**Supplementary Table 1. Synopsis of Development of Other Glucokinase Activators (GKAs)**

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| **Molecule** | **Types of GKAs** | **Major Safety Issues and Other Notes** | **Status** | **Company** |
| RO4389620 (piragliatin)1 | Dual acting full GKA Pancreas and liver | Hypoglycemia, alanine transaminase elevation | Discontinued | Roche |
| MK-09412 | Dual acting full GKA Pancreas and liver | Hypoglycemia, hypertriglyceridaemia,hypertension, loss of efficacy | Discontinued | Merck |
| AMG 151 (ARRY-403)3 | Dual acting full GKA Pancreas and liver | Hypoglycemia, hypertriglyceridaemia | Discontinued | Amgen |
| AZD16564 | Dual acting partial GKAPancreas and liver | Increase in triglycerides, hypoglycemia, loss of efficacy | Phase 2 | AstraZeneca |
| LY2608204 (Globalagliatin) | Dual acting full GKA Pancreas and liver | Undisclosed | Phase 2 | Yabao Pharmaceutical/Eli Lilly |
| PF-04937319 (PB-201) | Dual acting partial GKAPancreas and liver | Hypoglycemia | Phase 2 | Pfizer |
| GK1-399 (TTP399) | Liver targeting full GKA | Not found yet | Phase 2 | vTv Therapeutics |
| GKM-001 (ADV-1002401) | Liver targeting full GKA | Not found yet | Phase 2 | Impetis Biosciences Limited  |

Reference:

[1]Sarabu R, Bizzarro F T, Corbett W L, et al. Discovery of piragliatin--first glucokinase activator studied in type 2 diabetic patients [J]. J Med Chem, 2012, 55(16): 7021-7036.

[2]Meininger G E, Scott R, Alba M, et al. Effects of MK-0941, a novelglucokinase activator, on glycemic control in insulin-treated patientswith type 2 diabetes [J]. Diabetes Care, 2011, 34(12): 2560-2566.

[3]Katz L, Manamley N, Snyder W J, et al. AMG 151 (ARRY-403), a novel glucokinase activator, decreases fasting and postprandial glycemia in patients with type 2 diabetes [J]. Diabetes Obes Metab, 2015, 18 (2):195.

[4]Wilding J P H, Leonsson-Zachrisson M, Wessman C, et al. Dose-ranging study with the glucokinase activator AZD1656 in patients with type 2 diabetes mellitus on metformin [J].Diabetes Obes Metab, 2013, 15(8):750-759.

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| **Supplementary Table 2. Changes in Glycated Hemoglobin (%) by Scheduled Visits in 24-Week Double-blind Treatment Period.\*** |  |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** | **Dorzagliatin vs. Placebo** |
|  | N | Mean(SD) | vs. Baseline | N | Mean(SD) | vs. Baseline | LS Mean | P Value |
|  | Mean(SD) | LS Mean(SE) | 95% CI | Mean(SD) | LS Mean(SE) | 95% CI |
| Baseline | 307 | 8.35(0.671) | - | - | - | 150 | 8.37(0.731) | - | - | - | - | - |
| Week 4 | 305 | 7.54(0.823) | -0.81(0.452) | -0.80(0.027) | (-0.85, -0.75) | 148 | 8.10(0.794) | -0.28(0.459) | -0.27(0.038) | (-0.34, -0.19) | -0.53(-0.62，-0.44) | - |
| Week 8 | 299 | 7.18(0.958) | -1.17(0.711) | -1.15(0.040) | (-1.23, -1.07) | 136 | 7.93(0.844) | -0.40(0.647) | -0.39(0.058) | (-0.50, -0.28) | -0.75(-0.89，-0.62) | - |
| Week 12 | 296 | 7.05(0.966) | -1.29(0.836) | -1.25(0.047) | (-1.35, -1.16) | 134 | 7.89(0.920) | -0.43(0.729) | -0.41(0.068) | (-0.54, -0.27) | -0.85(-1.01，-0.69) | - |
| Week 16 | 290 | 7.07(1.011) | -1.26(0.939) | -1.21(0.052) | (-1.31, -1.11) | 126 | 7.82(0.957) | -0.48(0.786) | -0.42(0.077) | (-0.57, -0.27) | -0.79(-0.97，-0.61) | - |
| Week 20 | 286 | 7.10(1.026) | -1.22(0.982) | -1.14(0.056) | (-1.25, -1.03) | 122 | 7.72(0.939) | -0.57(0.776) | -0.49(0.084) | (-0.66, -0.33) | -0.65(-0.85，-0.45) | - |
| Week 24 | 284 | 7.18(1.139) | -1.15(1.095) | -1.07(0.061) | (-1.19, -0.95) | 122 | 7.71(0.923) | -0.58(0.788) | -0.50(0.091) | (-0.68, -0.32) | -0.57(-0.79，-0.36) | <0.001 |

\* SD: standard deviation; Least-squares(LS) mean differences, corresponding 95% confidence interval (CI) and P value were estimated using a mixed model for repeated measures in the full-analysis set; SE: standard error.

