# Roche Group development pipeline

**Marketed products development programmes**

**Roche Pharma global development programmes**

**Roche Pharma research and early development (pRED)**

**Genentech research and early development (gRED)**

**Spark**

# Changes to the development pipeline

*Q4 2022 update*

## New to phase I

**6 NMEs:**
**RG6209** NME – retinal disease
**RG6421** TMEM16A potentiator – cystic fibrosis
**RG6524** NME – solid tumors
**RG6411** NME – solid tumors
**CHU** anti-HLA-DQ2.5 x gluten peptides – celiac disease
**CHU** RAY121 – immunology

## New to phase II

**1 NME:**
**RG1662** basmisanil – Dup15q syndrome

**1 NME (moved from phase III):**
**RG6042** tominersen – Huntington's

## New to phase III

**2 NMEs:**
**RG6179** anti-IL-6 – UME
**RG6330** KRAS G12C – 2L NSCLC

## New to registration

**1 NME (US):**
**RG6026** glofitamab – 3L+ DLBCL

**1 AI (US & EU):**
**RG7446** Tecentriq SC – subcutaneous formulation, all approved indications

## Removed from phase I

**1 NME:**
**RG7880** efmarodocokin alfa – aGVHD

## Removed from phase II

## Removed from phase III

**2 NMEs:**
**RG1450** gantenerumab – prodromal to mild Alzheimer's
**RG7440** ipatasertib + abiraterone - 1L CRPC

**5 AIs:**
**RG7446** Tecentriq + chemo – 1L mUC
**RG7446** Tecentriq + cabozantinib – 2L NSCLC
**RG3502** Kadcyla + Tecentriq – 2L+ HER-2+ PD-L1+ mBC
**RG1450** gantenerumab – preclinical Alzheimer's
**RG6354** zinpentraxin alfa (PRM-151 ) – IPF

## Approvals

**1 NME (US):**
**RG7828** Lunsumio – 3L+ FL

**3 AIs (US):**
**RG7446** Tecentriq – ASPS
**RG1569** Actemra – COVID-19 pneumonia
**RG7421** Cotellic – histiocytosis

**2 AIs (EU):**
**RG6152** Xofluza – influenza pediatric
**RG6013** Hemlibra – moderate hemophilia A

Status as of February 2, 2023

# Roche Group development pipeline

## Phase I (55 NMEs + 12 AIs)

| | | |
|---|---|---|
| RG6007 | HLA-A2-WT1 x CD3 | AML |
| RG6026 | glofitamab monotherapy + combos | heme tumors |
| RG6058 | tiragolumab combos | heme & solid tumors |
| RG6076 | CD19-4-1BBL combos | heme tumors |
| RG6129 | HLA-A2-MAGE-A4 x CD3 | solid tumors |
| RG6160 | cevostamab (FcRH5 x CD3) | r/r multiple myeloma |
| RG6171 | giredestrant (SERD) | solid tumors |
| RG6114 | inavolisib (mPI3K alpha inh) | solid tumors |
| RG6156 | EGFRvIII x CD3 | glioblastoma |
| RG6180 | autogene cevumeran ± T | solid tumors |
| RG6185 | belvarafenib (pan-RAF inh) + Cotellic ± T | solid tumors |
| RG6189 | FAP-CD40 ± T | solid tumors |
| RG6194 | runimotamab (HER2 x CD3) | BC |
| RG6234 | forimtamig (GPRC5D x CD3) | multiple myeloma |
| RG6264 | Phesgo OBI | HER2+ BC |
| RG6279 | PD1-IL2v ± T | solid tumors |
| RG6286 | - | colorectal cancer |
| RG6290 | MAGE-A4 ImmTAC ± T | solid tumors |
| RG6292 | CD25 MAb combos | heme & solid tumors |
| RG6323 | IL15/IL15Ra-Fc ± T | solid tumors |
| RG6330 | KRAS G12C | solid tumors |
| RG6333 | CD19 x CD28 + glofitamab | r/r NHL |
| RG6344 | BRAF inhibitor (3) | solid tumors |
| RG6392 | - | oncology |
| RG6411 | - | solid tumors |
| RG6433 | SHP2i combos | solid tumors |
| RG6440 | TGFβ (SOF10) | solid tumors |
| RG6512 | FIXa x FX | hemophilia |
| RG6524 | - | solid tumors |
| RG6526[1] | camonsertib | solid tumors |
| RG6538[2] | P-BCMA-ALLO1 | multiple myeloma |
| RG7446 | Morpheus platform | solid tumors |
| RG7601 | Venclexta ± azacitidine | r/r MDS |
| RG7802 | cibisatamab ± T | solid tumors |
| RG7827 | FAP-4-1BBL monotherapy + combos | solid tumors |
| RG7828 | Lunsumio monotheraphy + combos | heme tumors |
| CHU | glypican-3 x CD3 | solid tumors |
| CHU | codrituzumab | HCC |
| CHU | CD137 switch antibody | solid tumors |
| CHU | RAS inhibitor | solid tumors |
| CHU | SPYK04 | solid tumors |
| SQZ | PBMC vaccine | solid tumors |
| RG6287 | - | IBD |
| RG6315 | - | immunologic disorders |
| RG6341 | - | asthma |
| RG6421 | TMEM16A potentiator | cystic fibrosis |
| RG6536[3] | vixarelimab | immunology |
| RG7828 | Lunsumio | SLE |
| CHU | anti-HLA-DQ2.5 x gluten peptides | celiac disease |
| CHU | RAY121 | immunology |
| RG6006 | Abx MCP | bacterial infections |
| RG6319 | LepB inhibitor | complicated urinary tract infection |
| RG6035 | BS-CD20 MAb | multiple sclerosis |
| RG6091 | rugonersen (UBE3A LNA) | Angelman syndrome |
| RG6163 | - | psychiatric disorders |
| RG6182 | - | neurodegenerative diseases |
| RG6237 | latent myostatin | neuromuscular disorders |
| RG6289 | - | Alzheimer´s |
| RG6418* | selnoflast | inflammation |
| RG7637 | - | psychiatric disorders |
| RG6120 | VEGF-Ang2 DutaFab | nAMD |
| RG6209 | - | retinal disease |
| RG6312 | - | geographic atrophy |
| RG6351 | - | retinal disease |
| RG6501[4] | OpRegen | geographic atrophy |
| RG7921 | - | RVO |
| CHU | anti-IL-8 recycling antibody | endometriosis |

## Phase II (23 NMEs + 8 AIs)

| | | |
|---|---|---|
| RG6026 | glofitamab + chemo | 1L ctDNA high risk DLBCL |
| RG6058 | tiragolumab + T | NSCLC |
| | tiragolumab + T + chemo | NSCLC neoadj-adj |
| | tiragolumab + T | cervical cancer |
| | tiragolumab + T | 1L PD-L1+ mSCCHN |
| RG6107 | crovalimab | sickle cell disease |
| RG6139 | PD1 x LAG3 | solid tumors |
| RG6180 | autogene cevumeran + pembrolizumab | 1L melanoma |
| RG6354 | zinpentraxin alfa (PRM-151) | myelofibrosis |
| RG6357 | SPK-8011 | hemophilia A |
| RG6358 | SPK-8016 | hemophilia A with inhibitors to factor VIII |
| RG6149 | astegolimab (Anti-ST2) | COPD |
| RG6299[5] | ASO factor B | IgA nephropathy |
| RG7854/ RG6346/ RG6084** | ruzotolimod (TLR7 ago[3])/ xalnesiran (siRNA)/ PDL1 LNA | HBV |
| RG6359 | SPK-3006 | Pompe disease |
| RG1662 | basmisanil | Dup15q syndrome |
| RG6042 | tominersen | Huntington's |
| RG6100 | semorinemab | Alzheimer's |
| RG6102 | trontinemab | Alzheimer's |
| RG6237 | latent myostatin + Evrysdi | SMA |
| RG6416 | bepranemab | Alzheimer's |
| RG7314 | balovaptan | post-traumatic stress disorder |
| RG7412 | crenezumab | familial Alzheimer's healthy pts |
| RG7816 | alogabat (GABA Aa5 PAM) | ASD |
| RG7906 | ralmitaront | schizophrenia |
| RG7935 | prasinezumab | Parkinson's |
| RG6179 | anti-IL-6 | DME |
| RG7774 | vicasinabin (CB2 receptor agonist) | DR |
| RG6299[5] | ASO factor B | geographic atrophy |

New Molecular Entity (NME)
Additional Indication (AI)
Oncology / Hematology
Immunology
Infectious Diseases
Metabolism
Neuroscience
Ophthalmology
Other

Status as of February 2, 2023

RG-No - Roche/Genentech; CHU - Chugai managed; SQZ - SQZ Biotechnology managed; [1]Repare Therapeutics managed; [2]Poseida Therapeutics managed; [3]Kiniksa Pharmaceuticals managed; [4]Lineage Cell Therapeutics managed; [5]IONIS managed; T=Tecentriq; BS=Brain Shuttle; OBI=On-Body Delivery System; *also developed in Immunology; **combination platform

# Roche Group development pipeline

## Phase III (8 NMEs + 41 AIs)

| | | |
|---|---|---|
| RG3502 | Kadcyla + T | HER-2+ eBC high-risk |
| RG6026 | glofitamab + chemo | 2L+ DLBCL |
| RG6058 | tiragolumab + T | 1L PD-L1+ NSCLC |
| | tiragolumab + T | 1L esophageal cancer |
| | tiragolumab + T | locally advanced esophageal cancer |
| | tiragolumab + T | stage III unresectable 1L NSCLC |
| | tiragolumab + T | 1L non-squamous NSCLC |
| RG6107 | crovalimab* | PNH |
| | crovalimab | aHUS |
| RG6114 | inavolisib (mPI3K alpha inh) | 1L HR+ mBC |
| RG6171 | giredestrant (SERD) | 1L ER+/HER2- mBC |
| | giredestrant (SERD) | ER+ BC adj |
| | giredestrant (SERD) + Phesgo | 1L ER+/HER2+ BC |
| RG6330 | KRAS G12C | 2L NSCLC |
| RG7446 | Tecentriq + platinum chemo | NSCLC periadj |
| | Tecentriq | NMIBC, high-risk |
| | Tecentriq + cabozantinib | RCC adv |
| | T ± chemo | SCCHN adj |
| | T + capecitabine or carbo/gem | 1L TNBC |
| | T + paclitaxel | TNBC adj |
| | T + Avastin | HCC adj |
| | Tecentriq | ctDNA+ high-risk MIBC |
| | T+ lurbinectedin | 1L maintenance SCLC |
| RG7601 | Venclexta | r/r MM t(11:14) |
| | Venclexta + azacitidine | 1L MDS |
| RG7828 | Lunsumio + lenalidomide | 2L+ FL |
| | Lunsumio + Polivy | 2L+ DLBCL |
| RG7853 | Alecensa | ALK+ NSCLC adj |
| RG3648 | Xolair | food allergy |
| RG7159 | Gazyva | lupus nephritis |
| | Gazyva | membranous nephropathy |
| | Gazyva | systemic lupus erythematosus |
| RG6152 | Xofluza | influenza, pediatric (0-1 year) |
| | Xofluza | influenza direct transmission |
| RG1594 | Ocrevus higher dose | RMS & PPMS |
| | Ocrevus SC | RMS & PPMS |
| RG3625 | TNKase | stroke |
| RG6168 | Enspryng | myasthenia gravis |
| RG6168 | Enspryng | MOG-AD |
| RG6168 | Enspryng | autoimmune encephalitis |
| RG6356 | delandistrogene moxeparvovec (SRP-9001) | DMD |
| RG7845 | fenebrutinib | RMS |
| RG7845 | fenebrutinib | PPMS |
| RG6179 | anti-IL-6 | UME |
| RG6321 | Susvimo (PDS) | DME |
| | Susvimo (PDS) | DR |
| | Susvimo (PDS) | wAMD, 36-week |
| RG7716 | Vabysmo (faricimab) | BRVO |
| | Vabysmo (faricimab) | CRVO |

New Molecular Entity (NME)
Additional Indication (AI)
Oncology / Hematology
Immunology
Infectious Diseases

