Investor science call: American Society of Nephrology Kidney Week 2019

Conference call for investors and analysts

10 November 2019
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Agenda

Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

Roxadustat Phase III ‘pooled’ safety and efficacy

Commercial opportunity

Q&A
### 2019: a very busy year for the pipeline
Investor science events in each therapy area

<table>
<thead>
<tr>
<th>Oncology</th>
<th>Cardiovascular, renal and metabolism</th>
<th>Respiratory (and immunology)</th>
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</thead>
<tbody>
<tr>
<td><strong>American Society of Clinical Oncology</strong> (Jun)</td>
<td><strong>European Society of Cardiology</strong> (Sep)</td>
<td><strong>American College of Rheumatology</strong> (Nov)</td>
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<tr>
<td>• Meet AZN management event(s)</td>
<td>• Conference call</td>
<td>• Conference call</td>
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<td>• Conference call</td>
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<tr>
<td><strong>European Society of Medical Oncology</strong> (Sep)</td>
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<tr>
<td>• Meet AZN management event(s)</td>
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<td>• Conference call</td>
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For AstraZeneca investor and analyst events, please visit [https://www.astrazeneca.com/investor-relations/results-and-presentations.html](https://www.astrazeneca.com/investor-relations/results-and-presentations.html).
Presenters

Elisabeth Bjork  
Senior Vice President, BioPharmaceuticals R&D, CVRM

John Houghton  
Global Medicines Leader, BioPharmaceuticals R&D, roxadustat

Joris Silon  
Senior Vice President, BioPharmaceuticals Business Unit, CVRM

Dr Steven Fishbane  
Zucker School of Medicine at Hofstra/Northwell, Great Neck, New York

Dr Robert Provenzano  
Associate clinical Professor of Medicine Wayne State University. Vice President, Medical Affairs, DaVita Inc.
Agenda

Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

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Q&A
Anaemia can be a serious medical condition; it is associated with increased risk of hospitalisation, cardiovascular (CV) complications and death.

200 million adult patients have chronic kidney disease (CKD) worldwide.
Roxadustat is a first in class hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor

**Past**

Patients were previously treated with transfusion-only care when iron supplementation was insufficient.

**Present**

CKD anaemia is currently characterised as erythropoietin (EPO) and iron deficiency.

Patients receive EPO supplements and extra iron to encourage erythrocyte production.
Future

Treating CKD anaemia enables the body to stimulate complete erythropoiesis.

Roxadustat has the potential to revolutionise the treatment paradigm of patients with anaemia from CKD.
Agenda

Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

Roxadustat Phase III ‘pooled’ safety and efficacy

Commercial opportunity

Q&A
Roxadustat Phase III ROCKIES trial
Design: Phase 3, Randomized, Open Label, Active Controlled

Patients with anemia of CKD on hemo- or peritoneal dialysis

R 1:1

Oral roxadustat TIW

Parenteral epoetin alfa

Dose titrated to Hb 11±1 g/dL

Dosed per prescribing information

Week
Visits

-6
Screening

1st wk

2

Every 2nd wk

20

Every 4th wk

EOT

EOS

Period

Screening

(6 wks)

Treatment (up to 4 y)

Follow-up

(4 wks)

Study end depended on number of CV events

CKD, chronic kidney disease; CV, cardiovascular; EOS, end of study; EOT, end of treatment; Hb, hemoglobin; R, randomization; TIW, three times weekly; wk, week(s)
Patient Disposition

Patients enrolled N=2941

Patients randomized N=2133

Roxadustat n=1068

Received Tx n=1048

Completed Tx n=696 (66%)

Discontinued Tx n=352
  Pt decision 135
  AE 54
  Severe non-compliance 6
  Met discontinuation criteria 32
  Other 125

Completed study n=982 (94%)

Life or death confirmed: 99.5%

Study withdrawal n=69
  Pt decision 67
  Missing 2

Epoetin alfa n=1065

Received Tx n=1053

Completed Tx n=796 (76%)

Discontinued Tx n=257
  Pt decision 88
  AE 22
  Severe non-compliance 3
  Other 142
  Missing 2

Study withdrawal n=65
  Pt decision 64
  Incorrect enrolment 1

Completed study n=990 (94%)

Life or death confirmed: 99.4%

Excluded from analysis due to GCP violations n=17

Excluded from analysis due to GCP violations n=10

AE, adverse event; GCP, good clinical practice; Pt, patient; Tx, treatment
Primary Efficacy Endpoint for US: Hb Change from Baseline to Average Hb in Weeks 28–52

Adjusted LSM (95% CI)

Hb change from baseline (g/dL)

Roxadustat (n=1003)

Epoetin alfa (n=1016)

0.77

0.68

P=0.036

Intent-to-treat analysis set. Error bars are 95% confidence intervals.

