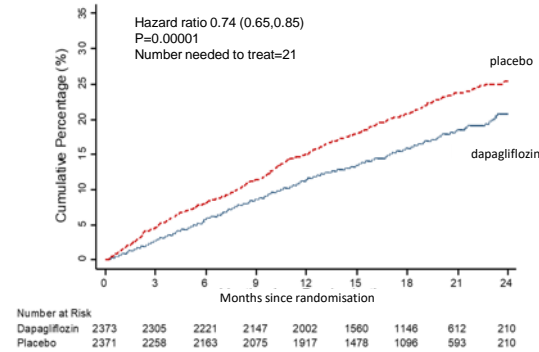
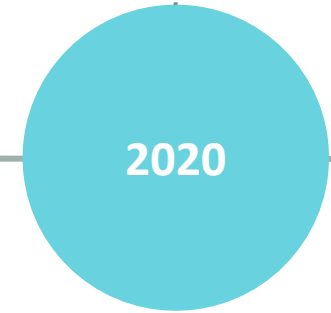


**DAPA-HF Phase III (HFrEF<sup>2</sup>)**  
26% risk reduction



**DAPA-CKD Phase III (CKD<sup>3</sup>)**  
Reduced the worsening of renal function or renal or CV<sup>4</sup> death by 39%<sup>5</sup>

**DAPA-HF Phase III (HFref<sup>2</sup>)**  
Approved in US, EU, JP and CN



1. Type-2 diabetes 2. Heart failure (NYHA class II-IV) with reduced ejection fraction in patients with and without T2D 3. Chronic kidney disease. In patients with and without T2D 4. Cardiovascular 5. Defined as a composite of a sustained  $\geq 50\%$  estimated glomerular filtration rate (eGFR) decline, onset of end-stage kidney disease and death from CV or renal cause. Compared to placebo ( $p < 0.0001$ ).



## New and upcoming milestones

### DAPA-CKD Phase III (CKD)

Regulatory decision US (H1 2021)  
EU, JP, CN (H2 2021)

### DELIVER Phase III (HFpEF<sup>1</sup>)

Data readout H2 2021

2021

### NEW trials

Phase III DAPA-MI<sup>2</sup>  
Achieved FPCD<sup>3</sup>

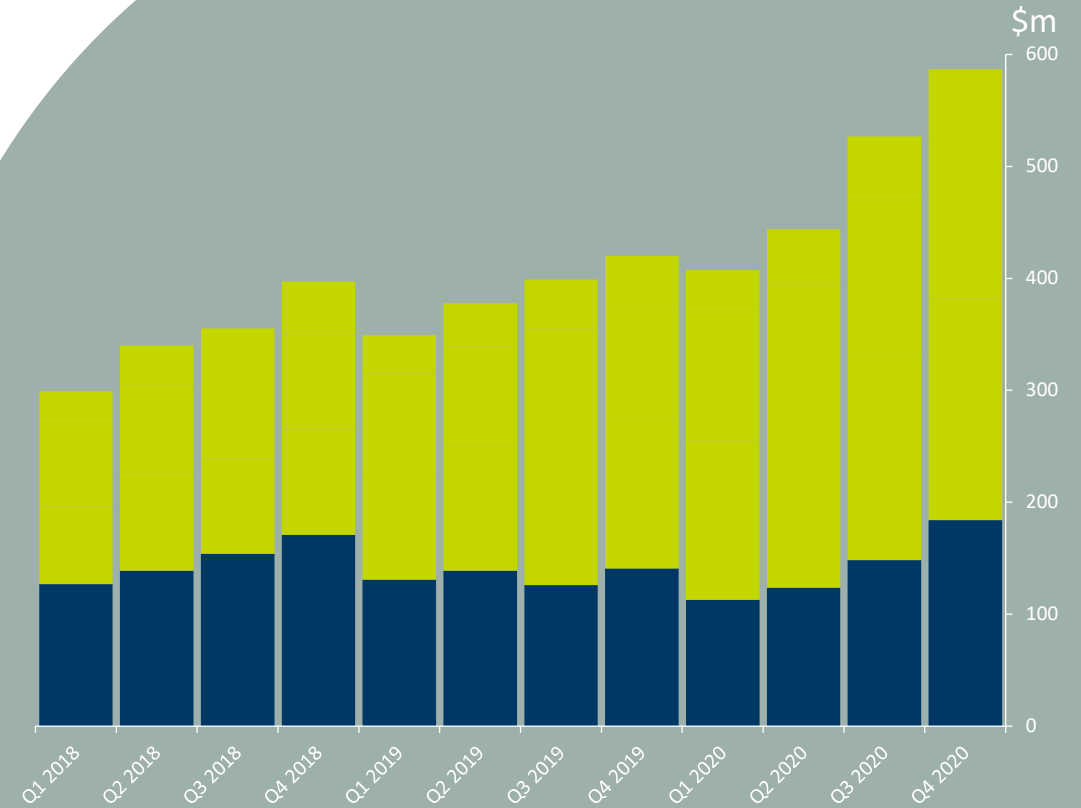
Phase II (CKD) AZD9977 +  
*Farxiga*  
H1 2021