Metabolism
Neuroscience
Ophthalmology
Other

## Registration US & EU (1 NME + 4 AIs)

| | | |
|---|---|---|
| RG6026 | glofitamab | 3L+ DLBCL |
| RG7446 | Tecentriq SC | all approved indications |
| RG7596 | Polivy[1] | 1L DLBCL |
| RG6413+ RG6412 | Ronapreve[2] | SARS-CoV-2 hospitalised |
| RG7916 | Evrysdi[3] | SMA pediatric <2months |

[1]Approved in EU, filed in US
[2]Filed in EU
[3]Approved in US, filed in EU

T=Tecentriq
PDS=Port Delivery System with ranibizumab
*First filed in China in Q3 2022

Status as of February 2, 2023

# NME submissions and their additional indications

## *Projects in phase II and III*

New Molecular Entity (NME)
Additional Indication (AI)
Oncology / Hematology
Immunology
Infectious Diseases
Metabolism
Neuroscience
Ophthalmology
Other

✓ Indicates submission to health authorities has occurred
Unless stated otherwise submissions are planned to occur in US and EU
PDS=Port Delivery System with ranibizumab
Mosun=mosunetuzumab
*First filed in China
[1]IONIS managed

### 2022

| | |
|---|---|
| RG6026 | **glofitamab** 3L+ DLBCL ✓ |
| RG6107 | **crovalimab*** PNH (CN) ✓ |

### 2023

| | |
|---|---|
| RG6058 | **tiragolumab + T** 1L PD-L1+ NSCLC |
| RG6058 | **tiragolumab + T** 1L esophageal cancer (CN) |
| RG6107 | **crovalimab*** PNH (EU, US) |
| RG6321 | **Susvimo (PDS)** DME (US) |
| RG6321 | **Susvimo (PDS)** DR (US) |
| RG7716 | **Vabysmo (faricimab)** BRVO/CRVO |

### 2024

| | |
|---|---|
| RG6026 | **glofitamab + chemo** 2L DLBCL |
| RG6058 | **tiragolumab + T** Stage III unresectable 1L NSCLC |
| RG6107 | **crovalimab** aHUS |
| RG6114 | **inavolisib (mPI3K alpha inh)** 1L HR+ BC |
| RG6356 | **delandistrogene moxeparvovec (SRP-9001)** DMD (EU) |

### 2025 and beyond

| | |
|---|---|
| RG6026 | **glofitamab + chemo** 1L ctDNA+ high risk DLBCL |
| RG6058 | **tiragolumab + T** 1L PD-L1+ cervical cancer |
| RG6058 | **tiragolumab + T** locally adv esophageal cancer |
| RG6058 | **tiragolumab + T** 1L non-sq NSCLC |
| RG6058 | **tiragolumab + T** 1L PD-L1+ mSCCHN |
| RG6058 | **tiragolumab+T+/- chemo** NSCLC neoadj/adj |
| RG6107 | **crovalimab** sickle cell disease |
| RG6139 | **PD1xLAG3** solid tumors |
| RG6171 | **giredestrant (SERD)** 1L ER+/HER2- mBC |
| RG6171 | **giredestrant (SERD)** ER+ BC adj |
| RG6171 | **giredestrant (SERD) + Phesgo** 1L ER+/HER2+ BC |
| RG6180 | **autogene cevumeran** 1L melanoma |
| RG6330 | **KRAS G12 C** 2L NSCLC |
| RG6354 | **zinpentraxin alfa (PRM-151)** myelofibrosis |
| RG7828 | **Lunsumio (mosun) + lenalidomide** 2L FL |
| RG7828 | **Lunsumio (mosun) + Polivy** 2L+ DLBCL (US) |
| RG6149 | **astegolimab (anti-ST2)** COPD |
| RG6299[1] | **ASO factor B** IgA nephropathy |
| RG7854/ RG6346/ RG6084 | **ruzotolimod (TLR7 ago [3])/ xalnesiran (siRNA)/ PDL1 LNA** HBV |
| RG1662 | **basmisanil** Dup15q syndrome |
| RG6042 | **tominersen** Huntington's |
| RG6100 | **semorinemab** Alzheimer's |
| RG6102 | **trontinemab** Alzheimer's |
| RG6237 | **latent myostatin + Evrysdi** SMA |
| RG6416 | **bepranemab** Alzheimer's |
| RG7314 | **balovaptan** post-traumatic stress disorder |
| RG7816 | **alogabat (GABA Aa5 PAM)** ASD |
| RG7845 | **fenebrutinib** RMS |
| RG7845 | **fenebrutinib** PPMS |
| RG7906 | **ralmitaront** schizophrenia |
| RG7935 | **prasinezumab** Parkinson's |
| RG6179 | **anti-IL-6** UME |
| RG6179 | **anti-IL-6** DME |
| RG6299[1] | **ASO factor B** geographic atrophy |
| RG6321 | **Susvimo (PDS)** wAMD, 36-week refill |
| RG7774 | **vicasinabin (CB2 receptor agonist)** DR |

Status as of February 2, 2023

# AI submissions for existing products

*Projects in phase II and III*

New Molecular Entity (NME)
Additional Indication (AI)
Oncology / Hematology
Immunology
Infectious Diseases

Metabolism
Neuroscience
Ophthalmology
Other

| 2022 | | 2023 | | 2023 | | 2024 | | 2025 and beyond | |
|---|---|---|---|---|---|---|---|---|---|
| RG6413+ RG6412 | **Ronapreve**** SARS-CoV-2 hospitalized (EU) ✓ | RG6264 | **Phesgo OBI** HER2+ BC | | | RG7446 | **Tecentriq**[1] NSCLC periadj | RG3502 | **Kadcyla + Tecentriq** HER-2+ eBC high-risk |
| | | RG6396 | **Gavreto** Tumor agnostic (US) | | | RG7446 | **Tecentriq** SCCHN adj | RG7446 | **Tecentriq** High-risk NMIBC |
| | | RG7446 | **Tecentriq + cabozantinib** RCC adv | RG1594 | **Ocrevus SC** RMS & PPMS | RG7446 | **Tecentriq + paclitaxel** TNBC adj | RG7446 | **Tecentriq+ lurbinectedin** 1l maintenance SCLC |
| RG1569 | **Actemra** COVID-19 pneumonia ✓ | RG7446 | **Tecentriq + Avastin** HCC adj | RG3625 | **TNKase** stroke | RG7446 | **Tecentriq** ctDNA+ high-risk MIBC | RG7159 | **Gazyva** membranous nephropathy |
| RG7446 | **Tecentriq SC** all approved indications ✓ | RG7601 | **Venclexta** r/r MM t(11:14) | RG3648 | **Xolair** food allergy | RG7601 | **Venclexta + azacitidine** 1L MDS | RG7159 | **Gazyva** systemic lupus erythematosus |
| RG7596 | **Polivy** 1L DLBCL (US) ✓ | RG7446 | **Tecentriq + capecitabine or carbo/gem** TNBC | RG6152 | **Xofluza** direct transmission | RG7159 | **Gazyva** lupus nephritis | RG1594 | **Ocrevus higher dose** RMS & PPMS |
| | | RG7853 | **Alecensa** ALK+ NSCLC adj | RG6152 | **Xofluza** influenza, pediatric (0-1 year) | RG6168 | **Enspryng** myasthenia gravis | RG6168 | **Enspryng** MOG-AD |
| | | | | | | | | RG6168 | **Enspryng** autoimmune encephalitis |

Status as of February 2, 2023

✓ Indicates submission to health authorities has occurred
Unless stated otherwise submissions are planned to occur in US and EU
[1]filing timeline based on data from interim analysis

OBI=On-Body Delivery System
**Ronapreve (casirivimab+imdevimab also known as REGEN-COV in the US) developed in collaboration with Regeneron Pharmaceuticals

# Major pending approvals 2022

| US | | EU | | China | | Japan-Chugai | |
|---|---|---|---|---|---|---|---|
| RG7596 | **Polivy**<br>1L DLBCL (US)<br>Filed Aug 2022 | RG7916 | **Evrysdi**<br>SMA presymptomatic pediatric <2mo<br>Filed Nov 2021 | RG7916 | **Evrysdi**<br>SMA presymptomatic pediatric <2mo<br>Filed June 2022 | RG6264 | **Phesgo**<br>HER-2+ BC/CC<br>Filed Sept 2022 |
| RG7446 | **Tecentriq SC**<br>all approved indications<br>Filed Nov 2022 | RG6413+ RG6412 | **Ronapreve***<br>SARS-CoV-2 hospitalized<br>Filed Jan 2022 | RG6264 | **Phesgo**<br>HER-2+ BC<br>Filed July 2022 | | |
| RG6026 | **glofitamab**<br>3L+ DLBCL<br>Filed Dec 2022 | RG6026 | **glofitamab**<br>3L+ DLBCL<br>Filed April 2022 | RG6107 | **crovalimab**<br>PNH<br>Filed Aug 2022 | | |
| | | RG1569 | **Actemra**<br>SS-ILD<br>Filed Aug 2022 | RG6026 | **glofitamab**<br>3L+ DLBCL<br>Filed Dec 2022 | | |
| | | RG7446 | **Tecentriq SC**<br>all approved indications<br>Filed Nov 2022 | | | | |

Status as of February 2, 2023

- New Molecular Entity (NME)
- Additional Indication (AI)
- Oncology / Hematology
- Immunology
- Infectious Diseases
- Metabolism
- Neuroscience
- Ophthalmology
- Other

PDS=Port Delivery System with ranibizumab
SC=Subcutaneous
*Ronapreve (casirivimab+imdevimab also known as REGEN-COV in the US) developed in collaboration with Regeneron Pharmaceuticals

# Major granted approvals 2022 and 2023 YTD

| US | |
|---|---|
| RG7716 | **Vabysmo (faricimab)**<br>DME<br>Jan 2022 |
| RG7716 | **Vabysmo (faricimab)**<br>wAMD<br>Jan 2022 |
| RG1569 | **Actemra**<br>GCA IV<br>Feb 2022 |
| RG7916 | **Evrysdi**<br>SMA presymptomatic pediatric <2mo<br>May 2022 |
| RG6152 | **Xofluza**<br>influenza pediatric<br>Aug 2022 |
| RG7421 | **Cotellic**<br>histiocytosis<br>Oct 2022 |
| RG7446 | **Tecentriq**<br>ASPS<br>Dec 2022 |
| RG7828 | **Lunsumio (mosunetuzumab)**<br>3L+ FL<br>Dec 2022 |
| RG1569 | **Actemra**<br>COVID-19 pneumonia<br>Dec 2022 |

| EU | |
|---|---|
| RG7596 | **Polivy**<br>1L DLBCL<br>May 2022 |
| RG7446 | **Tecentriq**<br>NSCLC adj<br>June 2022 |
| RG7828 | **Lunsumio (mosunetuzumab)**<br>3L+ FL<br>June 2022 |
| RG7716 | **Vabysmo (faricimab)**<br>DME<br>Sept 2022 |
| RG7716 | **Vabysmo (faricimab)**<br>wAMD<br>Sept 2022 |
| RG6152 | **Xofluza**<br>influenza pediatric<br>Jan 2023 |
| RG6013 | **Hemlibra**<br>moderate hemophilia A<br>Jan 2023 |

| China | |
|---|---|
| RG7446 | **Tecentriq**<br>NSCLC adj<br>March 2022 |
| RG1569 | **Actemra**<br>RA SC<br>April 2022 |
| RG6268 | **Rozlytrek**<br>NTRK+ solid tumors<br>July 2022 |
| RG6268 | **Rozlytrek**<br>ROS1+ NSCLC<br>Aug 2022 |
| RG7596 | **Polivy**<br>1L DLBCL<br>Jan 2023 |
| RG7596 | **Polivy**<br>r/r DLBCL<br>Jan 2023 |

| Japan-Chugai | |
|---|---|
| RG1569 | **Actemra**<br>COVID-19 pneumonia<br>Jan 2022 |
| RG7716 | **Vabysmo (faricimab)**<br>DME<br>March 2022 |
| RG7716 | **Vabysmo (faricimab)**<br>wAMD<br>March 2022 |
| RG1273 | **Perjeta + Herceptin**<br>HER-2+ CRC<br>March 2022 |
| RG7446 | **Tecentriq**<br>NSCLC adj<br>May 2022 |
| RG6013 | **Hemlibra**<br>acquired Hemophilia A<br>June 2022 |
| RG105 | **Rituxan**<br>NMOSD<br>June 2022 |
| RG7596 | **Polivy**<br>1L DLBCL<br>Aug 2022 |
| RG7159 | **Gazyva**<br>1L CLL<br>Dec 2022 |