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| **Supplementary Table 3. Changes in Fasting Plasma Glucose (mg/dl) by Scheduled Visits in 24-Week Double-blind Treatment Period.\*** |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** | **Dorzagliatin vs. Placebo** |
|  | N | Mean(SD) | vs. Baseline | N | Mean(SD) | vs. Baseline | LS Mean |
|  | Mean(SD) | LS Mean(SE) | 95% CI | Mean(SD) | LS Mean(SE) | 95% CI |
| Baseline | 307 | 176.04 (32.238) | - | - | - | 150 | 174.78 (27.63) | - | - | - | - |
| Week 4 | 305 | 154.98 (33.678) | -21.24 (25.074) | -20.70 (1.386) | (-23.40, -18.00) | 148 | 175.86 (33.174) | 0.90 (23.112) | 1.08 (1.944) | (-2.70, 5.04) | -21.78 (-26.46, -17.28) |
| Week 8 | 299 | 158.58 (34.596) | -17.46 (28.818) | -16.74 (1.548) | (-19.80, -13.68) | 136 | 173.52 (32.256) | 0.18 (23.004) | -0.18 (2.25) | (-4.50, 4.32) | -16.56 (-21.96, -11.34) |
| Week 12 | 296 | 160.56 (35.694) | -14.94 (31.662) | -14.04 (1.764) | (-17.64, -10.62) | 134 | 174.78 (35.244) | 1.44 (27.162) | 1.80 (2.574) | (-3.42, 6.84) | -15.84 (-21.96, -9.72) |
| Week 16 | 290 | 162 (36.27) | -12.6 (36.918) | -11.70 (1.926) | (-15.48, -7.74) | 126 | 168.66 (32.166) | -3.24 (24.408) | -2.34 (2.862) | (-8.10, 3.24) | -9.18 (-15.84, -2.52) |
| Week 20 | 286 | 159.30 (35.586) | -15.48 (36.864) | -13.68 (1.926) | (-17.46, -9.90) | 122 | 167.58 (29.376) | -3.78 (22.734) | -2.52 (2.88) | (-8.28, 3.06) | -11.16 (-17.82, -4.50) |
| Week 24 | 284 | 162.54 (41.112) | -12.60 (42.012) | -10.44 (2.214) | (-14.76, -6.12) | 122 | 165.24 (31.23) | -6.12 (23.49) | -4.68 (3.33) | (-11.16, 1.98) | -5.94 (-13.68, 1.98) |

\* SD: standard deviation; Least-squares(LS) mean differences and corresponding 95% confidence interval (CI) were estimated using a mixed model for repeated measures in the full-analysis set; SE: standard error.

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| **Supplementary Table 4. Changes in 2-hour Postprandial Glucose (mg/dl) in 24-Week Double-blind Treatment Period.\*** |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** | **Dorzagliatin vs. Placebo** |
|  | N | Mean(SD) | vs. Baseline | N | Mean(SD) | vs. Baseline | LS Mean |
|  | Mean(SD) | LS Mean(SE) | 95% CI | Mean(SD) | LS Mean(SE) | 95% CI |  |
| Baseline | 304 | 320.58 (57.060)- | - | - | - | 149 | 321.30 (57.186) | - | - | - | - |
| Week 12 | 293  | 260.46 (72.054) | -58.86 (66.852) | -56.88 (3.618) | (-63.90, -49.68) | 133 | 313.02 (68.220) | -7.02 (51.858) | -4.50 (5.256) | (-14.94, 5.76) | -52.20 (-64.44, -40.14) |
| Week 24 | 281 | 263.34 (78.282) | -54.90 (82.314) | -50.94 (4.392) | (-59.58, -42.3) | 121 | 304.38 (70.092) | -14.04 (54.990) | -9.00 (6.552) | (-21.96, 3.78) | -41.90 (-57.06, -26.82) |

\* SD: standard deviation; Least-squares(LS) mean differences and corresponding 95% confidence interval (CI) were estimated using a mixed model for repeated measures in the full-analysis set; SE: standard error.