### zibotentan + *Farxiga*

### AZD9977 + *Farxiga*

Data readout

2022+



~\$2 billion

FY 2020 revenue

71%

Revenue ex. US

US Ex. US

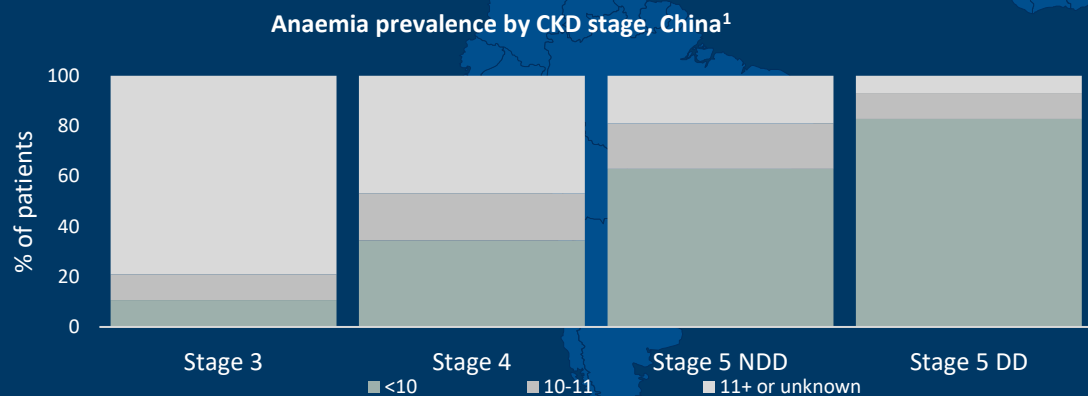
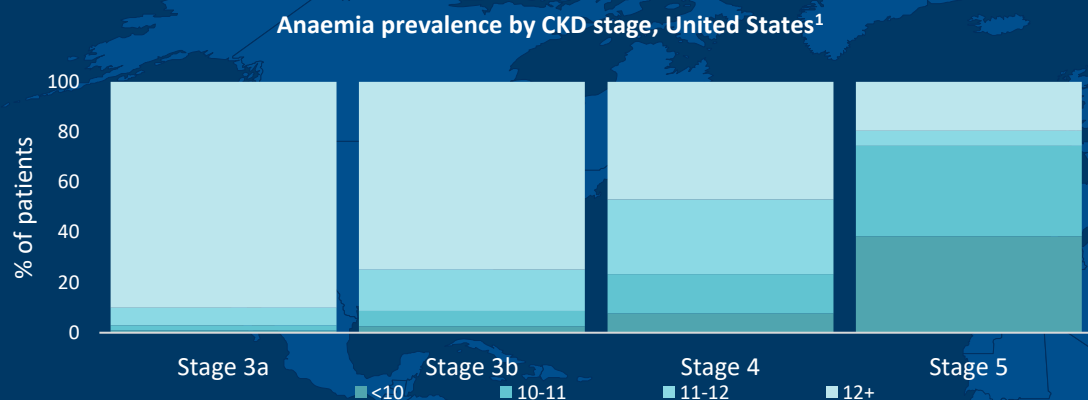
Total revenue at actual exchange rates.