New Molecular Entity (NME)
Additional Indication (AI)
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Status as of February 2, 2023

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Roche Pharma global development programmes

Roche Pharma research and early development (pRED)

Genentech research and early development (gRED)

Spark

# Hemlibra (emicizumab, RG6013)

*Factor VIII mimetic for treatment of hemophilia A*

| Indication | Hemophilia A patients without inhibitors to factor VIII | Hemophilia A patients with and without inhibitors to Factor VIII, dosing every 4 weeks |
|---|---|---|
| **Phase/study** | **Phase III<br>HAVEN 3** | **Phase III<br>HAVEN 4** |
| **# of patients** | N=135 | N=46 |
| **Design** | Patients on FVIII episodic treatment prior to study entry:<br>▪ **ARM A:** Hemlibra prophylaxis qw<br>▪ **ARM B:** Hemlibra prophylaxis q2w<br>▪ **ARM C:** Episodic FVIII treatment; switch to Hemlibra prophylaxis possible after 24 weeks<br>Patients on FVIII prophylaxis prior to study entry:<br>▪ **ARM D:** Hemlibra prophylaxis qw | ▪ **Part I:** Pharmacokinetic run-in part (N=6); Hemlibra q4w<br>▪ **Part II:** Expansion part (N=40); Hemlibra q4w |
| **Primary endpoint** | ▪ Number of bleeds over 24 weeks | ▪ Number of bleeds over 24 weeks |
| **Status** | ▪ Study met primary and key secondary endpoints Q4 2017<br>▪ FDA granted Breakthrough Therapy Designation April 2018<br>▪ Data presented at WFH 2018<br>▪ Filed in US (priority review) and EU in Q2 2018<br>▪ Data published in *NEJM* 2018; 379: 811-822 | ▪ Pharmacokinetic run-in data at ASH 2017<br>▪ Positive interim analysis outcome reported Q4 2017<br>▪ Data presented at WFH 2018<br>▪ Interim data filed in US and EU in Q2 2018<br>▪ Data published in Lancet Haematology 2019 Jun;6(6):e295-e305 |
| | ▪ Approved in US Q4 2018 and EU Q1 2019 | |
| **CT Identifier** | NCT02847637 | NCT03020160 |

In collaboration with Chugai

ASH=American Society of Hematology; WFH=World Federation of Hemophilia; NEJM=New England Journal of Medicine

# Hemlibra (emicizumab, RG6013)

*Factor VIII mimetic for treatment of hemophilia A*

| Indication | Hemophilia A patients with and without inhibitors to Factor VIII | Hemophilia A mild to moderate patients without inhibitors to Factor VIII |
|---|---|---|
| **Phase/study** | **Phase III<br>HAVEN 5** | **Phase III<br>HAVEN 6** |
| **# of patients** | N=85 | N=70 |
| **Design** | Patients with Hemophilia regardless of FVIII inhibitor status on prophylactic or episodic treatment prior to study entry:<br>▪ **ARM A**: Hemlibra prophylaxis qw<br>▪ **ARM B**: Hemlibra prophylaxis q4w<br>▪ **ARM C**: No prophylaxis (control arm) | Patients with mild or moderate Hemophilia A without FVIII inhibitors<br>▪ Hemlibra qw (1.5mg/kg), q2w (3.0mg/kg) or q4w (6.0mg/kg) (patients preference) |
| **Primary endpoint** | ▪ Number of bleeds over 24 weeks | ▪ Safety and efficacy |
| **Status** | ▪ FPI Q2 2018<br>▪ Recruitment completed Q1 2019<br>▪ Filed in China Q2 2020<br>▪ Approved in China Q2 2021 | ▪ FPI Q1 2020, recruitment completed Q1 2021<br>▪ Interim data presented at ASH 2021 and primary data presented at ISTH 2022<br>▪ Filed in EU Q4 2021<br>▪ Data presented at ASH 2022<br>▪ Approved in EU for moderate Hemophilia A Jan 2023 |
| **CT Identifier** | NCT03315455 | NCT04158648 |

In collaboration with Chugai
ASH=American Society of Hematology; ISTH=International Society on Thrombosis and Haemostasis

# Alecensa (alectinib, RG7853)

*New CNS-active inhibitor of anaplastic lymphoma kinase*

| Indication | Treatment-naïve ALK+ advanced NSCLC | Adjuvant ALK+ NSCLC |
|---|---|---|
| **Phase/study** | **Phase III ALEX** | **Phase III ALINA** |
| **# of patients** | N=286 | N=255 |
| **Design** | ▪ **ARM A:** Alecensa 600mg BID<br>▪ **ARM B:** Crizotinib 250mg BID | ▪ **ARM A:** Alecensa 600mg BID<br>▪ **ARM B:** Platinum-based chemotherapy |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Disease-free survival |
| **Status** | ▪ Data presented at ASCO 2017, 2018, ESMO 2017, 2018 and CNS data presented at ESMO 2017<br>▪ Data published in *NEJM* 2017; 377:829-838<br>▪ Final PFS and updated OS presented at ESMO 2019<br>▪ Approved in US Q4 2017 (priority review) and in EU Q4 2017 | ▪ FPI Q3 2018<br>▪ Recruitment completed Q4 2021 |
| **CT Identifier** | NCT02075840 | NCT03456076 |

In collaboration with Chugai

ALK=anaplastic lymphoma kinase; CNS= Central nervous system; NSCLC=non-small cell lung cancer; OS=Overall survival, PFS=Progression-free survival; ASCO=American Society of Clinical Oncology; *NEJM*=New England Journal of Medicine; ESMO=European Society for Medical Oncology

# Kadcyla (trastuzumab emtansine, RG3502)

*First ADC for HER2-positive breast cancer*

| Indication | HER2-positive early breast cancer (BC) high-risk patients | 2L+ HER-2 positive PD-L1 positive metastatic breast cancer (mBC) | HER2-positive early breast cancer (BC) high-risk patients |
|---|---|---|---|
| Phase/study | **Phase III KATHERINE** | **Phase III KATE 3** | **Phase III ASTEFANIA** |
| # of patients | N=1,484 | N=320 | N=1,700 |
| Design | ▪ **ARM A:** Kadcyla 3.6mg/kg q3w<br>▪ **ARM B:** Herceptin | ▪ **ARM A:** Kadcyla plus Tecentriq<br>▪ **ARM B:** Kadcyla plus placebo | ▪ **ARM A:** Kadcyla plus Tecentriq<br>▪ **ARM B:** Kadcyla plus placebo |
| Primary endpoint | ▪ Invasive disease-free survival | ▪ Progression-free survival and overall survival | ▪ Invasive disease-free survival |
| Status | ▪ Recruitment completed Q4 2015<br>▪ Stopped at pre-planned interim data analysis for efficacy Q4 2018<br>▪ Data presented at SABCS 2018<br>▪ BTD granted by FDA in Q1 2019<br>▪ US filling completed under RTOR Q1 2019 and filed in EU Q1 2019<br>▪ Approved in US Q2 2019 and in EU Q4 2019<br>▪ Data published in *NEJM* 2019; 380:617-628 | ▪ FPI Q1 2021<br>▪ Study closed Q4 2022 | ▪ FPI Q2 2021 |
| CT Identifier | NCT01772472 | NCT04740918 | NCT04873362 |

In collaboration with ImmunoGen, Inc.

ADC=antibody drug conjugate; BTD=Breakthrough therapy designation; HER2=Human Epidermal growth factor Receptor 2; SABCS=San Antonio Breast Cancer Symposium; RTOR=Real time oncology review; *NEJM*=New England Journal of Medicine

# Phesgo (pertuzumab/trastuzumab, RG6264)

## *FDC of Perjeta and Herceptin for subcutaneous administration*

| Indication | HER2-positive early breast cancer (BC) | | HER2-positive breast cancer (BC) |
|---|---|---|---|
| **Phase/study** | **Phase III FeDeriCa** | **Phase II PHranceSCa** | **Pivotal Phase I[1]** |
| **# of patients** | N=500 | N=160 | N=144 |
| **Design** | FDC of Perjeta and Herceptin for SC administration (Phesgo) in combination with chemotherapy in neoadjuvant/adjuvant setting<br>▪ **ARM A:** Perjeta IV plus Herceptin IV plus chemotherapy<br>▪ **ARM B:** Phesgo plus chemotherapy | ▪ **ARM A:** Perjeta and Herceptin IV followed by Phesgo<br>▪ **ARM B:** Phesgo followed by IV | ▪ **ARM A:** Phesgo administered using a handheld syringe with hypodermic needle (SC)<br>▪ **ARM B:** Phesgo administered using the on-body delivery system (OBI) |
| **Primary endpoint** | ▪ Trough Serum Concentration (Ctrough) of Perjeta during cycle 7 | ▪ Percentage of patients who preferred Perjeta and Herceptin FDC SC | ▪ AUC0-62*, Cmax** |
| **Status** | ▪ Primary endpoint met Q3 2019<br>▪ Data presented at SABCS 2019<br>▪ Data published in Lancet Oncology 2021 Jan;22(1):85-97 | ▪ Final analysis completed, 85% patients preferred FDC SC<br>▪ Data presented at ESMO 2020<br>▪ Data published in *Eur J Cancer* 2021 Jul;152:223-232 | ▪ FPI Q2 2022 |
| | ▪ Filed in US Dec 2019 & in EU Jan 2020; Approved in US Q2 2020 and EU Q4 2020 | | |
| **CT Identifier** | NCT03493854 | NCT03674112 | NCT05275010 |

[1]In collaboration with West Pharmaceuticals and Halozyme

*AUC0-62=comparability of area under the time-concentration curve from the start of dosing to 63 days; **Cmax=maximum serum concentration for pertuzumab and trastuzumab within Phesgo; FDC=Fixed-dose combination; Phesgo=FDC of Perjeta and Herceptin for SC administration;HER2=Human Epidermal growth factor Receptor 2, IV=intravenous; SC=Subcutaneous; ASCO=American Society of Clinical Oncology; NEJM=New England Journal of Medcine; SABCS=San Antonio Breast Cancer Symposium; Eur J Cancer=European Journal of Cancer; ESMO=European Society for Medical Oncology

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – lung cancer*

| Indication | Adjuvant NSCLC | Periadjuvant NSCLC |
|---|---|---|
| **Phase/study** | **Phase III**<br>**IMpower010** | **Phase III**<br>**IMpower030** |
| **# of patients** | N=1,280 | N=450 |
| **Design** | Following adjuvant cisplatin-based chemotherapy<br>▪ **ARM A:** Tecentriq<br>▪ **ARM B:** Best supportive care | ▪ **ARM A:** Tecentriq plus platinum-based chemotherapy<br>▪ **ARM B:** Platinum-based chemotherapy |
| **Primary endpoint** | ▪ Disease-free survival | ▪ Event-free survival |
| **Status** | ▪ Recruitment completed Q3 2018<br>▪ Study met primary endpoint Q1 2021<br>▪ Data presented at ASCO, WCLC and ESMO 2021<br>▪ Filed in US (priority review) and EU Q2 2021<br>▪ Approved in US Q4 2021 and EU Q2 2022 | ▪ FPI Q2 2018<br>▪ Recruitment completed Q3 2021 |
| **CT Identifier** | NCT02486718 | NCT03456063 |

NSCLC=non-small cell lung cancer; PD-L1=Programmed cell death-ligand 1; ASCO=American Society of Clinical Oncology; ESMO=European Society for Medical Oncology; WCLC=World Conference on Lung Cancer

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – lung cancer*

| Indication | 1L maintenance extensive-stage SCLC | 2L NSCLC previously treated with an immune checkpoint inhibitor | Stage IV NSCLC |
|---|---|---|---|
| **Phase/study** | **Phase III**<br>**IMforte**[1] | **Phase III**<br>**CONTACT-01**[2] | **Phase Ib/III**<br>**IMscin001**[3] |
| **# of patients** | N=450 | N=366 | N=371 |
| **Design** | ▪ **ARM A:** Platinum-etoposide + Tecentriq followed by maintenance Tecentriq plus lurbinectedin<br>▪ **ARM B:** Platinum-etoposide + Tecentriq followed by maintenance Tecentriq | ▪ **ARM A:** Tecentriq plus cabozantinib<br>▪ **ARM B:** Docetaxel | **Phase Ib**<br>▪ Dose finding, Tecentriq SC followed by Tecentriq IV<br>**Phase III**<br>▪ 2L NSCLC non inferiority of Tecentriq SC vs Tecentriq IV |
| **Primary endpoint** | ▪ Progression-free survival and overall survival | ▪ Overall survival | ▪ Observed concentration of Tecentriq in serum at cycle 1 |
| **Status** | ▪ FPI Q4 2021 | ▪ FPI Q3 2020<br>▪ Recruitment completed Q4 2021<br>▪ Study did not meet its primary endpoint Q4 2022 | ▪ FPI Phase Ib Q4 2018 and FPI Phase III Q4 2020<br>▪ Recruitment completed Q1 2022<br>▪ Study met its primary end point Q3 2022<br>▪ Data presented at ESMO-IO 2022<br>▪ Filed in US and EU Q4 2022 |
| **CT Identifier** | NCT05091567 | NCT04471428 | NCT03735121 |