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| **Supplementary Table 5. Response Rates (Glycated Hemoglobin <7.0%) in 24-Week Double-blind Treatment Period.\*** |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** | **Dorzagliatin vs. Placebo** |
|  | N | n, % | N | n, % | Odds Ratio(95% CI) |
| Baseline | 307 | 1(0.3) | 150 | 0(0.0) | - |
| Week 4 | 305 | 69(22.6) | 150 | 9(6.0) | - |
| Week 8 | 306 | 125(40.8) | 150 | 15(10.0) | - |
| Week 12 | 306 | 143(46.7) | 150 | 21(14.0) | - |
| Week 16 | 306 | 144(47.1) | 150 | 21(14.0) | - |
| Week 20 | 306 | 133(43.5) | 150 | 28(18.7) | - |
| Week 24 | 306 | 130(42.5) | 150 | 26(17.3) |  4.20(2.51, 7.02) |

\* The glycated hemoglobin response rate (percentage of patients who reached a glycated hemoglobin level of less than 7.0%) was estimated based on the data imputed by last observation carried forward approach in the full analysis set. Odds ratio (OR) and 95% confidence interval (CI) between two treatment groups were estimated using the logistic regression model.

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| **Supplementary Table 6. Homeostatic Control Rates in 24-Week Double-blind Treatment Period.\*** |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** | **Dorzagliatin vs. Placebo** |
|  | N | n, % | N | n, % | Odds Ratio(95% CI) |
| Baseline | 307 | 1(0.3) | 150 | 0(0.0) | - |
| Week 4 | 305 | 68(22.3) | 150 | 9(6.0) | - |
| Week 8 | 306 | 124(40.5) | 150 | 15(10.0) | - |
| Week 12 | 306 | 142(46.4) | 150 | 21(14.0) | - |
| Week 16 | 306 | 143(46.7) | 150 |  21(14.0) | - |
| Week 20 | 306 | 132(43.1) | 150 | 28(18.7) | - |
| Week 24 | 306 | 129(42.2) | 150 | 26(17.3) |  4.10(2.46, 6.85) |

\* Homeostatic control rates: a glycated hemoglobin level of less than 7.0% and without hypoglycemia.

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| **Supplementary Table 7. Changes in the Glycated Hemoglobin(%) by Scheduled Visits in 52-Week Treatment Period.\*** |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** |
|  | **52-week Treatment** | **Open-label Treatment** | **52-week Treatment** | **Open-label Treatment** |
|  | N | Mean(SD) | Change from Baseline | N | Mean(SD) | Change from Open-Label Baseline | N | Mean(SD) | Change from Baseline | N | Mean(SD) | Change from Open-Label Baseline |
| Baseline | 307 | 8.35(0.671) | - | - | - | - | 150 | 8.37(0.731) | - | - | - | - |
| Week 4 | 305 | 7.54(0.823) | -0.81(0.452) | - | - | - | 148 | 8.10(0.794) | -0.28(0.459) | - | - | - |
| Week 8 | 299 | 7.18(0.958) | -1.17(0.711) | - | - | - | 136 | 7.93(0.844) | -0.40(0.647) | - | - | - |
| Week 12 | 296 | 7.05(0.966) | -1.29(0.836) | - | - | - | 134 | 7.89(0.920) | -0.43(0.729) | - | - | - |
| Week 16 | 290 | 7.07(1.011) | -1.26(0.939) | - | - | - | 126 | 7.82(0.957) | -0.48(0.786) | - | - | - |
| Week 20 | 286 | 7.10(1.026) | -1.22(0.982) | - | - | - | 122 | 7.72(0.939) | -0.57(0.776) | - | - | - |
| Week 24 | 284 | 7.18(1.139) | -1.15(1.095) | 281 | 7.17(1.133) | - | 122 | 7.71(0.923) | -0.58(0.788) | 120 | 7.70(0.924) | - |
| Week 28 | 276 | 7.14(1.122) | -1.18(1.075) | 276 | 7.14(1.122) | 0.01(0.346) | 120 | 7.15(0.977) | -1.14(0.807) | 120 | 7.15(0.977) | -0.55(0.353) |
| Week 34 | 271 | 7.16(1.097) | -1.16(1.072) | 271 | 7.16(1.097) | 0.05(0.623) | 118 | 6.89(1.110) | -1.39(0.955) | 118 | 6.89(1.110) | -0.79(0.621) |
| Week 40 | 263 | 7.21(1.149) | -1.11(1.105) | 263 | 7.21(1.149) | 0.12(0.770) | 113 | 6.83(1.084) | -1.41(1.019) | 113 | 6.83(1.084) | -0.80(0.766) |
| Week 46 | 257 | 7.20(1.108) | -1.12(1.048) | 257 | 7.20(1.108) | 0.13(0.897) | 110 | 6.93(1.106) | -1.30(1.030) | 110 | 6.93(1.106) | -0.70(0.792) |
| Week 52 | 245 | 7.20(1.073) | -1.11(0.999) | 245 | 7.20(1.073) | 0.14(0.965) | 105 | 6.95(1.077) | -1.27(1.021) | 105 | 6.95(1.077) | -0.68(0.798) |