CI, confidence interval; Hb, hemoglobin; LSM, least squares mean; US, United States.
## Adverse Events in the Population*

<table>
<thead>
<tr>
<th>AE category</th>
<th>Roxadustat (N=1048)</th>
<th>Epoetin alfa (N=1053)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N pts w/ event</td>
<td>%</td>
</tr>
<tr>
<td>Any AE</td>
<td>891</td>
<td>85.0</td>
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<tr>
<td>Any AE leading to discontinuation of drug</td>
<td>57</td>
<td>5.4</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>604</td>
<td>57.6</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>167</td>
<td>15.9</td>
</tr>
</tbody>
</table>

*Followed on-treatment and for 28 days off-treatment

AE, adverse event; pts, patients; P-Y, patient years; w/, with
Common AEs and SAEs in the Population*

<table>
<thead>
<tr>
<th>AE category</th>
<th>Roxadustat (N=1048)</th>
<th>Epoetin alfa (N=1053)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N pts w/ event</td>
<td>%</td>
</tr>
<tr>
<td><strong>Most reported AEs</strong></td>
<td></td>
<td></td>
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<tr>
<td>Diarrhea</td>
<td>117</td>
<td>11.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>92</td>
<td>8.8</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>91</td>
<td>8.7</td>
</tr>
<tr>
<td>Headache</td>
<td>82</td>
<td>7.8</td>
</tr>
<tr>
<td>Arteriovenous fistula thrombosis</td>
<td>78</td>
<td>7.4</td>
</tr>
<tr>
<td><strong>Most reported SAEs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>70</td>
<td>6.7</td>
</tr>
<tr>
<td>Sepsis</td>
<td>40</td>
<td>3.8</td>
</tr>
<tr>
<td>Acute MI</td>
<td>39</td>
<td>3.7</td>
</tr>
<tr>
<td>Arteriovenous fistula thrombosis</td>
<td>37</td>
<td>3.5</td>
</tr>
</tbody>
</table>

*Followed on-treatment and for 28 days off-treatment

AE, adverse event; FAIR, follow-up adjusted incidence rate; MI, myocardial infarction; pts, patients; P-Y, patient years; SAE, serious adverse event, w/, with
Roxadustat Phase III OLYMPUS trial
**Design: Phase 3, Double-Blind, Randomized**

- **Hb <10 g/dL with Stage 3, 4 or 5 CKD not on dialysis**
  - Randomization (R 1:1)
  - Oral roxadustat
  - Oral placebo

- **Screening** (6 wks)
- **Treatment (up to 4 years)**
  - (Study end date depended on number of CV events)
- **Follow-up** (4 wks)

- **Weeks**
  - -6
  - 2
  - 20
  - 52
  - EOT
  - EOS

- **Visits**
  - Screening
  - 1st wk
  - Every 2nd wk
  - Every 4th wk
  - Every 8th wk

- **Started at 70 mg TIW, titrated to Hb 10–12 g/dL**

**KDD, chronic kidney disease; CV, cardiovascular; EOS, end of study; EOT, end of treatment; Hb, hemoglobin; R, randomization; TIW, three times weekly; wk, week(s)**
Patients enrolled: N=5222

Patients randomized: n=2781

Roxadustat: n=1393

Placebo: n=1388

Received Tx: n=1384

Completed TX: n=575 (42%)

Completed study: n=1247 (91%)

Patients who discontinued treatment were followed for concomitant medications, adverse events, vital status and hospitalization. GCP, good clinical practice; Pt, patient; Tx, treatment
Primary Efficacy Endpoint for US: Change in Hemoglobin from Baseline to the Average Over Weeks 28–52

Adjusted LSM change in Hb (g/dL)

Roxadustat (n=1334) 1.75 ± 0.40
Placebo (n=1330) 0.40 ± 0.20

P<0.001

Intent-to-treat analysis set. Error bars are 95% confidence intervals
Hb, hemoglobin; LSM, least squares mean
## Adverse Events (ITT*)