[1]In collaboration with Jazz Pharma, [2]In collaboration with Exelixis, [3]SC with Halozyme's rHuPH20/ Halozyme's human hyaluronidase
NSCLC=non-small cell lung cancer; PD-L1=Programmed cell death-ligand 1; SCLC=small cell lung cancer, SC=Subcutaneous, IV=Intravenous; ESMO-IO=European Society for Medical Oncology-Immuno-Oncology

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – SCCHN and melanoma*

| Indication | Adjuvant squamous cell carcinoma of the head and neck (SCCHN) |
|---|---|
| Phase/study | **Phase III**<br>**IMvoke010** |
| # of patients | N=406 |
| Design | ▪ **ARM A:** Tecentriq 1200mg q3w<br>▪ **ARM B:** Placebo |
| Primary endpoint | ▪ Event-free survival and overall survival |
| Status | ▪ FPI Q1 2018<br>▪ Recruitment completed Q1 2020 |
| CT Identifier | NCT03452137 |

SCCHN=squamous cell carcinoma of the head and neck

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – urothelial carcinoma*

| Indication | 1L metastatic urothelial carcinoma (UC) | High-risk non-muscle-invasive bladder cancer (NMIBC) | ctDNA+, high-risk muscle-invasive bladder cancer (MIBC) |
|---|---|---|---|
| **Phase/study** | **Phase III<br>IMvigor130** | **Phase III<br>ALBAN** | **Phase III<br>IMvigor011** |
| **# of patients** | N=1,200 | N=516 | N=495 |
| **Design** | ▪ **ARM A:** Tecentriq plus gemcitabine and carboplatin or cisplatin<br>▪ **ARM B:** Tecentriq monotherapy<br>▪ **ARM C:** Placebo plus gemcitabine and carboplatin or cisplatin | ▪ **ARM A**: BCG induction and maintenance<br>▪ **ARM B:** Tecentriq plus BCG induction and maintenance | ▪ **ARM A**: Tecentriq monotherapy<br>▪ **ARM B:** Placebo |
| **Primary endpoint** | ▪ Progression-free survival, overall survival and safety | ▪ Recurrence-free survival | ▪ Recurrence-free survival |
| **Status** | ▪ Recruitment completed Q3 2018<br>▪ Study met co-primary endpoint of PFS Q3 2019<br>▪ Data presented at ESMO 2019 and AACR 2021<br>▪ Data published in Lancet 2020 May 16;395(10236):1547-1557<br>▪ Study did not meet co-primary endpoint of OS Q4 2022; US indication voluntarily withdrawn Q4 2022<br>▪ Data will be presented at ASCO-GU 2023 | ▪ FPI Q4 2018 | ▪ FPI Q2 2021 |
| **CT Identifier** | NCT02807636 | NCT03799835 | NCT04660344 |

BCG=Bacille Calmette-Guérin; PD-L1=Programmed cell death-ligand 1; PFS=Progression-free survival; AACR=American Association for Cancer Research; ESMO=European Society for Medical Oncology, ASCO-GU=American Society of Clinical Oncology Genitourinary

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – renal cell cancer*

| Indication | Advanced renal cell carcinoma (RCC) after immune checkpoint inhibitor treatment |
|---|---|
| Phase/study | **Phase III**<br>**Contact-03**[1] |
| # of patients | N=500 |
| Design | ▪ **ARM A:** Tecentriq plus cabozantinib<br>▪ **ARM B:** Cabozantinib |
| Primary endpoint | ▪ Progression-free survival and overall survival |
| Status | ▪ FPI Q3 2020<br>▪ Recruitment completed Q4 2021 |
| CT Identifier | NCT04338269 |

[1]In collaboration with Exelixis
PD-L1=Programmed cell death-ligand 1; DFS=Disease-free survival

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – hepatocellular carcinoma*

| Indication | Adjuvant hepatocellular carcinoma (HCC) |
|---|---|
| Phase/study | **Phase III**<br>**IMbrave050** |
| # of patients | N=668 |
| Design | ▪ **ARM A:** Tecentriq plus Avastin<br>▪ **ARM B:** Active surveillance |
| Primary endpoint | ▪ Recurrence-free survival |
| Status | ▪ FPI Q4 2019<br>▪ Recruitment completed Q4 2021<br>▪ Study met its primary endpoint Jan 2023 |
| CT Identifier | NCT04102098 |

PD-L1=Programmed cell death-ligand 1; ESMO=European Society for Medical Oncology; NEJM=New England Journal of Medicine; RTOR=Real time oncology review

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – breast cancer*

| Indication | Previously untreated metastatic triple negative breast cancer (TNBC) | |
|---|---|---|
| **Phase/study** | **Phase III IMpassion130** | **Phase III IMpassion132** |
| **# of patients** | N=902 | N=572 |
| **Design** | ▪ **ARM A:** Tecentriq plus nab-paclitaxel<br>▪ **ARM B:** Placebo plus nab-paclitaxel | ▪ **ARM A:** Tecentriq plus capecitabine or carbo/gem<br>▪ **ARM B:** Placebo plus capecitabine or carbo/gem |
| **Primary endpoint** | ▪ Progression-free survival and overall survival (co-primary endpoint) | ▪ Overall survival |
| **Status** | ▪ Study met co-primary endpoint of PFS in both PD-L1+ and ITT populations Q3 2018<br>▪ Primary PFS and interim OS data presented at ESMO 2018 and ASCO 2019<br>▪ Data published in *NEJM* 2018; 379:2108-2121<br>▪ US accelerated approval Q1 2019 – US indication voluntarily withdrawn Q3 2021<br>▪ Approved in EU Q3 2019<br>▪ Final OS presented at ESMO Asia 2020 | ▪ FPI Q1 2018 |
| **CT Identifier** | NCT02425891 | NCT03371017 |

Carbo/gem=gemcitabine and carboplatin; ITT=Intention to treat; PD-L1=Programmed cell death-ligand 1; PFS=Progression-free survival; OS=Overall survival; ESMO=European Society for Medical Oncology; ASCO=American Society of Clinical Oncology; NEJM=New England Journal of Medicine

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – breast cancer*

| Indication | Neoadjuvant triple negative breast cancer (TNBC) | Adjuvant triple negative breast cancer (TNBC) |
|---|---|---|
| Phase/study | **Phase III**<br>**IMpassion031** | **Phase III**<br>**IMpassion030** |
| # of patients | N=333 | N=2,300 |
| Design | ▪ **ARM A:** Tecentriq plus nab-paclitaxel<br>▪ **ARM B:** Placebo plus nab-paclitaxel | ▪ **ARM A:** Tecentriq plus paclitaxel followed by Tecentriq plus AC, followed by Tecentriq maintenance<br>▪ **ARM B:** Placebo plus paclitaxel followed by AC followed by placebo |
| Primary endpoint | ▪ Percentage of participants with pathologic complete response | ▪ Invasive disease-free survival |
| Status | ▪ Study met primary endpoint Q2 2020<br>▪ Data presented at ESMO 2020<br>▪ Data published in Lancet 2020;396 (10257):1090-1100<br>▪ Filed in EU Q4 2020 - application withdrawn Q3 2021 | ▪ FPI Q3 2018 |
| CT Identifier | NCT03197935 | NCT03498716 |

PD-L1=Programmed cell death-ligand 1; ESMO=European Society for Medical Oncology

# Venclexta (venetoclax, RG7601)

*Novel small molecule Bcl-2 selective inhibitor – chronic lymphocytic leukemia*

| Indication | Untreated chronic lymphocytic leukemia (CLL) patients with coexisting medical conditions | Relapsed or refractory chronic lymphocytic leukemia (CLL) | Untreated fit chronic lymphocytic leukemia (CLL) patients |
|---|---|---|---|
| **Phase/study** | **Phase III CLL14** | **Phase III MURANO** | **Phase III CristaLLo** |
| **# of patients** | N=445 | N=389 | N=165 |
| **Design** | ▪ **ARM A:** Venclexta plus Gazyva<br>▪ **ARM B:** Chlorambucil plus Gazyva | ▪ **ARM A:** Venclexta plus Rituxan<br>▪ **ARM B:** Rituxan plus bendamustine | ▪ **ARM A:** Venclexta plus Gazyva<br>▪ **ARM B:** Fludarabine plus cyclophosphamide plus Rituxan or bendamustine plus Rituxan |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Progression-free survival | ▪ MRD negativity rate in peripheral blood at 15 months |
| **Status** | ▪ Study met primary endpoint Q4 2018<br>▪ BTD granted by FDA Q1 2019<br>▪ US filing completed under RTOR Q1 2019<br>▪ Filed in EU Q2 2019<br>▪ Data presented at ASCO 2019, ASH 2019, ASH 2020 and EHA 2021 and EHA 2022<br>▪ Data published in *NEJM* 2019; 380:2225-2236<br>▪ Approved US Q2 2019 and EU Q1 2020 | ▪ Study met primary endpoint at interim analysis<br>▪ Data presented at ASH 2017<br>▪ Filed in US Q4 2017 and EU Q1 2018<br>▪ Data published in *NEJM* 2018; 378:1107–20<br>▪ Data presented at ASCO 2018 and ASH 2019, 2020<br>▪ Approved in US Q2 2018 (priority review) and EU Q4 2018 | ▪ FPI Q2 2020 |
| **CT Identifier** | NCT02242942 | NCT02005471 | NCT04285567 |

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute

Bcl-2=B-cell lymphoma 2; BTD=Breakthrough therapy designation; CLL=chronic lymphocytic leukemia; MRD=Minimal Residual Disease; ASH=American Society of Hematology; ASCO=American Society of Clinical Oncology; EHA=European Hematology Association; RTOR=Real time oncology review; NEJM=New England Journal of Medicine

# Venclexta (venetoclax, RG7601)

*Novel small molecule Bcl-2 selective inhibitor – multiple myeloma*

| Indication | Relapsed or refractory multiple myeloma (MM) | |
|---|---|---|
| **Phase/study** | **Phase I** | **Phase III CANOVA** |
| **# of patients** | N=117 | N=244 |
| **Design** | ▪ **Dose escalation cohort:** Venclexta dose escalation<br>▪ **Safety expansion cohort (t11;14):** Venclexta expansion<br>▪ **Combination cohort:** Venclexta plus dexamethasone | ▪ **ARM A:** Venclexta plus dexamethazone<br>▪ **ARM B:** Pomalidomide plus dexamethasone in t(11;14) positive r/r MM |
| **Primary endpoint** | ▪ Safety and maximum tolerated dose | ▪ Progression-free survival |
| **Status** | ▪ Data presented at ASCO 2015 and updated data presented at ASCO 2016 and ASH 2016<br>▪ Data published in Blood 2017; 130(22):2401-2409 and Am *J Hematol* 2021 Apr 1;96(4):418-427 | ▪ FPI Q4 2018 |
| **CT Identifier** | NCT01794520 | NCT03539744 |

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute;
Bcl-2=B-cell lymphoma 2; MM=multiple myeloma; r/r=Relapsed or refractory ; ASCO=American Society of Clinical Oncology; ASH=American Society of Hematology

