SUPPLEMENTAL MATERIAL

Bempedoic acid in patients with type 2 diabetes mellitus, prediabetes, and normoglycaemia: a post hoc analysis of efficacy and glycaemic control using pooled data from phase 3 clinical trials.

| Baseline Glycaemic Control Status | Normoglycaemia$^d$ | Prediabetes$^e$ | New Onset Diabetes$^f$ | Undetermined$^g$ |
|----------------------------------|---------------------|-----------------|------------------------|-------------------|
| Normoglycaemia$^a$               |                    |                 |                        |                   |
| Bempedoic acid (n = 410)         | 67.8 (278)         | 22.9 (94)       | 0.5 (2)                | 8.8 (36)          |
| Placebo (n = 208)                | 70.7 (147)         | 21.6 (45)       | 0.5 (1)                | 7.2 (15)          |
| Prediabetes$^b$                  |                    |                 |                        |                   |
| Bempedoic acid (n = 1259)        | 23.4 (295)         | 64.0 (806)      | 4.5 (57)               | 8.0 (101)         |
| Placebo (n = 609)                | 25.8 (157)         | 63.5 (387)      | 5.9 (36)               | 4.8 (29)          |

| Diabetes with HbA1c ≥ 6.5% at baseline$^c$ | Normoglycaemia$^d$ | Prediabetes$^e$ | New Onset Diabetes$^f$ | Undetermined$^g$ |
|-------------------------------------------|---------------------|-----------------|------------------------|-------------------|
| Bempedoic acid (n = 455)                 | 1.1 (5)             | 15.2 (69)       | 74.5 (339)             | 9.2 (42)          |
| Placebo (n = 232)                        | 0                   | 14.2 (33)       | 80.6 (187)             | 5.2 (12)          |

| Last HbA1c Level, % (n)                  | ≤ 5.6% | 5.7 – 6.4% | ≥ 6.5% | Undetermined |
|-----------------------------------------|--------|------------|--------|--------------|
| Bempedoic acid (n = 455)                |        |            |        |              |
| Placebo (n = 232)                       |        |            |        |              |

$^a$Patients not fulfilling the criteria for diabetes or prediabetes.
$^b$Patients with all the following: no medical history of diabetes; not receiving diabetes medication prior to baseline; and HbA1c of 5.7% to 6.4% (inclusive) at baseline, or ≥1 fasting glucose value of ≥100 mg/dL, but not more than 1 value ≥126 mg/dL between screening and randomization.
$^c$Patients with 1 or more of the following: history of type 1 or type 2 diabetes; receiving diabetes medication prior to baseline; and/or HbA1c ≥6.5% at baseline, or ≥1 fasting plasma glucose value ≥100 mg/dL, but not more than 1 value ≥126 mg/dL between screening and randomization. All patients with diabetes in this analysis had HbA1c ≥6.5% at baseline.
$^d$Post-baseline criteria for normoglycemic included HbA1c ≤5.6% and no diabetes medication added.
$^e$Post-baseline criteria for prediabetes included HbA1c 5.7 – 6.4% and no diabetes medication added.
$^f$Patients with 1 or more of the following: ≥1 HbA1c value ≥6.5%; ≥2 fasting serum glucose values ≥126 mg/dL; an investigator-reported diabetes-related adverse event; and/or initiation of diabetes medication at any point after baseline.
$^g$Undetermined due to absence of post-baseline HbA1c levels.

Abbreviations: HbA1c, glycated haemoglobin.
TABLE S2  Safety overview

| Parameter                                      | Exposure-Adjusted Incidence, per 100 Person-Years (n) |
|------------------------------------------------|-------------------------------------------------------|
|                                                | Diabetes a                                        | Prediabetes b                                    | Normoglycaemia c                                   |
|                                                | BA (n = 755)                                      | BA (n = 1259)                                     | BA (n = 410)                                       | Placebo (n = 208)                                     |
| Any TEAE                                       | 86.5 (552)                                        | 86.7 (917)                                        | 89.6 (302)                                        | 88.6 (151)                                         |
| TEAE leading to IMP discontinuation           | 12.4 (79)                                         | 14.4 (152)                                        | 12.5 (42)                                         | 12.3 (21)                                           |
| Most common TEAEs ≥5 per 100 PY (n) in any group |                                                     |                                                     |                                                     |                                                     |
| Nasopharyngitis                               | 8.0 (51)                                          | 8.4 (89)                                          | 13.0 (70)                                         | 11.9 (40)                                          | 7.6 (13)                                           |
| Urinary tract infection                       | 6.7 (43)                                          | 5.2 (28)                                          | 5.9 (20)                                          | 7.6 (13)                                           |                                                     |
| Myalgia                                       | 4.9 (31)                                          | 6.5 (69)                                          | 5.7 (31)                                          | 5.3 (18)                                           | 6.5 (11)                                           |
| Upper respiratory tract infection             | 4.9 (31)                                          | 4.5 (48)                                          | 4.5 (15)                                          |                                                     |                                                     |
| Hypoglycaemia                                 | 4.5 (29)                                          | 0.6 (6)                                           | 1.5 (5)                                           | 0.6 (1)                                            |                                                     |
| Arthralgia                                    | 4.4 (28)                                          | 5.2 (55)                                          | 4.8 (26)                                          | 5.0 (17)                                           | 7.6 (13)                                           |
| Dizziness                                     | 4.4 (28)                                          | 3.5 (37)                                          | 3.3 (18)                                          | 5.3 (18)                                           | 2.9 (5)                                            |
| Diarrhoea                                     | 4.1 (26)                                          | 4.1 (43)                                          | 3.0 (16)                                          | 3.9 (13)                                           | 1.8 (3)                                            |
| Muscle spasm                                  | 3.4 (22)                                          | 4.5 (48)                                          | 3.1 (17)                                          | 5.6 (19)                                           | 1.8 (3)                                            |
| Osteoarthritis                                | 3.0 (19)                                          | 1.9 (20)                                          | 2.8 (15)                                          | 2.7 (9)                                            | 5.3 (9)                                            |
| Angina pectoris                               | 2.4 (15)                                          | 2.5 (26)                                          | 2.0 (11)                                          | 2.4 (8)                                            | 5.3 (9)                                            |

Note: TEAE incidence is defined as the number of patients having an event started in a certain period divided by the total person-time (in 100 PY) at risk during this period.

aPatients with 1 or more of the following: history of type 1 or type 2 diabetes; receiving diabetes medication prior to baseline; and/or HbA1c ≥6.5% (48 mmol/mol) at baseline, or ≥1 fasting plasma glucose value ≥100 mg/dL, but not more than 1 value ≥126 mg/dL between screening and randomization.

bPatients with all the following: no medical history of diabetes; not receiving diabetes medication prior to baseline; and HbA1c of 5.7% (39 mmol/mol) to 6.4% (46 mmol/mol) (inclusive) at baseline, or ≥1 fasting glucose value of ≥100 mg/dL, but not more than 1 value ≥126 mg/dL between screening and randomization.

cPatients not fulfilling the criteria for diabetes or prediabetes.

Abbreviations: BA, bempedoic acid; HbA1c, glycated haemoglobin; IMP, investigational medicinal product; PY, person-years; TEAE, treatment-emergent adverse event.