<table>
<thead>
<tr>
<th>OLYMPUS Events</th>
<th>Roxadustat (N=1384)</th>
<th>Placebo (N=1377)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N pts w/ event</td>
<td>% N per 100 P-Y†</td>
<td>N pts w/ event</td>
</tr>
<tr>
<td>Any AE</td>
<td>1243 89.8 182.9</td>
<td>1216 88.3 171.9</td>
</tr>
<tr>
<td>Any AE leading to discontinuation of drug</td>
<td>78 5.6 2.8</td>
<td>57 4.1 2.1</td>
</tr>
<tr>
<td>Any serious AE</td>
<td>795 57.4 42.1</td>
<td>749 54.4 40.0</td>
</tr>
<tr>
<td>All-cause mortality‡</td>
<td>284 20.5 9.6</td>
<td>245 17.8 8.4</td>
</tr>
</tbody>
</table>

*ITT analysis; includes events on-treatment + off-treatment until study end date. †N per 100 P-Y calculated by FAIR
‡Includes deaths from adverse events and public record searches

### Pooled data from non-dialysis patients (Phase 3: OLYMPUS, ANDES, ALPS)

<table>
<thead>
<tr>
<th></th>
<th>Roxadustat (N=2386)</th>
<th>Placebo (N=1884)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality‡</td>
<td>400 16.8 8.3</td>
<td>301 16.0 8.1</td>
</tr>
</tbody>
</table>

AE, adverse event; FAIR, follow-up adjusted incidence rate; ITT, intent-to-treat; pts, patients; P-Y, patient years; w/, with
# Common Adverse Events (ITT*)

<table>
<thead>
<tr>
<th>AE category</th>
<th>Roxadustat (N=1384)</th>
<th>Placebo (N=1377)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N pts w/ event</td>
<td>%</td>
</tr>
<tr>
<td>Most reported AEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End stage renal disease</td>
<td>209</td>
<td>21.0</td>
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<tr>
<td>Urinary tract infection</td>
<td>177</td>
<td>12.8</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>165</td>
<td>11.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>159</td>
<td>11.5</td>
</tr>
<tr>
<td>Most reported SAEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End stage renal disease</td>
<td>199</td>
<td>14.4</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>113</td>
<td>8.2</td>
</tr>
<tr>
<td>Azotemia</td>
<td>61</td>
<td>4.4</td>
</tr>
<tr>
<td>Sepsis</td>
<td>49</td>
<td>3.5</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>41</td>
<td>3.0</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>41</td>
<td>3.0</td>
</tr>
</tbody>
</table>

*ITT analysis; includes events on-treatment + off-treatment in long term follow-up until study end date
†N per 100 P-Y calculated by FAIR

AE, adverse event; FAIR, follow-up adjusted incidence rate; ITT, intent-to-treat; pts, patients; P-Y, patient years; w/, with
Conclusions for both trials

**ROCKIES**

- Compared with epoetin alfa, roxadustat:
  - Increased Hb at least as effectively in dialysis patients with anaemia
  - Increased Hb more effectively in those with inflammation
  - Required significantly less monthly IV iron use
  - Lowered hepcidin to a greater extent
  - Common adverse events with roxadustat were generally similar to those of epoetin alfa and commonly found in dialysis-dependent patients

**OLYMPUS**

- Compared with placebo, roxadustat treatment:
  - Significantly increased Hb levels
    - regardless of iron-repletion
    - regardless of inflammation
  - Reduced the need for rescue therapy, including red blood cell (RBC) transfusion
  - More patients on placebo discontinued study drug earlier than roxadustat, especially in patients with more advanced CKD (lower eGFR\(^1\))
  - Overall safety findings are generally consistent with the patient population
  - Risks and benefits of roxadustat will be determined across all trials in the development program


Oral Presentation #TH-OR023, OLYMPUS: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, International Study of Roxadustat Efficacy in Patients with Non-Dialysis-Dependent (NDD) Chronic Kidney Disease (CKD) and Anemia, ASN Kidney Week 2019, Washington D.C., US. 1. glomerular filtration rate
Agenda

Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

Roxadustat Phase III ‘pooled’ safety and efficacy

Commercial opportunity

Q&A
Roxadustat Phase III ‘pooled’ safety and efficacy
### Phase 3 CKD non-dialysis-dependent (NDD) Pool

