**Supplemental Table 3. Systemic adverse events by system organ class**

| Medical Condition                                      | Once-daily netarsudil 0.02% (n=839) | Twice-daily timolol 0.5% (n=839) |
|--------------------------------------------------------|-------------------------------------|---------------------------------|
| General Disorders and Administration Site Conditions   | 8 (1.0)                             | 8 (1.0)                         |
| Treatment-related                                      | 1 (0.1)                             | 1 (0.1)                         |
| Serious                                                | 0 (0)                               | 0 (0)                           |
| Infections and infestations                            | 89 (10.6)                           | 79 (9.4)                        |
| Treatment-related                                      | 0 (0)                               | 0 (0)                           |
| Serious                                                | 1 (0.1)                             | 5 (0.6)                         |
| Nervous system disorders                               | 34 (4.1)                            | 43 (5.1)                        |
| Treatment-related                                      | 11 (1.3)                            | 7 (0.8)                         |
| Serious                                                | 3 (0.4)                             | 5 (0.6)                         |
| Skin and subcutaneous tissue disorders                 | 23 (2.7)                            | 16 (1.9)                        |
| Treatment-related                                      | 11 (1.3)                            | 0 (0)                           |
| Serious                                                | 0 (0)                               | 0 (0)                           |
| Musculoskeletal and connective tissue disorders        | 32 (3.8)                            | 33 (3.9)                        |
| Treatment-related                                      | 1 (0.1)                             | 1 (0.1)                         |
| Serious                                                | 2 (0.2)                             | 1 (0.1)                         |
| Respiratory, thoracic, and mediastinal disorders       | 25 (3.0)                            | 26 (3.1)                        |
| Treatment-related                                      | 1 (0.1)                             | 5 (0.6)                         |
| Serious                                                | 2 (0.2)                             | 2 (0.2)                         |
| Investigations                                         | 31 (3.7)                            | 26 (3.1)                        |
| Treatment-related                                      | 5 (0.6)                             | 2 (0.2)                         |
| Serious                                                | 0 (0)                               | 1 (0.1)                         |
| Gastrointestinal disorders                             | 19 (2.3)                            | 24 (2.9)                        |
| Treatment-related                                      | 2 (0.2)                             | 2 (0.2)                         |
| Serious                                                | 1 (0.1)                             | 2 (0.2)                         |
| Metabolism and nutrition disorders                     | 13 (1.5)                            | 14 (1.7)                        |
| Treatment-related                                      | 0 (0)                               | 0 (0)                           |
| Serious                                                | 1 (0.1)                             | 0 (0)                           |
| Cardiac disorders                                      | 15 (1.8)                            | 13 (1.5)                        |
| Treatment-related                                      | 2 (0.2)                             | 2 (0.2)                         |
| Serious                                                | 10 (1.2)                            | 4 (0.5)                         |
| Neoplasms                                              | 13 (1.5)                            | 11 (1.3)                        |
| Treatment-related                                      | 0 (0)                               | 0 (0)                           |
| Serious                                                | 8 (1.0)                             | 3 (0.4)                         |
| Vascular disorders                                     | 7 (0.8)                             | 18 (2.1)                        |
| Treatment-related                                      | 0 (0)                               | 0 (0)                           |
| Serious                                                | 2 (0.2)                             | 1 (0.1)                         |
| Immune system disorders                                | 9 (1.1)                             | 2 (0.2)                         |
| Treatment-related                                      | 2 (0.2)                             | 0 (0)                           |
| Serious                                                | 0 (0)                               | 0 (0)                           |
| Medical Condition                        | Treatment-related | Serious |
|-----------------------------------------|-------------------|---------|
| Renal and urinary disorders             | 0 (0)             | 0 (0)   |
| Blood and lymphatic system disorders    | 0 (0)             | 0 (0)   |
| Ear and labyrinth disorders             | 0 (0)             | 0 (0)   |
| Psychiatric disorders                   | 0 (0)             | 0 (0)   |
| Endocrine disorders                     | 0 (0)             | 0 (0)   |
| Reproductive system and breast disorders| 0 (0)             | 0 (0)   |
| Hepatobiliary disorders                 | 0 (0)             | 0 (0)   |

Data are expressed as number (%) of patients. To include only adverse events plausibly related to study medication, the following system organ classes were omitted: “social circumstances,” “surgical and medical procedures,” “congenital, familial, and genetic disorders,” and “injury, poisoning, and procedural complications.”