1. Heart failure with preserved ejection fraction 2. Myocardial infarction 3. First patient commenced dosing.



# CKD affects c.840m adults worldwide

Silent, progressive, high-mortality disease; significantly underdiagnosed



>2 billion

People at risk of developing CKD<sup>2</sup>

c.840 million

Estimated people with CKD<sup>3</sup>

12%

Diagnosed with Stage 3 CKD<sup>4</sup>

+40%

Increase in dialysis, transplant or death<sup>5</sup>

## Approach

**Revolutionise:** early diagnosis of CKD

**Establish:** *Farxiga* as SoC<sup>6</sup> from prevention to treatment

**Transform:** management of complications with *Lokelma* and roxadustat

1. National Health and Nutrition Examination Survey (NHANES), AstraZeneca 2. Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, Zhao MH, Lv J, Garg AX, Knight J, Rodgers A, Gallagher M, Kotwal S, Cass A, Perkovic V. Worldwide access to treatment for end-stage kidney disease: a systematic review. *The Lancet*. 2015 May 16;385(9981):1975-82. doi: 10.1016/S0140-6736(14)61601-9. Epub 2015 Mar 13. PMID: 25777665 3. Kitty J Jager, Csaba Kovesdy, Robyn Langham, Mark Rosenberg, Vivekanand Jha, Carmine Zoccali, A single number for advocacy and communication - worldwide more than 850 million individuals have kidney diseases, *Nephrology Dialysis Transplantation*, Volume 34, Issue 11, November 2019, Pages 1803-1805, <https://doi.org/10.1093/ndt/gfz174> 4. Ravera M et al. *Am J Kidney Dis* 2011;57:71-77; 3; Ryan TP et al. *Am J Med*. 2007;120:981-986 5. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systemic analysis of the Global Burden of Disease Study 2017. Available at: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30045-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30045-3/fulltext) (Accessed Oct 2020) 6. Standard of care.



## Rapid and sustained potassium control for patients with hyperkalaemia

HK<sup>1</sup> is common in patients with chronic conditions<sup>2</sup>



**44%**

of patients with HK also had CKD

**22%**

of patients with HK also had HF<sup>3</sup>

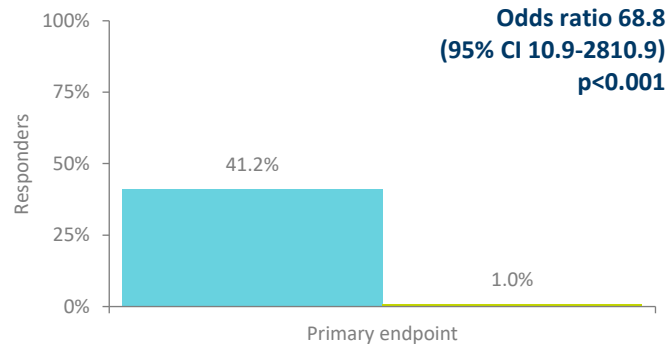
**58%**

of patients with HK were also, on RAASI<sup>4</sup> therapy

1. Hyperkalaemia 2. Retrospective analysis 3. Heart failure 4. Renin angiotensin aldosterone system inhibitor. Source: Betts KA et al. *Curr Med Res Opin.* 2018;34(6):971-978.