<table>
<thead>
<tr>
<th>Study</th>
<th>Sponsor 1</th>
<th>Sponsor 2</th>
<th>Sponsor 3</th>
<th>Treatment 1</th>
<th>Treatment 2</th>
<th>N</th>
<th>Avg PEY</th>
</tr>
</thead>
<tbody>
<tr>
<td>D5740C00001</td>
<td>FGCL-4592-060</td>
<td>1517-CL-0608</td>
<td>NDD Pooled</td>
<td>Roxadustat</td>
<td>Placebo</td>
<td>2761</td>
<td>1.62</td>
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<td>OLYMPUS</td>
<td>ANDES</td>
<td>ALPS</td>
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<td>922</td>
<td>1.23</td>
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<td>AstraZeneca</td>
<td>FibroGen</td>
<td>Astellas</td>
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<td>N=2761</td>
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<td></td>
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<td>2391</td>
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<td>R 1:1</td>
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<td>1886</td>
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**Number of patients:** 4277  
**Patient exposure years:** 6194

### Phase 3 CKD dialysis-dependent (DD) Pool

<table>
<thead>
<tr>
<th>Study</th>
<th>Sponsor 1</th>
<th>Sponsor 2</th>
<th>Sponsor 3</th>
<th>Treatment 1</th>
<th>Treatment 2</th>
<th>N</th>
<th>Avg PEY</th>
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<tbody>
<tr>
<td>D5740C00002</td>
<td>FGCL-4592-064</td>
<td>FGCL-4592-063</td>
<td>DD Pooled</td>
<td>Roxadustat</td>
<td>EPO</td>
<td>2106</td>
<td>1.71</td>
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<td>ROCKIES</td>
<td>SIERRAS</td>
<td>HIMALAYAS</td>
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<td>741</td>
<td>1.92</td>
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<td>AstraZeneca</td>
<td>FibroGen</td>
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<td>Global</td>
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<td>N=2106</td>
<td>N=741</td>
<td>N=1043</td>
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<td>Correction &amp; maintenance</td>
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<td>Early &amp; Stable DD</td>
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</tbody>
</table>

**Number of patients:** 3880  
**Patient exposure years:** 7059

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EPO, epoetin alfa; Hb, hemoglobin; PEY, patient exposure year; R, Randomization, Roxa, roxadustat
Roxadustat NDD Program: Evaluation of Anemia Therapy In A Broad Range of Patients Not Included In Prior CKD Anemia Trials

**Roxadustat NDD Patient Features**
- Advanced CKD: 42% CKD 5
- Low Iron stores: 40% non-iron replete
- Low Mean Baseline Hb: 9.1

**Graphic comparison of patients baseline Hb/eGFR of roxadustat NDD vs historical studies***

*Historical study patients baseline Hb & eGFR characteristics in figure is based on approximations from published manuscripts eGFR, estimated glomerular filtration rate
NDD Efficacy: Met Primary Efficacy Endpoint
Roxadustat is superior to placebo, regardless of iron-repletion

Primary efficacy endpoint (change in Hb from baseline to Hb averaged over Weeks 28–52) was met in individual studies and pooled analyses

Hb change from baseline to Week 28–52
Studies: ANDES, ALPS, OLYMPUS

<table>
<thead>
<tr>
<th>Individual Study</th>
<th>LS mean (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDES</td>
<td>1.85 (1.74, 1.97)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALPS</td>
<td>1.69 (1.52, 1.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OLYMPUS</td>
<td>1.35 (1.27, 1.43)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Iron Replete: TSAT ≥20% and ferritin ≥100 ng/mL
CI, confidence interval; LS, least squares; SE, standard error

NDD (N=4277): Mean Hb over time up to Week 52 (g/dL)
Hb change to Week 28–52: 1.85 (Roxa) vs 0.13 (Placebo) P<0.001

Mean Hb (g/dL) ± SE

ΔHb (g/dL)

Mean change from baseline Hb (g/dL)

Iron replete*

<table>
<thead>
<tr>
<th>Roxadustat (n=1433)</th>
<th>Placebo (n=1127)</th>
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</thead>
<tbody>
<tr>
<td>1.94</td>
<td>0.13</td>
</tr>
<tr>
<td>P&lt;0.001</td>
<td></td>
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</tbody>
</table>

Iron non-replete

<table>
<thead>
<tr>
<th>Roxadustat (n=956)</th>
<th>Placebo (n=755)</th>
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</thead>
<tbody>
<tr>
<td>1.94</td>
<td>0.33</td>
</tr>
<tr>
<td>P&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Baseline Hb = 9.1 g/dL