# Venclexta (venetoclax, RG7601)

*Novel small molecule Bcl-2 selective inhibitor – myelodysplastic syndromes*

| Indication | Relapsed or refractory myelodysplastic syndromes (MDS) | Treatment-naive myelodysplastic syndromes (MDS) | Newly diagnosed higher-risk myelodysplatic syndrome (MDS) |
|---|---|---|---|
| **Phase/study** | **Phase Ib** | **Phase Ib** | **Phase III VERONA** |
| **# of patients** | N=70 | N=129 | N=500 |
| **Design** | **Cohort 1:**<br>▪ **ARM A:** Venclexta 400 mg<br>▪ **ARM B:** Venclexta 800 mg<br>**Cohort 2:**<br>▪ **ARM A:** Venclexta plus azacitidine<br>**Study expansion:**<br>▪ Venclexta or Venclexta plus azacitidine | **Dose escalation cohort:**<br>▪ Venclexta plus azacitidine dose escalation<br>**Safety expansion cohort** | ▪ **ARM A:** Venclexta plus azacitidine<br>▪ **ARM B:** Placebo plus azacitidine |
| **Primary endpoint** | ▪ Safety, efficacy, Pharmacokinetics and Pharmacodynamics | ▪ Safety, Pharmacokinetics, RPTD | ▪ Complete remission rate and overall survival |
| **Status** | ▪ FPI Q1 2017<br>▪ Recruitment completed Q1 2022 | ▪ FPI Q1 2017<br>▪ Data presented at ASH 2019, ASH 2020 and ASCO 201<br>▪ BTD granted by FDA July 2021<br>▪ Recruitment completed Q1 2022 | ▪ FPI Q4 2020<br>▪ Recruitment completed Q3 2022 |
| **CT Identifier** | NCT02966782 | NCT02942290 | NCT04401748 |

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute

Bcl-2=B-cell lymphoma 2; BTD=Breakthrough therapy designation; RPTD=Recommended phase II dose ; ASH=American Society of Hematology

# Polivy (polatuzumab vedotin, RG7596)

*ADC targeting CD79b to treat B cell malignancies*

| Indication | 1L DLBCL |
|---|---|
| Phase/study | **Phase III**<br>**POLARIX** |
| # of patients | N=879 |
| Design | ▪ **ARM A:** Polivy plus R-CHP<br>▪ **ARM B:** R-CHOP |
| Primary endpoint | ▪ Progression-free survival |
| Status | ▪ Recruitment completed Q2 2019<br>▪ Study met primary endpoint Q3 2021<br>▪ Data presented at ASH 2021 and 2022<br>▪ Filed in EU, Japan and China Q4 2021<br>▪ Published in *NEJM* 2022 Jan 27;386(4):351-363<br>▪ Approved in EU Q2 2022, Japan Q3 2022 and China Jan 2023<br>▪ Filed in US Q3 2022 |
| CT Identifier | NCT03274492 |

In collaboration with Seagen Inc.

DLBCL=diffuse large B cell lymphoma; R-CHP=Rituxan, cyclophosphamide, hydroxydoxorubicin, prednisone; R-CHOP=Rituxan, cyclophosphamide, doxorubicin, vincristine, and prednisone; ASH=American Society of Hematology, NEJM=New England Journal of Medicine

# Gavreto (pralsetinib, RG6396)

*Highly selective RET inhibitor*

| Indication | RET+ NSCLC, thyroid cancer and other advanced solid tumors | 1L RET fusion-positive, metastatic NSCLC |
|---|---|---|
| Phase/study | **Phase I/II ARROW** | **Phase III AcceleRET Lung** |
| # of patients | N=647 | N=250 |
| Design | ▪ **Part I:** Gavreto 30-600mg dose escalation<br>▪ **Part II:** Gavreto 400mg dose expansion | ▪ **ARM A:** Gavreto 400mg<br>▪ **ARM B:** Platinum-based chemotherapy +/- pembrolizumab |
| Primary endpoint | ▪ Safety and efficacy | ▪ Progression-free survival |
| Status | ▪ Filed in US and EU for RET fusion-positive NSCLC and US for RET-mutant MTC and RET fusion-positive thyroid cancer<br>▪ Approved in US Q3 2020 in RET fusion-positive NSCLC, in Q4 2020 in RET-mutant MTC and RET fusion-positive thyroid cancer<br>▪ Updated data presented at ASCO 2021 and 2022<br>▪ Data published in Lancet Oncol 2021 Jul;22(7):959-969 and Lancet Diabetes & Endocrinology Aug 2021;9(8):491-501<br>▪ Approved in EU for RET fusion-positive NSCLC Q4 2021<br>▪ Filing withdrawn in EU Q4 2022 for RET-mutant MTC and RET fusion-positive thyroid cancer | ▪ Study initiated in Q1 2020 |
| CT Identifier | NCT03037385 | NCT04222972 |

In collaboration with Blueprint Medicines

NSCLC=non-small cell lung cancer; MTC=medullary thyroid cancer; RET=Rearranged during transfection; ASCO=American Society of Clinical Oncology; ESMO=European Society for Medical Oncology

# Lunsumio (mosunetuzumab, CD20 x CD3, RG7828)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | 3L+ FL, 3L+ DLBCL & other relapsed or refractory NHL | 1L DLBCL | Relapsed or refractory DLBCL |
|---|---|---|---|
| **Phase/study** | **Phase I/II** | **Phase Ib/II** | **Phase Ib/II** |
| **# of patients** | N=746 | N=160 | N=262 |
| **Design** | ▪ Dose escalation study of Lunsumio as single agent and in combination with Tecentriq<br>▪ Expansion cohorts for r/r FL, r/r DLBCL and SC in r/r NHL | ▪ Lunsumio plus CHOP<br>▪ Lunsumio plus CHP plus Polivy<br>▪ Lunsumio plus CHP-Polivy vs Rituximab plus CHP-Polivy | Lunsumio plus Polivy, randomised cohorts<br>▪ **ARM A:** Lunsumio SC plus Polivy<br>▪ **ARM B:** Rituximab plus Polivy |
| **Primary endpoint** | ▪ Safety, tolerability, dose/schedule, PK and response rates | ▪ Safety/tolerability and response | ▪ Safety/tolerability and response |
| **Status** | ▪ Data in r/r NHL presented at ASH 2018, 2019, and in r/r FL at ASH 2020, 2021 and 2022<br>▪ BTD granted by FDA Q2 2020<br>▪ Filed in EU and rolling submission in US Q4 2021; Filed in US (priority review) Q2 2022<br>▪ Approved in EU Q2 2022 and US Q4 2022<br>▪ Data published in *J. Clin. Oncol.* 40(5)481-491 and in the *Lancet* July 2022: doi.org/10.1016/S1470-2045(22)00335-7 | ▪ FPI Q1 2019<br>▪ Data for Lunsumio plus CHOP presented at ASH 2020 | ▪ FPI Q3 2018<br>▪ Initial data presented at ASCO and ASH 2021 and 2022 |
| **CT Identifier** | NCT02500407 | NCT03677141 | NCT03671018 |

FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma; r/r=relapsed/refractory; NHL=non-Hodgkin's lymphoma; R=Rituximab; SC=subcutaneous; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; CHP=cyclophosphamide, doxorubicin, and prednisone); PK=Pharmacokinetics; BTD=Breakthrough Therapy Designation; ASH=American Society of Hematology; ASCO=American Society of Clinical Oncology

# Lunsumio (mosunetuzumab, CD20 x CD3, RG7828)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | 1L DLBCL & 2L DLBCL following 1L induction | Relapsed or refractory 2L+ FL |
|---|---|---|
| **Phase/study** | **Phase I** | **Phase Ib** |
| **# of patients** | N=92 + 80 (cohort C) | N=27 |
| **Design** | ▪ **Cohort A:** Lunsumio monotherapy (after a response to prior systemic chemotherapy)<br>▪ **Cohort B:** Lunsumio monotherapy (1L treatment in elderly/frail)<br>▪ **Cohort C:** Lunsumio SC plus Polivy in 1L elderly/unfit | ▪ Lunsumio plus lenalidomide safety run-in for phase III<br>▪ Lunsumio SC plus lenalidomide |
| **Primary endpoint** | ▪ Safety/tolerability and response | ▪ Safety/tolerability and response |
| **Status** | ▪ FPI Q2 2019 – Cohort B<br>▪ FPI Q3 2019 – Cohort A<br>▪ FPI Q1 2021 – Cohort C<br>▪ Initial data presented at ASH 2020 (Cohort B) and ASH 2022 | ▪ FPI Q3 2020<br>▪ Initial data presented at ASH 2021 and 2022 |
| **CT Identifier** | NCT03677154 | NCT04246086 |

FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma; r/r=relapsed/refractory; SC=subcutaneous; ASH=American Society of Hematology

# Lunsumio (mosunetuzumab, CD20 x CD3, RG7828)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | 2L+ FL | Relapsed or refractory FL | Relapsed or refractory CLL |
|---|---|---|---|
| **Phase/study** | **Phase III CELESTIMO** | **Phase Ib/II** | **Phase Ib/II** |
| **# of patients** | N=400 | N=118 | N=56 |
| **Design** | ▪ **ARM A**: Lunsumio plus lenalidomide<br>▪ **ARM B:** Rituxan plus lenalidomide | Dose escalation (Phase Ib) and expansion (Phase II)<br>▪ **ARM A**: Lunsumio plus tiragolumab<br>▪ **ARM B:** Lunsumio plus tiragolumab plus Tecentriq | ▪ Lunsumio monotherapy (3L+ CLL) |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Phase Ib: Dose-limiting toxicity<br>▪ Phase II: Best complete response | ▪ Safety, dose-limiting toxicity and RPTD |
| **Status** | ▪ FPI Q4 2021 | ▪ FPI Phase Ib Q2 2022 | ▪ FPI Q1 2022 |
| **CT Identifier** | NCT04712097 | NCT05315713 | |

FL=follicular lymphoma; r/r=relapsed/refractory; RPTD=Recommended Phase II Dose; CLL=Chronic lymphocytic leukemia

# Lunsumio (mosunetuzumab, CD20 x CD3, RG7828)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | 2L+ SCT ineligible DLBCL |
|---|---|
| Phase/study | **Phase III**<br>**SUNMO** |
| # of patients | N=222 |
| Design | ▪ **ARM A:** Lunsumio plus Polivy<br>▪ **ARM B:** R + GemOx |
| Primary endpoint | ▪ Progression-free survival |
| Status | ▪ FPI Q2 2022 |
| CT Identifier | NCT05171647 |

DLBCL=diffuse large B cell lymphoma; SCT=stem cell transplant; R=Rituxan/MabThera; GemOx=Gemcitabin und Oxaliplatin

# Ocrevus (ocrelizumab, RG1594)

*Humanized monoclonal antibody selectively targeting CD20+ B cells*

| Indication | Relapsing multiple sclerosis (RMS) | | Primary progressive multiple sclerosis (PPMS) |
|---|---|---|---|
| **Phase/study** | **Phase III OPERA I** | **Phase III OPERA II** | **Phase III ORATORIO** |
| **# of patients** | N=821 | N=835 | N=732 |
| **Design** | 96-week treatment period:<br>▪ **ARM A:** Ocrevus 2x300mg IV followed by 600mg IV q24w<br>▪ **ARM B:** Interferon β-1a (Rebif) | 96-week treatment period:<br>▪ **ARM A:** Ocrevus 2x300mg IV followed by 600mg IV q24w<br>▪ **ARM B:** Interferon β-1a (Rebif) | 120-week treatment period:<br>▪ **ARM A:** Ocrevus 2x300mg IV q24w<br>▪ **ARM B:** Placebo |
| **Primary endpoint** | ▪ Annualized relapse rate at 96 weeks versus Rebif | ▪ Annualized relapse rate at 96 weeks versus Rebif | ▪ Sustained disability progression versus placebo by EDSS |
| **Status** | ▪ Primary endpoint met Q2 2015, OLE ongoing<br>▪ Data presented at ECTRIMS 2015, AAN and ECTRIMS 2017, AAN and EAN 2018<br>▪ Data published in *NEJM* 2017; 376:221-234<br>▪ Data published on COVID-19 in *Mult Scler Relat Disord* on Ocrevus treated people with MS, doi.org/10.1016/j.msard.2020.102725 | | ▪ Primary endpoint met Q3 2015<br>▪ Data presented at ECTRIMS 2015, AAN and ECTRIMS 2017, AAN and EAN 2018<br>▪ Data published in *NEJM* 2017; 376:209-220 |
| | ▪ Approved in US Q1 2017 and EU Q1 2018 | | |
| **CT Identifier** | NCT01247324 | NCT01412333 | NCT01194570 |