\* Change from baseline and change from open-label baseline values are arithmetic means(SD). SD: standard deviation.

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| **Supplementary Table 8. Changes in Fasting Plasma Glucose (mg/dl) by Scheduled Visits in 52-Week Treatment Period.\*** |  |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** |
|  | **52-week Treatment** | **Open-label Treatment** | **52-week Treatment** | **Open-label Treatment** |
|  | N | Mean(SD) | Change from Baseline | N | Mean(SD) | Change from Open-Label Baseline | N | Mean(SD) | Change from Baseline | N | Mean(SD) | Change from Open-Label Baseline |
| Baseline | 307 | 176.04 (32.238) | - | - | - | - | 150 | 174.78 (27.630) | - | - | - | - |
| Week 4 | 305 | 154.98 (33.678) | -21.24 (25.074) | - | - | - | 148 | 175.86 (33.174) | 0.90 (23.112) | - | - | - |
| Week 8 | 299 | 158.58 (34.596) | -17.46 (28.818) | - | - | - | 136 | 173.52 (32.256) | 0.18 (23.004) | - | - | - |
| Week 12 | 296 | 160.56 (35.694) | -14.94 (31.662) | - | - | - | 134 | 174.78 (35.244) | 1.44 (27.162) | - | - | - |
| Week 16 | 290 | 162.00 (36.270) | -12.60 (36.918) | - | - | - | 126 | 168.66 (32.166) | -3.24 (24.408) | - | - | - |
| Week 20 | 286 | 159.30 (35.586) | -15.48 (36.864) | - | - | - | 122 | 167.58 (29.376) | -3.78 (22.734) | - | - | - |
| Week 24 | 284 | 162.54 (41.112) | -12.60 (42.012) | 281 | 162 (40.284) | - | 122 | 165.24 (31.230) | -6.12 (23.49) | 120 | 165.24 (31.482) | - |
| Week 28 | 276 | 158.76 (34.974) | -16.38 (36.126) | 276 | 158.76 (34.974) | -1.44 (25.722) | 120 | 145.08 (31.986) | -26.28 (27.108) | 120 | 145.08 (31.986) | -20.16 (20.052) |
| Week 34 | 271 | 160.38 (38.412) | -14.76 (38.322) | 271 | 160.38 (38.412) | 0.72 (31.536) | 118 | 151.2 (43.362) | -19.80 (38.502) | 118 | 151.20 (43.362) | -13.50 (31.212) |
| Week 40 | 263 | 158.94 (37.044) | -15.30 (39.006) | 263 | 158.94 (37.044) | 0.36 (37.224) | 113 | 152.1 (36.558) | -17.46 (33.372) | 113 | 152.10 (36.558) | -10.62 (26.046) |
| Week 46 | 257 | 158.76 (35.046) | -15.66 (37.368) | 257 | 158.76 (35.046) | 0.54 (38.232) | 110 | 152.82 (40.32) | -16.02 (36.126) | 110 | 152.82 (40.32) | -9.18 (30.744) |
| Week 52 | 245 | 160.56 (35.226) | -13.86 (37.98) | 245 | 160.56 (35.226) | 2.34 (37.854) | 105 | 151.38 (34.29) | -17.10 (32.778) | 105 | 151.38 (34.29) | -10.62 (27.324) |

\* Change from baseline and change from open-label baseline values are arithmetic means(SD). SD: standard deviation.