NDD (N=4277): Mean Hb over time up to Week 52 (g/dL)
Mean Hb (g/dL)

*Iron Replete: TSAT ≥20% and ferritin ≥100 ng/mL
CI, confidence interval; LS, least squares; SE, standard error
**Primary efficacy endpoint (change in Hb from baseline to Hb averaged over Weeks 28 to 52): Roxadustat achieved larger Hb increase over epoetin alfa in individual studies & in pooled DD**

<table>
<thead>
<tr>
<th>Group</th>
<th>Hb (g/dL) Change from Baseline to Week 28–52</th>
<th>DD (N=3857): Mean Hb (g/dL) Over Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Individual Studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROCKIES</td>
<td></td>
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<tr>
<td>HIMALAYAS</td>
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</tr>
<tr>
<td>SIERRAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Roxadustat</strong></td>
<td>0.090 (0.010, 0.180) <em>P</em>=0.036</td>
<td>Mean Hb (g/dL) ± SE: 11.4</td>
</tr>
<tr>
<td><strong>Epoetin alfa</strong></td>
<td>0.180 (0.079, 0.287) <em>P</em>&lt;0.001</td>
<td>∆Hb = 1.22 (Roxa) vs 0.99 (Epoetin alfa)</td>
</tr>
<tr>
<td></td>
<td>0.480 (0.365, 0.591) <em>P</em>&lt;0.001</td>
<td><em>P</em>&lt;0.001</td>
</tr>
</tbody>
</table>

---

CRP, C-reactive protein; EPO, epoetin alfa
**"comparable" based on hazard ratio (HR) upper bound of 95% confidence interval (95%CI) below reference non-inferiority margin of 1.3

**ITT analysis = Intent to treat analysis evaluation period to include on-treatment and off-treatment long term follow-up, until end of study
**DD Pooled: Cardiovascular Safety Endpoints**

- Risk of MACE and all cause mortality in roxadustat patients were not increased compared to epoetin alfa in DD patients*
- Roxadustat patients had a lower risk of MACE+ than epoetin alfa patients

### MACE+ Components Incidence Rates, N (%)

<table>
<thead>
<tr>
<th>Events</th>
<th>Events</th>
<th>Roxadustat</th>
<th>Epoetin alfa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>1940</td>
<td>1940</td>
</tr>
<tr>
<td>Death (all-cause mortality)</td>
<td></td>
<td>207 (10.7%)</td>
<td>232 (12.0%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td>103 (5.3%)</td>
<td>109 (5.6%)</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td>45 (2.3%)</td>
<td>50 (2.6%)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td></td>
<td>18 (0.9%)</td>
<td>22 (1.1%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td></td>
<td>120 (6.2%)</td>
<td>166 (8.6%)</td>
</tr>
</tbody>
</table>

**Time to event endpoints using Cox model, on-treatment analysis DD (ROCKIES, HIMALAYAS, SIERRAS), N=3880**

- MACE: HR (95% CI) 0.96 (0.82, 1.13)
- MACE+: HR (95% CI) 0.86 (0.74, 0.98) \(P=0.028\)
- All Cause Mortality: HR (95% CI) 0.96 (0.79, 1.17)

*“risk not increased” based on hazard ratio (HR) upper bound of 95% confidence interval (95%CI) below reference non-inferiority margin of 1.3
Roxadustat had 30% lower risk of MACE and 34% lower risk of MACE+ than epoetin alfa* and with a trend towards lower all-cause mortality relative to epoetin alfa, in incident dialysis patients.

**Incident Dialysis Pool: Cardiovascular Safety Endpoints**

**Proportion of Patients Without MACE+ Over Time**

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Roxadustat</th>
<th>Epoetin alfa</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>0.65</td>
<td>0.70</td>
</tr>
<tr>
<td>6</td>
<td>0.62</td>
<td>0.63</td>
</tr>
<tr>
<td>9</td>
<td>0.58</td>
<td>0.60</td>
</tr>
<tr>
<td>12</td>
<td>0.53</td>
<td>0.55</td>
</tr>
<tr>
<td>18</td>
<td>0.48</td>
<td>0.49</td>
</tr>
<tr>
<td>24</td>
<td>0.44</td>
<td>0.45</td>
</tr>
<tr>
<td>30</td>
<td>0.40</td>
<td>0.40</td>
</tr>
<tr>
<td>36</td>
<td>0.36</td>
<td>0.36</td>
</tr>
<tr>
<td>42</td>
<td>0.32</td>
<td>0.32</td>
</tr>
<tr>
<td>48</td>
<td>0.28</td>
<td>0.28</td>
</tr>
<tr>
<td>54</td>
<td>0.24</td>
<td>0.24</td>
</tr>
</tbody>
</table>

