

## Supplementary Tables

### **Sandoz rituximab biosimilar Rixathon<sup>®</sup>/Riximyo<sup>®</sup> is stable after temperature excursions up to 21 days at room temperature**

Roman Borišek<sup>a</sup>, André Mischo<sup>b</sup>, Ida Šmid<sup>a</sup>

<sup>a</sup>Lek Pharmaceuticals d.d., Menges, Slovenia

<sup>b</sup>Novartis AG, Biochemiestraße 10, 6336 Langkampfen, Austria

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Corresponding author:

Roman Borišek

Email: roman.borisek@novartis.com

**Supplementary Table 1 Physicochemical and microbiological tests of SDZ-RTX: OOF condition I (25 ± 2°C/60 ± 5% RH)**

| Duration of the OOF exposure (days) | CCIT              | Clarity (NTU) | Particulate contamination |   |                   | Identity - CEX     | Identity – Peptide mapping | Sterility         | BET (EU/mg) |
|-------------------------------------|-------------------|---------------|---------------------------|---|-------------------|--------------------|----------------------------|-------------------|-------------|
|                                     |                   |               | Visible particles         | Sub visible particles (particles/container) |                   |                    |                            |                   |             |
|                                     |                   |               |                           | Particles ≥ 10 µm                           | Particles ≥ 25 µm |                    |                            |                   |             |
| <b>SDZ-RTX Batch 1 (10 mL)</b>      |                   |               |                           |   |                   |                    |                            |                   |             |
| 0                                   | n.t. <sup>a</sup> | 6             | n.t. <sup>a</sup>         | 205   | 7                 | Corr. <sup>b</sup> | Corr. <sup>b</sup>         | n.t. <sup>a</sup> |             |
| 7                                   |                   | 6             |                           | n.t.  | n.t.              | n.t.               | n.t.                       |                   |             |
| 14                                  |                   | 6             |                           | n.t.  | n.t.              | n.t.               | n.t.                       |                   |             |
| 21                                  |                   | 6             |                           | 317   | 35                | Corr. <sup>b</sup> | Corr. <sup>b</sup>         |                   |             |
| <b>SDZ-RTX Batch 2 (50 mL)</b>      |                   |               |                           |   |                   |                    |                            |                   |             |
| 0                                   | n.t. <sup>a</sup> | 6             | n.t. <sup>a</sup>         | 620   | 3                 | Corr. <sup>b</sup> | Corr. <sup>b</sup>         | n.t. <sup>a</sup> |             |
| 7                                   |                   | 6             |                           | n.t.  | n.t.              | n.t.               | n.t.                       |                   |             |
| 14                                  |                   | 6             |                           | n.t.  | n.t.              | n.t.               | n.t.                       |                   |             |
| 21                                  |                   | 6             |                           | 267   | 7                 | Corr. <sup>b</sup> | Corr. <sup>b</sup>         |                   |             |
| <b>SDZ-RTX Batch 3 (50 mL)</b>      |                   |               |                           |   |                   |                    |                            |                   |             |
| 0                                   | n.t. <sup>a</sup> | 6             | n.t. <sup>a</sup>         | 367   | 10                | Corr. <sup>b</sup> | Corr. <sup>b</sup>         | n.t. <sup>a</sup> |             |
| 7                                   |                   | 6             |                           | n.t.  | n.t.              | n.t.               | n.t.                       |                   |             |
| 14                                  |                   | 6             |                           | n.t.  | n.t.              | n.t.               | n.t.                       |                   |             |
| 21                                  |                   | 6             |                           | 460   | 57                | Corr. <sup>b</sup> | Corr. <sup>b</sup>         |                   |             |

BET, bacterial endotoxin testing; CCIT, container closure integrity testing; CDC, complement-dependent cytotoxicity; CEX, cation exchange chromatography; Corr., corresponds; n.t., not tested; NTU, nephelometric turbidity unit; OOF, out-of-fridge; RH, relative humidity; SDZ-RTX, Sandoz rituximab

<sup>a</sup> Tested only at the worst-case condition (30°C / 65% RH)