### DIALIZE Phase IIIb trial

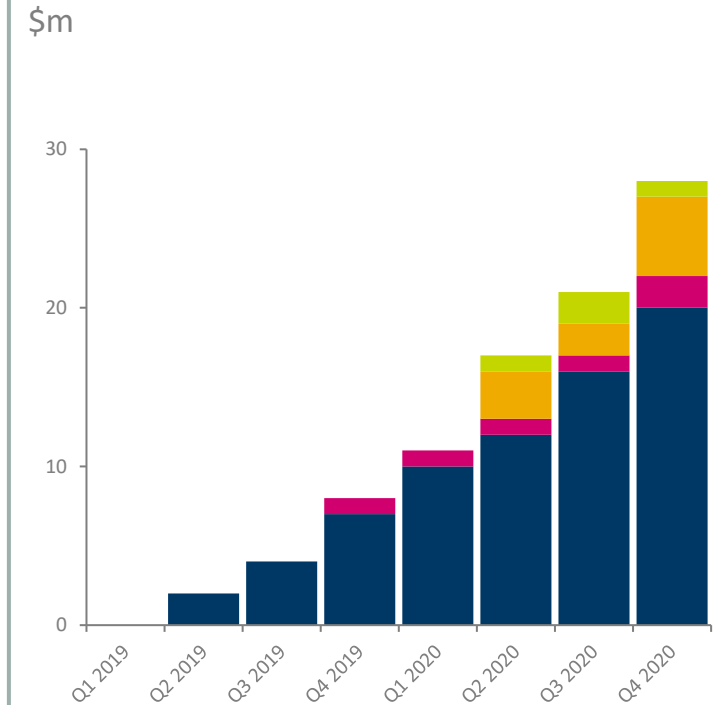
- The first randomised, placebo-controlled trial of a K<sup>+</sup> binder<sup>5</sup> in the treatment of HD<sup>6</sup> patients with HK



High efficacy in patients with normokalaemia 75% of the time

Lokelma Placebo  
5. Potassium binder.  
6. Haemodialysis.

### FY2020: Global \$76m; US \$57m



US market leadership helps expand market<sup>7</sup>

US Europe Established Rest of World Emerging Markets  
Total revenue at actual exchange rates. 7. Market leadership in new-to-medicine patients, IQVIA market research.



# Roxadustat<sup>1</sup>

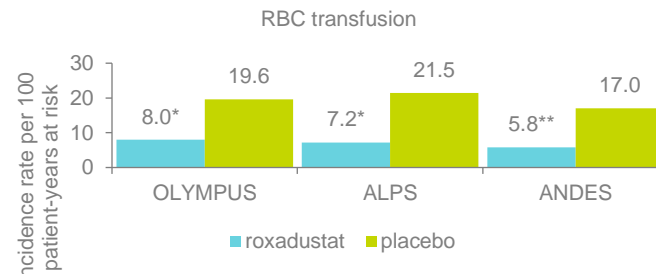
## Shifting the treatment paradigm for patients with anaemia from CKD

### Unique characteristics

- Leverages the body's natural response to hypoxia
- Consistent Hb<sup>2</sup> control across all patients<sup>3</sup>
- Reduction in RBC<sup>4</sup> transfusion risk
- Effect is independent of underlying inflammation
- Reduces the potential need for IV<sup>5</sup> iron
- Pooled analysis demonstrated CV safety
- Convenient oral administration