**Time to event endpoints using Cox model**

- **MACE**
  - HR (95% CI): 0.70 (0.51, 0.96)
  - P = 0.029
- **MACE+**
  - HR (95% CI): 0.66 (0.50, 0.89)
  - P = 0.005
- **All Cause Mortality**
  - HR (95% CI): 0.76 (0.52, 1.11)

**Incident Dialysis (ROCKIES, HIMALAYAS, SIERRAS), N=1526**

<table>
<thead>
<tr>
<th>Incident Dialysis</th>
<th>MACE+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roxadustat (n=760)</td>
<td>88</td>
</tr>
<tr>
<td>Epoetin alfa (n=766)</td>
<td>121</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># of patients with MACE+/100 PEY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roxadustat (8.0)</td>
</tr>
</tbody>
</table>

Epoetin alfa 699 605 511 401 316 246 171 111 50 24 0
Roxadustat 673 594 495 389 304 223 137 87 43 16 0

*Lower MACE & MACE+ risks – based on incident dialysis*
Conclusions: *Efficacy*

- **Roxadustat efficacy was demonstrated**
  - Achieved primary efficacy endpoint (change in Hb) in individual studies and pooled analyses
    - **NDD:** roxadustat was superior to placebo and efficacious regardless of iron-repletion
    - **DD:** roxadustat achieved larger mean Hb increase than epoetin alfa, especially in inflamed patients, and less IV iron was required in roxadustat arm than in epoetin alfa.
  - **Lower RBC transfusion risk**
    - **NDD:** In roxadustat patients compared with placebo
    - **DD:** In roxadustat patients compared with epoetin alfa
  - **Other potential benefits in NDD**
    - Reduced LDL cholesterol
    - Less decline in eGFR
Conclusions: **Roxadustat CV Safety**

- **CV safety was demonstrated in all study populations**
  - **Non-dialysis:** Risk of MACE, MACE+, and all-cause mortality in roxadustat patients were comparable to placebo in NDD patients
  - **Incident dialysis:** Roxadustat had 30% lower risk of MACE and 34% lower risk of MACE+ than epoetin alfa, and with a trend towards lower all-cause mortality relative to epoetin alfa
  - **Dialysis-dependent:**
    - Roxadustat patients had a lower risk of MACE+ than epoetin alfa patients
    - Risk of MACE and all-cause mortality in roxadustat patients were not increased compared to epoetin alfa in DD patients
Agenda

Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

Roxadustat Phase III ‘pooled’ safety and efficacy

Commercial opportunity

Q&A
How does roxadustat compare to currently approved treatments for anaemia from CKD in NDD or DD patients?
How do you see roxadustat fitting into or potentially changing the CKD treatment paradigm?
What factors will enable more patients, who require treatment of anaemia from CKD in NDD or DD, to benefit from roxadustat in the future?
Chronic kidney disease
The prevalence of anaemia increases as the disease progresses

30 million
US prevalence of patients with CKD

19 million
US prevalence of patients with CKD (Stage 3-5)

4 million
US diagnosed patients with anaemia from CKD

2 million
US treated patients with anaemia from CKD

120 million
China prevalence of patients with CKD

39 million
China prevalence of patients with CKD (Stage 3-5)

3 million
China diagnosed patients with anaemia from CKD

1.5 million
China treated patients with anaemia from CKD

Source: 1. National Health and Nutrition Examination Survey (NHANES), AstraZeneca. 2. NHANES, United States Renal Data System (USRDS), Decision Resources, Adelphi DSP, IMS data analysis and Beijing Renmin Hospital. 3. Stage 3-5. 4. Iron or ESA. 5. Hb <11 g/dL
US regulatory submission in Q4 2019

Roxadustat

Consistent Hb control across all patients\(^1\text{-}^6\)

Effect is independent of underlying inflammation\(^1, 7\)

Reduces the potential need for IV iron administration\(^3\)

Demonstrated CV safety in pooled analysis\(^8\text{-}^9\)

Agenda

Unmet medical need

Roxadustat Phase III OLYMPUS and ROCKIES trials

Roxadustat Phase III ‘pooled’ safety and efficacy

Commercial opportunity

Q&A
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