<sup>b</sup> Corresponds to reference

**Supplementary Table 2 Physicochemical and microbiological tests of SDZ-RTX: OOF condition II (30 ± 2°C/65 ± 5% RH)**

| Duration of the OOF exposure (days) | CCIT            | Clarity (NTU) | Particulate contamination |   |                   | Identity - CEX     | Identity – Peptide mapping | Sterility | BET (EU/mg) |
|-------------------------------------|-----------------|---------------|---------------------------|---|-------------------|--------------------|----------------------------|-----------|-------------|
|                                     |                 |               | Visible particles         | Sub visible particles (particles/container) |                   |                    |                            |           |             |
|                                     |                 |               |                           | Particles ≥ 10 µm                           | Particles ≥ 25 µm |                    |                            |           |             |
| <b>SDZ-RTX Batch 1 (10 mL)</b>      |                 |               |                           |   |                   |                    |                            |           |             |
| 0                                   | Container tight | 6             | pfp                       | 205   | 7                 | Corr. <sup>a</sup> | Corr. <sup>a</sup>         | Sterile   | < 0.20      |
| 7                                   | n.t.            | 6             | n.t.                      | n.t.  | n.t.              | n.t.               | n.t.                       | n.t.      | n.t.        |
| 14                                  | n.t.            | 6             | n.t.                      | n.t.  | n.t.              | n.t.               | n.t.                       | n.t.      | n.t.        |
| 21                                  | Container tight | 6             | pfp                       | 227   | 6                 | Corr. <sup>a</sup> | Corr. <sup>a</sup>         | Sterile   | < 0.20      |
| <b>SDZ-RTX Batch 2 (50 mL)</b>      |                 |               |                           |   |                   |                    |                            |           |             |
| 0                                   | Container tight | 6             | pfp                       | 620   | 3                 | Corr. <sup>a</sup> | Corr. <sup>a</sup>         | Sterile   | < 0.20      |
| 7                                   | n.t.            | 6             | n.t.                      | n.t.  | n.t.              | n.t.               | n.t.                       | n.t.      | n.t.        |
| 14                                  | n.t.            | 6             | n.t.                      | n.t.  | n.t.              | n.t.               | n.t.                       | n.t.      | n.t.        |
| 21                                  | Container tight | 6             | pfp                       | 440   | 0                 | Corr. <sup>a</sup> | Corr. <sup>a</sup>         | Sterile   | < 0.20      |
| <b>SDZ-RTX Batch 3 (50 mL)</b>      |                 |               |                           |   |                   |                    |                            |           |             |
| 0                                   | Container tight | 6             | pfp                       | 367   | 10                | Corr. <sup>a</sup> | Corr. <sup>a</sup>         | Sterile   | < 0.20      |
| 7                                   | n.t.            | 6             | n.t.                      | n.t.  | n.t.              | n.t.               | n.t.                       | n.t.      | n.t.        |
| 14                                  | n.t.            | 6             | n.t.                      | n.t.  | n.t.              | n.t.               | n.t.                       | n.t.      | n.t.        |
| 21                                  | Container tight | 6             | pfp                       | 293   | 3                 | Corr. <sup>a</sup> | Corr. <sup>a</sup>         | Sterile   | < 0.20      |

BET, bacterial endotoxin testing; CCIT, container closure integrity testing; CDC, complement-dependent cytotoxicity; CEX, cation exchange chromatography; Corr., corresponds; n.t., not tested; NTU, nephelometric turbidity unit; OOF, out-of-fridge; pfp, practically free from particles; RH, relative humidity; SDZ-RTX, Sandoz rituximab

<sup>a</sup> Corresponds to reference

**Supplementary Table 3 Physicochemical tests of SDZ-RTX: OOF condition II (30 ± 2°C/65 ± 5% RH)**

| Duration of the OOF exposure (days) | Appearance of container | Degree of coloration | pH   | Extractable volume (mL) | Osmolality (mOsmol/kg) | SDZ-RTX content by UV (mg/mL) |
|-------------------------------------|-------------------------|----------------------|------|-------------------------|------------------------|-------------------------------|
| <b>SDZ-RTX Batch 1 (10 mL)</b>      |                         |                      |      |                         |                        |                               |
| 0                                   | a                       | Colorless solution   | 6.5  | 10.33                   | 354                    | 10.1                          |
| 7                                   | n.t.                    | n.t.                 | n.t. | n.t.                    | n.t.                   | n.t.                          |
| 14                                  | n.t.                    | n.t.                 | n.t. | n.t.                    | n.t.                   | n.t.                          |
| 21                                  | a                       | Colorless solution   | 6.5  | 10.35                   | 354                    | 10.0                          |
| <b>SDZ-RTX Batch 2 (50 mL)</b>      |                         |                      |      |                         |                        |                               |
| 0                                   | a                       | Colorless solution   | 6.6  | 50.86                   | 354                    | 10.0                          |
| 7                                   | n.t.                    | n.t.                 | n.t. | n.t.                    | n.t.                   | n.t.                          |
| 14                                  | n.t.                    | n.t.                 | n.t. | n.t.                    | n.t.                   | n.t.                          |
| 21                                  | a                       | Colorless solution   | 6.6  | 51.00                   | 352                    | 10.0                          |
| <b>SDZ-RTX Batch 3 (50 mL)</b>      |                         |                      |      |                         |                        |                               |
| 0                                   | a                       | Colorless solution   | 6.5  | 50.81                   | 354                    | 10.1                          |
| 7                                   | n.t.                    | n.t.                 | n.t. | n.t.                    | n.t.                   | n.t.                          |
| 14                                  | n.t.                    | n.t.                 | n.t. | n.t.                    | n.t.                   | n.t.                          |
| 21                                  | a                       | Colorless solution   | 6.5  | 50.70                   | 353                    | 10.1                          |

Corr., corresponds; n.t., not tested; OOF, out-of-fridge; RH, relative humidity; SDZ-RTX, Sandoz rituximab; UV, ultraviolet

<sup>a</sup>Vial - Clear glass, rubber stopper and aluminum flip off cap, visually clean and correctly fitted