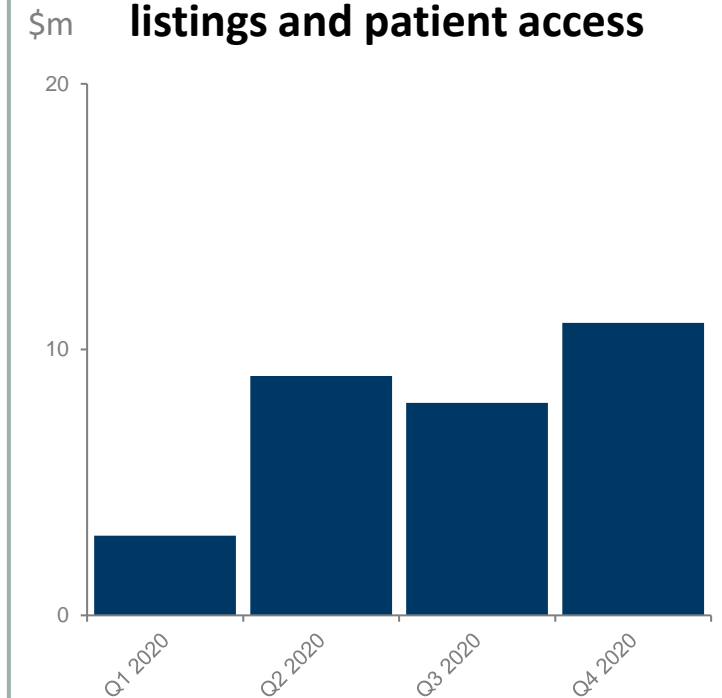
### Key data from ASN<sup>6</sup> 2020

- MACE<sup>7</sup>, MACE+<sup>8</sup>, and CV event rates were lowest at achieved Hb levels  $\geq 10$  g/dL, in DD<sup>9</sup> and NDD<sup>10</sup> CKD patients
- Reduced risk of hospitalisation for HF vs. ESA<sup>11</sup> in DD patients; consistent and large reduction in transfusion vs. placebo in NDD patients
- Not associated with an increased risk of neoplasm



\*p<0.001 vs. placebo. \*\* p<0.0001 vs. placebo using a Cox proportional hazards model. OLYMPUS: on-treatment +28 analysis. ALPS and ANDES: full analysis.

### China \$30m; focus on hospital listings and patient access



Next milestone: US FDA Cardiovascular and Renal Drugs Advisory Committee

1. Collaboration with FibroGen, Inc. 2. Haemoglobin 3. Non-dialysis dependant, incident dialysis, dialysis dependant 4. Red blood cell 5. Intravenous 6. American Society of Nephrology Kidney Week 2020.

7. All-cause mortality, myocardial infarction, and stroke 8. MACE plus HF or unstable angina requiring hospitalisation 9. Dialysis dependent 10. Non-dialysis dependent 11. Erythropoietin stimulating agents. Source: Abstract TH-OR05, ASN 2020.

China

Total revenue at actual exchange rates. FY 2020 \$73m in-market sales.



# Full pipeline and news flow

## Expanding *Farxiga* from T2D and HF to CKD

### New CVRM: near-term opportunities

Phase II	Phase III	Regulatory review
<b>roxadustat<sup>1</sup></b> HIF-PH <sup>2</sup> inhibitor chemo induced anaemia	<b>Farxiga DAPA-MI</b> SGLT <sup>3</sup> prevention of HF and CV death following a MI	<b>Farxiga DAPA-CKD</b> SGLT CKD
	<b>Farxiga DELIVER</b> SGLT HFpEF	
	<b>roxadustat<sup>1</sup></b> HIF-PH inhibitor anaemia MDS <sup>4</sup>	

### Upcoming milestones

#### H1 2021

- *Farxiga* - CKD: regulatory decision (US)

#### H2 2021

- *Forxiga* - CKD: regulatory decision (EU, JP, CN)
- *Farxiga* - HF (HFpEF): data readout
- roxadustat - anaemia in CKD: Advisory Committee, regulatory decision (US)

#### 2022

- *Farxiga* - HF (HFpEF): regulatory submission
- roxadustat - MDS: data readout, regulatory submission

Status as of 25 March 2021.

1. Collaboration with FibroGen, Inc. 2. Hypoxia-inducible factor prolyl hydroxylase 3. Sodium-glucose co-transporter-2 4. Anaemia in myelodysplastic syndrome.