IV=intravenous; EDSS=Expanded Disability Status Scale; OLE=Open label extension; ECTRIMS=European Committee for Treatment and Research in Multiple Sclerosis; AAN=Annual Meeting of the American Academy of Neurology; EAN=European Academy of Neurology; NEJM=New England Journal of Medicine

# Ocrevus (ocrelizumab, RG1594)

*Humanized monoclonal antibody selectively targeting CD20+ B cells*

| Indication | Relapsing and primary progressive multiple sclerosis (RMS & PPMS) | Primary progressive multiple sclerosis (PPMS) |
|---|---|---|
| **Phase/study** | **Phase IIIb**<br>**ENSEMBLE PLUS** | **Phase IIIb**<br>**ORATORIO-HAND** |
| **# of patients** | N=1,225 | N ~ 1,000 |
| **Design** | ▪ Substudy of ongoing phase IIIb, open-label, single-arm ENSEMBLE study<br>▪ Shorter two-hour infusion time | 120-week treatment period:<br>▪ **ARM A:** Ocrevus 600mg IV q24w<br>▪ **ARM B:** Placebo |
| **Primary endpoint** | ▪ Safety, measured by the proportion of patients with IRRs following the first randomised 600 mg infusion | ▪ Time to upper limb disability progression confirmed for at least 12 weeks |
| **Status** | ▪ Filed in US and EU Q1 2020<br>▪ Approved in EU Q2 2020 and US Q4 2020<br>▪ Data published *Neurol, Neuroimmunol* and *Neuroinflamm* Sept 2020; 7(5), e807 | ▪ FPI Q3 2019 |
| **CT Identifier** | NCT03085810 | NCT04035005 |

IV=intravenous; IRR=Infusion Related Reaction

# Ocrevus (ocrelizumab, RG1594)

*Humanized monoclonal antibody selectively targeting CD20+ B cells*

| Indication | Primary progressive multiple sclerosis (PPMS) | Relapsing multiple sclerosis (RMS) | PPMS & RMS |
|---|---|---|---|
| **Phase/study** | **Phase IIIb GAVOTTE** | **Phase IIIb MUSETTE** | **Phase III Ocarina II[1]** |
| **# of patients** | N ~ 699 | N ~ 786 | N ~ 232 |
| **Design** | 120-week treatment period:<br>▪ **ARM A:** Ocrevus 600mg IV q24w<br>▪ **ARM B:** Ocrevus 1200mg if BW <75kg or 1800mg if BW ≥75kg q24w | 120-week treatment period:<br>▪ **ARM A:** Ocrevus 600mg IV q24w<br>▪ **ARM B:** Ocrevus 1200mg if BW <75kg or 1800mg if BW ≥75kg q24w | ▪ **ARM A:** Ocrevus IV<br>▪ **ARM B:** Ocrevus SC |
| **Primary endpoint** | ▪ Superiority of Ocrevus higher dose versus approved dose on cCDP | ▪ Superiority of Ocrevus higher dose versus approved dose on cCDP | ▪ Serum Ocrevus area under the concentration-time curve (AUCW1-12) at week 12 |
| **Status** | ▪ FPI Q4 2020 | ▪ FPI Q4 2020<br>▪ Recruitment completed Q4 2021 | ▪ FPI Q2 2022<br>▪ Recruitment completed Q4 2022 |
| **CT Identifier** | NCT04548999 | NCT04544436 | NCT05232825 |

[1]SC with Halozyme's rHuPH20/ Halozyme's human hyaluronidase
cCDP=composite confirmed disability progression; IV=intravenous; SC=Subcutaneous

# Evrysdi (risdiplam, RG7916)

*Oral SMN2 splicing modifier*

| Indication | Spinal muscular atrophy (SMA) | | |
|---|---|---|---|
| **Phase/study** | **Phase II/III FIREFISH** | **Phase II/III SUNFISH** | **Phase II JEWELFISH** |
| **# of patients** | N=21 (Part 1), 41 (Part 2) | N=51 (Part 1), 180 (Part 2) | N=174 |
| **Design** | Infants with type 1 SMA<br>▪ **Part I (dose-finding):** ≥4 weeks<br>▪ **Part II (confirmatory):** 24 months | Adult & pediatric patients with type 2 or 3 SMA:<br>▪ **Part I (dose-finding):** At least 12 weeks<br>▪ **Part II (confirmatory):** 24 months | ▪ Adult and pediatric patients with previously treated SMA type 1, 2 and 3 |
| **Primary endpoint** | ▪ Safety, tolerability, PK/PD and efficacy | ▪ Safety, tolerability, PK/PD and efficacy | ▪ Safety, tolerability, PK/PD |
| **Status** | ▪ Part I 12-month data presented at AAN, CureSMA and EAN 2019; 16-month data presented at WMS 2019<br>▪ Part II 1-year data presented at AAN 2020, Part I 2-year data at WMS 2020<br>▪ Part I data published in *NEJM* 2021;384:915-923<br>▪ Part II 2-year data presented at AAN 2021<br>▪ Part II 1-year data published in *NEJM* 2021;385:427-435<br>▪ 3-year data presented at EPNS 2022 | ▪ Part I 12-month data presented at AAN, CureSMA and EAN 2019; 16-month data presented at WMS 2019<br>▪ Part II 1-year data presented at SMA Europe 2020, 2-year data at MDA 2021 and 3-year data at MDA 2022<br>▪ Part II 1-year data published in Lancet Neurology, 2022; 21 (1) 42-52 | ▪ Data presented at WMS 2017, AAN 2018, WMS 2018, CureSMA 2019, WMS 2019, CureSMA 2020 and 2021<br>▪ 2-year data presented at WMS 2022 |
| | ▪ ODD granted by FDA Q1 2017 and EU Q1 2019, PRIME designation in Q4 2018<br>▪ Approved in US Q3 2020 and EU Q1 2021 | | |
| **CT Identifier** | NCT02913482 | NCT02908685 | NCT03032172 |

In collaboration with PTC Therapeutics and SMA Foundation

SMA=Spinal muscular atrophy; SMN=survival motor neuron; PK/PD=Pharmacokinetics/Pharmacodynamics; PRIME=priority medicines; AAN=American Academy of Neurology; WMS=World Muscle Society; EAN=European Academy of Neurology; NEJM=New England Journal of Medicine; MDA=Muscular Dystrophy Association; CureSMA=Annual SMA Conference; EPNS=European Paediatric Neurology Society; ODD=Orphan drug designation

# Evrysdi (risdiplam, RG7916)

*Oral SMN2 splicing modifier*

| Indication | Spinal muscular atrophy (SMA) | |
|---|---|---|
| **Phase/study** | **Phase II**<br>**RAINBOWFISH** | **Phase II/III**<br>**MANATEE** |
| **# of patients** | N=25 | N=180 |
| **Design** | ▪ Infants aged from birth to 6 weeks who have been genetically diagnosed with SMA but are not yet presenting with symptoms | **ARM A:**<br>▪ **Part I**: GYM329 plus Evrysdi for 24 weeks, followed by GYM329 plus Evrysdi for 72 weeks<br>▪ **Part II:** GYM329 plus Evrysdi for 72 weeks<br>**ARM B:**<br>▪ Placebo plus Evrysdi |
| **Primary endpoint** | ▪ Proportion of participants with two copies of the SMN2 gene and baseline CMAP>=1.5 millivolt who are sitting without support | ▪ Change from baseline in RHS score after week 72 of treatment<br>▪ Safety, PK/PD and muscle biomarkers |
| **Status** | ▪ FPI Q3 2019<br>▪ Recruitment completed Q1 2022<br>▪ Initial data presented at CureSMA , WMS 2021, MDA and WMS 2022<br>▪ Filed in US and EU Q4 2021<br>▪ Approved in US Q2 2022 | ▪ FPI Part I Q2 2022<br>▪ ODD granted by FDA in Q4 2021 for GYM329 |
| **CT Identifier** | NCT03779334 | NCT05115110 |

In collaboration with PTC Therapeutics and SMA Foundation

SMN=survival motor neuron; CMAP=compound muscle action potential; PK/PD=Pharmacokinetics/Pharmacodynamics; WMS=World Muscle Society; CureSMA=Annual SMA Conference; MDA=Muscular Dystrophy Association; ODD=Orphan drug designation; RHS=Revised hammersmith scale

# Enspryng (satralizumab, RG6168, SA237)

*Anti-IL-6 receptor humanized monoclonal antibody*

| Indication | Neuromyelitis optica spectrum disorder (NMOSD) | |
|---|---|---|
| **Phase/study** | **Phase III**<br>**SAkuraStar** | **Phase III**<br>**SAkuraSky** |
| **# of patients** | N=95 | N=83 |
| **Design** | Enspryng monotherapy:<br>▪ **ARM A:** Enspryng 120mg SC monthly<br>▪ **ARM B:** Placebo SC monthly | Add-on therapy of Enspryng:<br>▪ **ARM A:** Enspryng 120mg SC monthly<br>▪ **ARM B:** Placebo SC monthly<br>▪ Both arms on top of baseline therapies: azathioprine, mycophenolate mofetil or oral corticosteroids |
| **Primary endpoint** | ▪ Efficacy (time to first relapse), safety and PK/PD | ▪ Efficacy (time to first relapse), safety and PK/PD |
| **Status** | ▪ Primary endpoint met Q4 2018<br>▪ Data presented at ECTRIMS 2019<br>▪ Published in Lancet Neurology 2020; 19(5): 402-412 | ▪ Primary endpoint met Q3 2018<br>▪ Data presented at ECTRIMS 2018 and AAN 2019<br>▪ Published in *NEJM* 2019; 381:2114-2124 |
| | ▪ BTD granted by FDA Q4 2018<br>▪ Filed in EU Q3 2019; US acceptance of filing Q4 2019<br>▪ Approved in US Q3 2020 and EU Q2 2021 | |
| **CT Identifier** | NCT02073279 | NCT02028884 |

*Trials managed by Chugai (Roche opted-in)

BTD=Breakthrough therapy designation; PK/PD=Pharmacokinetics/Pharmacodynamics; SC=Subcutaneous; ECTRIMS=European Committee for Treatment and Research in Multiple Sclerosis; AAN=American Academy of Neurology; NEJM=New England Journal of Medicine

# Enspryng (satralizumab, RG6168, SA237)

*Anti-IL-6 receptor humanized monoclonal antibody*

| Indication | Generalised myasthenia gravis (MG) | Myelin oligodendrocyte glycoprotein antibody disease (MOG-AD) | Autoimmune encephalitis (AIE) |
|---|---|---|---|
| Phase/study | **Phase III Luminesce** | **Phase III METEOROID** | **Phase III CIELO** |
| # of patients | N=240 | N=152 | N=152 |
| Design | ▪ **ARM A:** Enspryng plus standard of care<br>▪ **ARM B:** Placebo plus standard of care | ▪ **ARM A**: Enspryng at weeks 0, 2, 4 (loading doses) and maintenance doses q4w<br>▪ **ARM B:** Placebo | ▪ **ARM A**: Enspryng at weeks 0, 2, 4 (loading doses) and maintenance doses q4w<br>▪ **ARM B**: Placebo |
| Primary endpoint | ▪ Mean change from baseline in total MG-ADL score at week 24 in AChR+ population | ▪ Time from randomization to the first occurrence of a MOG-AD relapse | ▪ Efficacy (proportion of participants with mRS score improvement ≥ 1 from baseline and no use of rescue therapy at week 24) and safety |
| Status | ▪ ODD granted in US Q1 2021<br>▪ FPI Q4 2021 | ▪ FPI Q3 2022<br>▪ ODD granted by FDA in Q4 2021 | ▪ FPI Q3 2022<br>▪ ODD granted for NMDAR AIE in US Q3 22 |
| CT Identifier | NCT04963270 | NCT05271409 | NCT05503264 |

In collaboration with Chugai

MG-ADL= Myasthenia Gravis Activities of Daily Living; AChR=Acetylcholine receptor; MOG-AD=Myelin Oligodendrocyte Glycoprotein Antibody Disease, mRS=Modified Rankin Scale; AIE=Autoimmune encephalitis; NMDAR AIE= Anti-N-Methyl-D-Aspartic Acid Receptor Autoimmune Encephalitis; PK/PD=Pharmacokinetics/Pharmacodynamics; ODD=Orphan drug designation