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| **Supplementary Table 9. Changes in 2-hour Postprandial Glucose (mg/dl) by Scheduled Visits in 52-Week Treatment Period.\*** |  |
|  | **Dorzagliatin 75 mg Twice Daily** | **Placebo** |
|  | **52-week Treatment** | **Open-label Treatment** | **52-week Treatment** | **Open-label Treatment** |
|  | N | Mean(SD) | Change from Baseline | N | Mean(SD) | Change from Open-Label Baseline | N | Mean(SD) | Change from Baseline | N | Mean(SD) | Change from Open-Label Baseline |
| Baseline | 304 | 320.58 (57.060) | - | - | - | - | 149 | 321.30 (57.186) | - | - | - | - |
| Week 12 | 293 | 260.46 (72.054) | -58.86 (66.852) | - | - | - | 133 | 313.02 (68.220) | -7.02 (51.858) | - | - | - |
| Week 24 | 281 | 263.34 (78.282) | -54.90 (82.314) | 278 | 263.52 (78.138) | - | 121 | 304.38 (70.092) | -14.04 (54.990) | 119 | 302.58 (69.210) | - |
| Week 52 | 243 | 255.78 (76.662) | -62.28 (77.256) | 243 | 255.78 (76.662) | -2.88 (74.988) | 105 | 243.72 (77.652) | -71.28 (65.466) | 105 | 243.72 (77.652) | -54.36 (61.668) |

\* Change from baseline and change from open-label baseline values are arithmetic means(SD). SD: standard deviation.

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| Supplementary Table 10. Adverse events in 24-week double-blind treatment period and additional 28-week open-label treatment period |
| Event | **Double-blind treatment period (0-24 week)** | **Open-label treatment period (24-52 week)** |
| **Dorzagliatin** **(N=310)** | **Placebo****(N=153)** | **Dorzagliatin- Dorzagliatin****(N=281)** | **Placebo- Dorzagliatin****(N=120)** |
| *No. of Patients (%)* | *No. of Events* | *No. of Patients (%)* | *No. of Events* | *No. of Patients (%)* | *No. of Events* | *No. of Patients (%)* | *No. of Events* |
| Any adverse event | 240 ( 77.4) | 653 | 103 ( 67.3) | 301 | 191 ( 68.0) | 448 | 83 ( 69.2) | 206 |
| Mild | 235 ( 75.8) | 619 | 99 ( 64.7) | 281 | 190 ( 67.6) | 428 | 82 ( 68.3) | 195 |
| Moderate | 21 ( 6.8) | 33 | 16 ( 10.5) | 20 | 13 ( 4.6) | 19 | 7 ( 5.8) | 11 |
| Severe | 1 ( 0.3) | 1 | 0 | 0 | 1 ( 0.4) | 1 | 0 | 0 |
| Drug-related adverse event \*  | 25 ( 8.1) | 32 | 12 ( 7.8) | 17 | 12 ( 4.3) | 16 | 7 ( 5.8) | 9 |
| Mild | 24 ( 7.7) | 30 | 10 ( 6.5) | 14 | 12 ( 4.3) | 16 | 7 ( 5.8) | 9 |
| Moderate | 2 ( 0.6) | 2 | 2 (1.3) | 3 | 0 | 0 | 0 | 0 |
| Severe | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Adverse event leading to drug discontinuation |  0 | 0 | 2 ( 1.3)  | 3 |  0 | 0 |  0 | 0 |
| Adverse event leading to withdrawal from study |  0 | 0 | 2 ( 1.3)  | 3 |  0 | 0  |  0 |  0  |
| Any serious adverse event | 12 ( 3.9) | 18 | 9 ( 5.9) | 10 | 13 ( 4.6) | 14 | 6 ( 5.0) | 7 |
| Results in death | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Other serious adverse event | 12 ( 3.9) | 18 | 9 ( 5.9) | 10 | 13 ( 4.6) | 14 | 6 ( 5.0) | 7 |
| Serious adverse event leading to drug discontinuation | 2 ( 0.6) | 3 | 6 ( 3.9) | 7 | 3 ( 1.1)  | 3 | 2 ( 1.7) | 2 |
| Serious adverse event leading to withdrawal from study | 1 ( 0.3) | 1 | 5 ( 3.3) | 6 | 3 ( 1.1) | 3 | 1 ( 0.8) | 1 |
| Adverse events in ≥5% of patients‖ |  |  |  |  |  |  |  |  |
| Upper respiratory tract infection | 58 (18.7) | 66 | 27 (17.6) | 33 | 39 (13.9) | 46 | 25 (20.8) | 29 |
| Hyperlipidemia | 37 (11.9) | 43 | 16 (10.5) | 17 | 25 (8.9) | 29 | 20 (16.7) | 22 |
| Protein urine present | 26 (8.4) | 32 | 7 (4.6) | 10 | 10 (3.6) | 13 | 6 (5.0) | 6 |
| Urinary tract infection | 16 (5.2) | 16 | 8 (5.2) | 9 | 7 (2.5) | 8 | 3 (2.5) | 3 |
| Hepatic function abnormal | 18 (5.8) | 18 | 6 (3.9) | 6 | 9 (3.2) | 10 | 6 (5.0) | 6 |
| Hypertension | 16 (5.2) | 16 | 6 (3.9) | 7 | 6 (2.1) | 7 | 2 (1.7) | 2 |
| Adverse events in at least 5% of patients related to the study drug† |  |  |  |  |  |  |  |  |
| Upper respiratory tract infection | 3 (1.0) | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hyperlipidemia | 1 (0.3) | 1 | 0 | 0 | 0 | 0 | 2 (1.7) | 2 |
| Protein urine present | 1 (0.3) | 1 | 1 (0.7) | 1 | 0 | 0 | 0 | 0 |
| Urinary tract infection | 1 (0.3) | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hepatic function abnormal | 2 (0.6) | 2 | 2 (1.3) | 2 | 2 (0.7) | 2 | 2 (1.7) | 2 |
| Hypertension | 1 (0.3) | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hypoglycemia |  |  |  |  |  |  |  |  |
| Severe hypoglycemia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Clinically significant hypoglycemia (Blood glucose level <3.0 mmol/L) | 1 (0.3) | 1 | 0 | 0 | 0 | 0 | 1 (0.8) | 1 |
| Drop-out due to hypoglycemia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