# Questions & Answers

To ask a question

*Webinar*

Click 'Raise Hand' (preferred):



or type your question into the Q&A box  
(alternative)

*Phone*

\*6 - Toggle mute/unmute

\*9 - Raise hand



# Appendix



# Publications

<b>Farxiga</b>				
<b>Trial</b>	<b>Journal</b>	<b>Title</b>	<b>Author</b>	<b>Citation</b>
DAPA-CKD	<i>New England Journal of Medicine</i>	<a href="#">Dapagliflozin in Patients with Chronic Kidney Disease</a>	Heerspink, H.J.L et al.	<i>N Engl J Med</i> 2020; 383:1436-1446
DAPA-HF	<i>New England Journal of Medicine</i>	<a href="#">Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction</a>	McMurray, J.J.V et al.	<i>N Engl J Med</i> 2019; 381:1995-2008
DELIGHT	<i>The Lancet Diabetes &amp; Endocrinology</i>	<a href="#">Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT)</a>	Pollock, C et al.	<i>Lancet Diabetes Endocrinol</i> 2019; 7: 429–41
DECLARE-TIMI 58	<i>New England Journal of Medicine</i>	<a href="#">Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes</a>	Wiviott, S.D et al.	<i>N Engl J Med</i> 2019; 380:347-357
<b>Lokelma</b>				
Study 4, DIALIZE	<i>Journal of the American Society of Nephrology</i>	<a href="#">A Phase 3b, Randomized, Double-Blind, Placebo-Controlled Study of Sodium Zirconium Cyclosilicate for Reducing the Incidence of Predialysis Hyperkalemia</a>	Fishbane, S et al.	<i>JASN</i> September 2019, 30 (9) 1723-1733
Study 3	<i>Clinical Journal of the American Society of Nephrology</i>	<a href="#">Sodium Zirconium Cyclosilicate among Individuals with Hyperkalemia</a>	Spinowitz, B.S et al.	<i>CJASN</i> June 2019, 14 (6) 798-809
Study 2, HARMONIZE	<i>JAMA Network</i>	<a href="#">Effect of Sodium Zirconium Cyclosilicate on Potassium Lowering for 28 Days Among Outpatients With Hyperkalemia</a>	Kosiborod, M et al.	<i>JAMA</i> . 2014;312(21):22 23-2233
Study 1	<i>New England Journal of Medicine</i>	<a href="#">Sodium Zirconium Cyclosilicate in Hyperkalemia</a>	Packham, D.K et al.	<i>N Engl J Med</i> 2015; 372:222-231



# Publications, continued

Roxadustat				
Trial	Journal	Title	Author	Citation
OLYMPUS	<i>Journal of the American Society of Nephrology</i>	<a href="#">Roxadustat for Treating Anemia in Patients with CKD Not on Dialysis: Results from a Randomized Phase 3 Study</a>	Fishbane, S et al.	<i>JASN</i> March 2021, 32 (3) 737-755
Incident-dialysis patients	<i>Kidney International Reports</i>	<a href="#">Pooled Analysis of Roxadustat for Anemia in Patients With Kidney Failure Incident to Dialysis</a>	Provenzano, R et al.	<i>Kidney International Reports</i> Volume 6, Issue 3, March 2021, Pages 613-623
ALPS	<i>Nephrology Dialysis Transplantation</i>	<a href="#">Roxadustat for the treatment of anemia in chronic kidney disease patients not on dialysis: a phase 3, randomized, double-blind, placebo-controlled study (ALPS)</a>	Shutov, E et al.	<i>Nephrology Dialysis Transplantation</i> , gfab057
ANDES	<i>Kidney International Reports</i>	<a href="#">Roxadustat for CKD-related Anemia in Non-dialysis Patients</a>	Coyne, D.W et al.	<i>Kidney International Reports</i> , Clinical Research, Volume 6, Issue 3, P624-635, March 01, 2021
HIMALAYAS	<i>Nephrology Dialysis Transplantation</i>	<a href="#">Roxadustat for anemia in patients with end-stage renal disease incident to dialysis</a>	Provenzano, R et al.	<i>Nephrology Dialysis Transplantation</i> , gfab051



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