# Gazyva (obinutuzumab, RG7159)

## *Immunology development program*

| Indication | Lupus nephritis | | Membranous nephropathy |
|---|---|---|---|
| **Phase/study** | **Phase II NOBILITY** | **Phase III REGENCY** | **Phase III MAJESTY** |
| **# of patients** | N=126 | N=252 | N=140 |
| **Design** | ▪ **ARM A:** Gazyva 1000mg IV plus MFF / mycophenolic acid<br>▪ **ARM B:** Placebo IV plus MFF/ mycophenolic acid | ▪ **ARM A:** Gazyva 1000mg IV (6 doses through Week 52) plus MFF<br>▪ **ARM B:** Gazyva1000 mg IV (5 doses through Week 52) plus MFF<br>▪ **ARM C:** Placebo IV plus MFF | ▪ **ARM A:** Gazyva 1000mg IV on top of renin-angiotensin inhibitors<br>▪ **ARM B:** Tacrolimus treatment for 12 months |
| **Primary endpoint** | ▪ Percentage of participants who achieve complete renal response (CRR) | ▪ Percentage of participants who achieve complete renal response (CRR) | ▪ Percentage of patients who achieve complete remission at week 104 |
| **Status** | ▪ Recruitment completed Q4 2017<br>▪ Primary endpoint met Q2 2019<br>▪ BTD granted by the FDA Q3 2019<br>▪ Data presented at ASN and ACR 2019<br>▪ Published in *Ann Rheum Dis* 2022 Jan;81(1):100-107 | ▪ FPI Q3 2020 | ▪ FPI Q2 2021 |
| **CT Identifier** | NCT02550652 | NCT04221477 | NCT04629248 |

In collaboration with Biogen

BTD=Breakthrough therapy designation; IV=Intravenous; ASN=American Society of Nephrology; ACR=American College of Rheumatology; MFF=mycophenolate mofetil=

# Gazyva (obinutuzumab, RG7159)

*Immunology development program*

| Indication | Systemic lupus erythematosus (SLE) |
|---|---|
| Phase/study | **Phase III**<br>**ALLEGORY** |
| # of patients | N=200 |
| Design | ▪ **ARM A:** Gazyva 1000mg IV on Day 1 and Weeks 2, 24 and 26.<br>▪ **ARM B:** Placebo IV |
| Primary endpoint | ▪ Percentage of participants who achieve Systemic Lupus Erythematosus Responder Index (SRI) at week 52 |
| Status | ▪ FPI Q4 2021 |
| CT Identifier | NCT04963296 |

In collaboration with Biogen
IV=Intravenous

# Lunsumio (mosunetuzumab, CD20 x CD3, RG7828)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | Systemic lupus erythematosus (SLE) |
|---|---|
| Phase/study | **Phase I** |
| # of patients | N=50 |
| Design | ▪ **ARM A**: Lunsumio SC on either Day 1 or on Days 1 and 8<br>▪ **ARM B:** Fractionated (divided) dose of Lunsumio SC on Days 1 and 8 |
| Primary endpoint | ▪ Safety |
| Status | ▪ FPI Q1 2022 |
| CT Identifier | NCT05155345 |

SC=subcutaneous

# Actemra/RoActemra (tocilizumab, RG1569)

*Interleukin 6 receptor inhibitor*

| Indication | Adult hospitalised with severe COVID-19 pneumonia | |
|---|---|---|
| **Phase/study** | **Phase III COVACTA[1]** | **Phase III REMDACTA[2]** |
| **# of patients** | N=450 | N=650 |
| **Design** | ▪ **ARM A:** Actemra plus standard of care<br>▪ **ARM B:** Placebo plus standard of care | ▪ **ARM A:** Remdesivir plus Actemra<br>▪ **ARM B:** Remdesivir plus placebo |
| **Primary endpoint** | ▪ Clinical status assessed using 7-Category Ordinal Scale (Day 28) | ▪ Time to hospital discharge or ready for discharge |
| **Status** | ▪ Primary endpoint not met Q3 2020<br>▪ Published in *NEJM* 2021; 384:1503-1516 | ▪ Primary endpoint not met Q1 2021<br>▪ Published in *Intensive Care Med* 2021 doi: 10.1007/s00134-021-06507-x |
| | ▪ Filed in EU Q3 2021 and US Q1 2022<br>▪ Approved in EU Q4 2021 and US Q4 2022 | |
| **CT Identifier** | NCT04320615 | NCT04409262 |

[1]In collaboration with US Biomedical Advanced Research and Development Authority (BARDA); [2]In collaboration with Gilead Sciences, Inc.
NEJM=New England Journal of Medicine

# Actemra/RoActemra (tocilizumab, RG1569)

*Interleukin 6 receptor inhibitor*

| Indication | Adult hospitalised with severe COVID-19 pneumonia | |
|---|---|---|
| **Phase/study** | **Phase II**<br>**MARIPOSA** | **Phase III**<br>**EMPACTA** |
| **# of patients** | N=100 | N=379 |
| **Design** | ▪ **ARM A:** 8 mg/kg Actemra plus standard of care<br>▪ **ARM B:** 4mg/kg Actemra plus standard of care | Conducted in sites known to provide critical care to underserved and minority populations that often do not have access to clinical trials<br><br>▪ **ARM A:** Actemra plus standard of care<br>▪ **ARM B:** Placebo plus standard of care |
| **Primary endpoint** | ▪ Pharmacodynamics and pharmacokinetics | ▪ Cumulative proportion of participants requiring mechanical ventilation by day 28 |
| **Status** | ▪ FPI Q2 2020<br>▪ Recruitment completed Q2 2020<br>▪ Published in *Open Forum Infect Dis* 2021 Dec 4;9(1) | ▪ Primary endpoint met Q3 2020<br>▪ Published in *NEJM* 2021 Jan 7;384(1):20-30<br>▪ Filed in EU Q3 2021 and US Q1 2022<br>▪ Approved in EU Q4 2021 and US Q4 2022 |
| **CT Identifier** | NCT04363736 | NCT04372186 |

NEJM=New England Journal of Medicine

# Xolair (omalizumab, RG3648)

*Humanized monoclonal antibody that selectively binds to IgE*

| Indication | Food allergy |
|---|---|
| Phase/study | **Phase III**<br>**OUtMATCH[1]** |
| # of patients | N=225 |
| Design | ▪ Xolair by SC injection either q2w or q4w for 16 to 20 weeks |
| Primary endpoint | ▪ Number of participants who successfully consume ≥600mg of peanut protein without dose-limiting symptoms |
| Status | ▪ FPI Q3 2019 |
| CT Identifier | NCT03881696 |

In collaboration with Novartis; [1] Sponsor of the study is the National Institute of Allergy and Infectious Diseases (NIAID)
IgE=Immunoglobulin E; SC=Subcutaneous

# Susvimo (PDS, RG6321)

*First eye implant to achieve sustained delivery of a biologic medicine*

| Indication | Wet age-related macular degeneration (wAMD) | | |
|---|---|---|---|
| **Phase/study** | **Phase III<br>Archway** | **Phase II+III extension<br>Portal** | **Phase IIIb<br>Velodrome** |
| **# of patients** | N=418 | N=1,000 | N=442 |
| **Design** | ▪ **ARM A:** PDS q24w<br>▪ **ARM B:** Intravitreal ranibizumab q4w | ▪ Patients from LADDER or Archway receive refills of ranibizumab q24w (patients without the PDS will receive the PDS and subsequent refills) | ▪ **ARM A:** PDS q36w<br>▪ **ARM B:** PDS q24w |
| **Primary endpoint** | ▪ Change in BCVA from baseline at the average of week 36 and week 40 | ▪ Safety and long term efficacy | ▪ Change in BCVA from baseline averaged over weeks 68 and 72 |
| **Status** | ▪ Study met primary endpoint Q2 2020<br>▪ Data presented at ASRS 2020, 44/48 week data at Angiogenesis 2021 and 2-year data at Angiogenesis 2022<br>▪ Filed in US (PRIME) and EU Q2 2021<br>▪ Approved in US Q4 2021 | ▪ FPI Q3 2018 | ▪ FPI Q2 2021 |
| **CT Identifier** | NCT03677934 | NCT03683251 | NCT04657289 |

BCVA=best corrected visual acuity; wAMD=wet age-related macular degeneration; ASRS=American Society of Retinal Specialists; PDS=Port Delivery System with ranibizumab; PRIME=Priority review

# Susvimo (PDS, RG6321)

*First eye implant to achieve sustained delivery of a biologic medicine*

| Indication | Diabetic macular edema (DME) | Diabetic retinopathy (DR) without center-involved diabetic macular edema (DME) |
|---|---|---|
| Phase/study | **Phase III Pagoda** | **Phase III Pavilion** |
| # of patients | N=545 | N=160 |
| Design | ▪ **ARM A:** PDS q24w<br>▪ **ARM B:** Intravitreal ranibizumab q4w | ▪ **ARM A:** Intravitreal ranibizumab (X2) followed by PDS implant (refill q36w)<br>▪ **ARM B:** Q4w comprehensive clinical monitoring until participants receive PDS (refill q36w) |
| Primary endpoint | ▪ Change in BCVA from baseline at the average of week 48 and week 52 | ▪ Percentage of participants with a ≥2-step improvement from baseline on the ETDRS-DRSS at Week 52 |
| Status | ▪ FPI Q3 2019<br>▪ Recruitment completed Q2 2021<br>▪ Study met its primary endpoint Q4 2022 | ▪ FPI Q3 2020<br>▪ Recruitment completed Q3 2021<br>▪ Study met its primary endpoint Q4 2022 |
| CT Identifier | NCT04108156 | NCT04503551 |

BCVA=best corrected visual acuity; ETDRS=Early Treatment Diabetic Retinopathy Study; DRSS=Diabetic Retinopathy Severity Scale; PDS=Port Delivery System with ranibizumab

# Vabysmo (faricimab, RG7716)

*Bispecific antibody to simultaneously bind Ang-2 and VEGF-A*

| Indication | Center-involving diabetic macular edema (CI-DME) | |
|---|---|---|
| **Phase/study** | **Phase III<br>YOSEMITE** | **Phase III<br>RHINE** |
| **# of patients** | N=940 | N=951 |
| **Design** | ▪ **ARM A:** Faricimab q8w<br>▪ **ARM B:** Faricimab PTI up to q16w<br>▪ **ARM C:** Aflibercept, q8w | ▪ **ARM A:** Faricimab q8w<br>▪ **ARM B:** Faricimab PTI up to q16w<br>▪ **ARM C:** Aflibercept, q8w |
| **Primary endpoint** | ▪ Change from baseline in BCVA at 1 year | ▪ Change from baseline in BCVA at 1 year |
| **Status** | ▪ Study met primary endpoint Q4 2020<br>▪ Data presented at Angiogenesis 2021 | ▪ Study met primary endpoint Q4 2020<br>▪ Data presented at Angiogenesis 2021 |
| | ▪ Filed in US and EU Q2 2021<br>▪ Published in the Lancet 2022 Feb 19;399(10326):741-755.<br>▪ 2-year data presented at Angiogenesis 2022<br>▪ Approved in US Q1 2022 and EU Q3 2022 | |
| **CT Identifier** | NCT03622580 | NCT03622593 |

Ang-2=Angiopoietin-2; VEGF=Vascular endothelial growth factor; PTI=Personalized Treatment Interval; BCVA=best corrected visual acuity

# Vabysmo (faricimab, RG7716)

*Bispecific antibody to simultaneously bind Ang-2 and VEGF-A*

| Indication | Wet age related macular degeneration (wAMD) | |
|---|---|---|
| **Phase/study** | **Phase III<br>TENAYA** | **Phase III<br>LUCERNE** |
| **# of patients** | N=671 | N=658 |
| **Design** | ▪ **ARM A:** Faricimab 6.0mg q16w flexible after 4 IDs<br>▪ **ARM B:** Aflibercept 2.0mg q8w after 3 IDs | ▪ **ARM A:** Faricimab 6.0mg q16w flexible after 4 IDs<br>▪ **ARM B:** Aflibercept 2.0mg q8w after 3 IDs |
| **Primary endpoint** | ▪ Change from baseline in BCVA week 40, 44 & 48 | ▪ Change from baseline in BCVA week 40, 44 & 48 |
| **Status** | ▪ Study met primary endpoint Q1 2021<br>▪ Data presented at Angiogenesis 2021 | ▪ Study met primary endpoint Q1 2021<br>▪ Data presented at Angiogenesis 2021 |
| | ▪ Filed in US and EU Q2 2021<br>▪ Published in Lancet 2022 Feb 19;399(10326):729-740<br>▪ Approved in US Q1 2022 and EU Q3 2022<br>▪ 2-year data presented at ASRS 2022 | |
| **CT Identifier** | NCT03823287 | NCT03823300 |