\*Adverse events and serious adverse events that occurred in the 24-week double-blind treatment period and 28-week open-label treatment period among patients in the safety population are included in the table and presented with their preferred terms in the Medical Dictionary for Regulatory Activities, version 23.0. The safety population includes all randomized patients, who took at least one dose of study drugs. Events were included if the date of onset was between the first intake of double-blind study medications and the 7th day after the last dose of study medications.

‖Adverse events in at least 5% of patients and more frequently reported in the dorzagliatin group than in the placebo group were listed in the table. Urinary tract infection was reported in 5.2% of patients in both groups and is not listed in the table.

†Adverse events in at least 5% of patients related to the study drug was defined as adverse events that were deemed by the investigators to be very likely, or probably related to the study drug or placebo.

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| Supplementary Table 11 Serious adverse events in 24-week double-blind treatment period and additional 28-week open-label treatment period by System Organ Class (SOC) |
| System Organ Class（SOC）\* | **Double-blind treatment period (0-24 week)** | **Open-label treatment period (24-52 week)** |
| **Dorzagliatin****(N=310)** | **Placebo****(N=153)** | **Dorzagliatin- Dorzagliatin****(N=281)** | **Placebo- Dorzagliatin****(N=120)** |
| *No. of Patients (%)* | *No. of Patients (%)* | *No. of Patients (%)* | *No. of Patients (%)* |
| Nervous system disorders | 1 (0.3) | 2 (1.3) | 4 (1.4) | 1 (0.8) |
| Infections and infestations | 0 | 4 (2.6) | 2 (0.7) | 1 (0.8) |
| Cardiac disorders | 2 (0.6) | 1 (0.7) | 2 (0.7) | 0 |
| Injury, poisoning and procedural | 2 (0.6) | 0 | 2 (0.7) | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | 1 (0.3) | 2 (1.3) | 2 (0.7) | 0 |
| Musculoskeletal and connective tissue | 2 (0.6) | 0 | 0 | 1 (0.8) |
| Eye disorders | 1 (0.3) | 0 | 0 | 0 |
| Hepatobiliary disorders | 0 | 1 (0.7) | 1 (0.4) | 0 |
| Renal and urinary disorders | 0 | 0 | 0 | 1 (0.8) |
| Ear and labyrinth disorders | 1 (0.3) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal | 1 (0.3) | 0 | 0 | 0 |
| Gastrointestinal disorders | 0 | 0 | 0 | 1 (0.8) |
| Vascular disorders | 1 (0.3) | 0 | 0 | 0 |
| Reproductive system and breast disorders | 1 (0.3) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | 0 | 1 (0.7) | 0 | 1 (0.8) |

\* Serious adverse events that occurred in the 24-week double-blind treatment period and 28-week open-label treatment period among patients in the safety population are included in the table and classified by System Organ Class (SOC) in the Medical Dictionary for Regulatory Activities, version 23.0.