BCVA=best corrected visual acuity; Ang-2=Angiopoietin-2; VEGF=Vascular endothelial growth factor; IDs=initiating doses; ASRS=American Society of Retina Specialists

# Vabysmo (faricimab, RG7716)

*Bispecific antibody to simultaneously bind Ang-2 and VEGF-A*

| Indication | Macular edema (ME) secondary to branch retinal vein occlusion (RVO) | Macular edema (ME) secondary to central retinal vein occlusion (RVO) |
|---|---|---|
| Phase/study | **Phase III**<br>**BALATON** | **Phase III**<br>**COMINO** |
| # of patients | N=570 | N=750 |
| Design | ▪ **ARM A:** Faricimab, q4w/PTI<br>▪ **ARM B:** Aflibercept, q4w | ▪ **ARM A:** Faricimab, q4w/PTI<br>▪ **ARM B:** Aflibercept, q4w |
| Primary endpoint | ▪ Change from baseline in BCVA at week 24 | ▪ Change from baseline in BCVA at week 24 |
| Status | ▪ FPI Q1 2021<br>▪ Recruitment completed Q1 2022<br>▪ Study met its primary endpoint Q4 2022 | ▪ FPI Q1 2021<br>▪ Recruitment completed Q1 2022<br>▪ Study met its primary endpoint Q4 2022 |
| CT Identifier | NCT04740905 | NCT04740931 |

PTI=Personalized Treatment Interval; BCVA=best corrected visual acuity; Ang-2=Angiopoietin-2; VEGF=Vascular endothelial growth factor

# Xofluza (baloxavir marboxil, RG6152, S-033188 )

*Small molecule, novel CAP-dependent endonuclease inhibitor*

| Indication | Influenza | | |
|---|---|---|---|
| **Phase/study** | **Phase III**<br>**miniSTONE 1 (0-1 year old)** | **Phase III**<br>**miniSTONE 2 (1- <12 years old )** | **Phase IIIb**<br>**CENTERSTONE** |
| **# of patients** | N=30 | N=176 | N=3,160 |
| **Design** | Healthy pediatric patients from birth to <1 year with influenza-like symptoms receive Xofluza on Day 1 | Healthy pediatric patients 1 to <12 years of age with influenza-like symptoms<br>▪ **ARM A:** Xofluza<br>▪ **ARM B:** Tamiflu | Reduction of direct transmission of influenza from otherwise healthy patients to household contacts<br>▪ **ARM A:** Xofluza<br>▪ **ARM B:** Placebo |
| **Primary endpoint** | ▪ Safety | ▪ Safety | ▪ Percentage of household contacts who are PCR-positive for influenza by day 5 post randomization of index patients |
| **Status** | ▪ FPI Q1 2019 | ▪ Primary endpoint met Q2 2019<br>▪ Data presented at OPTIONS X 2019<br>▪ Filed in US Q1 2020 and EU Q4 2021<br>▪ Data published in *Pediatric Infectious Disease* 2020 Aug;39(8):700-705<br>▪ Approved in the US (age 5 years and older) Q3 2022 and EU Jan 2023 | ▪ FPI Q4 2019 |
| **CT Identifier** | NCT03653364 | NCT03629184 | NCT03969212 |

In collaboration with Shionogi & Co., Ltd.
CAP=Catabolite Activating Protein

Roche Group development pipeline

Marketed products development programmes

Roche Pharma global development programmes

Roche Pharma research and early development (pRED)

Genentech research and early development (gRED)

Spark

# Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

*Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT*

| Indication | 1L NSCLC PD-L1 TPS>50% | Stage III unresectable 1L NSCLC |
|---|---|---|
| Phase/study | **Phase III**<br>**SKYSCRAPER-01** | **Phase III**<br>**SKYSCRAPER-03** |
| # of patients | N=500-560 | N=800 |
| Design | ▪ **ARM A:** Tiragolumab plus Tecentriq<br>▪ **ARM B:** Placebo plus Tecentriq | ▪ **ARM A:** Tiragolumab plus Tecentriq for up to 12 months<br>▪ **ARM B:** Durvalumab for up to 12 months |
| Primary endpoint | ▪ Overall survival and progression-free survival | ▪ Progression-free survival |
| Status | ▪ FPI Q1 2020<br>▪ Recruitment completed Q3 2021<br>▪ Study did not meet one of its primary endpoints, PFS, Q2 2022 | ▪ FPI Q3 2020 |
| CT Identifier | NCT04294810 | NCT04513925 |

NSCLC=Non-small cell lung cancer; ES-SCLC=Extensive stage small cell lung cancer; PD-L1=Programmed cell death-ligand 1; TPS=Tumor Proportion Score; PFS=Progression-free survival

# Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

*Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT*

| Indication | Metastatic and/or recurrent PD-L1+ cervical cancer (CC) | Neoadjuvant and adjuvant NSCLC | 1L non-squamous NSCLC |
|---|---|---|---|
| Phase/study | **Phase II SKYSCRAPER-04** | **Phase II SKYSCRAPER-05** | **Phase III SKYSCRAPER-06** |
| # of patients | N=172 | N=82 | N=540 |
| Design | ▪ **ARM A:** Tiragolumab plus Tecentriq<br>▪ **ARM B:** Tecentriq | ▪ **ARM A:** (PD-L1 high) neoadjuvant tiragolumab plus Tecentriq followed by adjuvant tiragolumab plus Tecentriq or adjuvant chemotherapy<br>▪ **ARM B:** (PD-L1 all-comers) neoadjuvant tiragolumab plus Tecentriq plus chemo followed by adjuvant tiragolumab plus Tecentriq | ▪ **ARM A:** Tiragolumab plus Tecentriq plus pemetrexed plus chemotherapy followed by maintenance tiragolumab plus Tecentriq plus pemetrexed<br>▪ **ARM B:** Placebo plus pembrolizumab plus pemetrexed plus chemotherapy followed by maintenance placebo plus pembrolizumab plus pemetrexed |
| Primary endpoint | ▪ Objective response rate | ▪ Pathologic complete response, major pathological response and safety | ▪ Objective response rate, progression-free survival and overall survival |
| Status | ▪ FPI Q2 2020 | ▪ FPI Q2 2021 | ▪ FPI Q4 2020 |
| CT Identifier | NCT04300647 | NCT04832854 | NCT04619797 |

NSCLC=Non-small cell lung cancer; PD-L1=Programmed cell death-ligand 1

# Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

*Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT*

| Indication | Locally advanced esophageal cancer (EC) | 1L esophageal cancer (EC) | 1L recurrent/metastatic PD-L1 positive squamous cell head and neck carcinoma (SCCHN) |
|---|---|---|---|
| Phase/study | **Phase III SKYSCRAPER-07** | **Phase III SKYSCRAPER-08** | **Phase II SKYSCRAPER-09** |
| # of patients | N=750 | N=500 | N=120 |
| Design | ▪ **ARM A:** Tiragolumab plus Tecentriq<br>▪ **ARM B:** Tecentriq plus placebo<br>▪ **ARM C:** Placebo plus placebo | ▪ **ARM A:** Tiragolumab plus Tecentriq plus cisplatin and paclitaxel<br>▪ **ARM B:** Placebo plus placebo plus cisplatin and paclitaxel | ▪ **ARM A:** Tiragolumab plus Tecentriq<br>▪ **ARM B:** Tecentriq plus placebo |
| Primary endpoint | ▪ Progression-free survival (A vs C)<br>▪ Overall survival (A vs C, hierarchical, B vs C hierarchical) | ▪ Overall survival and progression-free survival | ▪ Objective response rate |
| Status | ▪ FPI Q3 2020 | ▪ FPI Q4 2020<br>▪ Recruitment completed Q4 2021 | ▪ FPI Q1 2021<br>▪ Recruitment completed Q2 2022 |
| CT Identifier | NCT04543617 | NCT04540211 | NCT04665843 |

NSCLC=Non-small cell lung cancer; PD-L1=Programmed cell death-ligand 1

# Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

*Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT*

| Indication | Solid tumors | NSCLC | Relapsed or refractory multiple myeloma (MM) or r/r B-cell NHL |
|---|---|---|---|
| **Phase/study** | **Phase I** | **Phase II CITYSCAPE** | **Phase I** |
| **# of patients** | N=540 | N=135 | N=52 |
| **Design** | ▪ **Phase Ia:** Dose escalation and expansion of tiragolumab<br>▪ **Phase Ib:** Dose escalation and expansion of tiragolumab in combination with Tecentriq and/or other anti-cancer therapies | ▪ **ARM A:** Tecentriq plus tiragolumab<br>▪ **ARM B:** Tecentriq monotherapy | ▪ **Phase Ia:** Tiragolumab monotherapy<br>▪ **Phase Ib:** Tiragolumab plus daratumumab (r/r MM) or rituximab (r/r NHL) |
| **Primary endpoint** | ▪ Safety, tolerability, PK variability and preliminary efficacy | ▪ Overall response rate and progression-free survival | ▪ Safety, tolerability, PK/PD and preliminary efficacy |
| **Status** | ▪ Data presented at AACR 2020 | ▪ Data presented at ASCO 2020 and WCLC and ESMO IO 2021<br>▪ BTD granted by FDA Q4 2020<br>▪ Published in *Lancet Oncol* 2022 Jun;23(6):781-792 | ▪ FPI Q2 2019 |
| **CT Identifier** | NCT02794571 | NCT03563716 | NCT04045028 |

BTD=Breakthrough therapy designation; MM=Multiple myeloma; NSCLC=Non-small cell lung cancer; r/r=Relapsed refractory; NHL=Non-Hodgkin's lymphoma; PK=Pharmacokinetics; PD=Pharmacodynamics; ASCO=American Society of Clinical Oncology; AACR=American Association for Cancer Research; WCLC=World Conference on Lung Cancer; ESMO IO=European Society for Medical Oncology - Immuno-Oncology

# Glofitamab (CD20-TCB, RG6026)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | Relapsed or refractory Non-Hodgkin's lymphoma (NHL) | | |
|---|---|---|---|
| **Phase/study** | **Phase I** | **Phase Ib** | **Phase I** |
| **# of patients** | N=700 | N=140 | N=18-36 |
| **Design** | **Cohort 1:** Single-agent dose escalation study<br>▪ Initial dose escalation<br>▪ Expansion cohort in r/r DLBCL<br>▪ Expansion cohort in r/r FL<br>▪ All patients will receive pretreatment with a single dose of Gazyva (1000mg)<br>**Cohort 2:** Glofitamab plus Gazyva (i.e. continuous treatment with Gazyva) | Dose escalation and expansion<br>▪ **ARM A:** Glofitamab plus Tecentriq<br>▪ **ARM B:** Glofitamab plus Polivy | Glofitamab SC<br>▪ Part 1 dose escalation |
| **Primary endpoint** | ▪ Efficacy, safety, tolerability and pharmacokinetics | ▪ Safety | ▪ Safety |
| **Status** | ▪ FPI Q1 2017<br>▪ Data presented at ASH 2018, ICML and ASH 2019; EHA and ASH 2020; ASCO, EHA, ICML and ASH 2021; ASCO, EHA and ASH 2022<br>▪ Data published in *J Clin Oncology* 2021; 39:18:1959-1970 and *NEJM* 2022; 387:2220-2231<br>▪ Filed in EU Q2 2022 and US Q4 2022 | ▪ ARM A: FPI Q2 2018<br>▪ Data presented at ASH 2019 and ASH 2021<br>▪ ARM B: FPI Q4 2020 | ▪ FPI Q3 2021 |
| **CT Identifier** | NCT03075696 | NCT03533283 | ISRCTN17975931 |

DLBCL=diffuse large B cell lymphoma; FL=Follicular lymphoma; r/r=Relapsed or refractory; SC=subcutenous; ASCO=American Society of Clinical Oncology; ASH=American Society of Hematology; EHA=European Hematology Association; ICML=International Conference on Malignant Lymphoma; NEJM=New England Journal of Medicine

# Glofitamab (CD20-TCB, RG6026)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | Non-Hodgkin's lymphoma (NHL) | 2L+ SCT-ineligible DLBCL | 1L ctDNA high risk DLBCL |
|---|---|---|---|
| **Phase/study** | **Phase Ib** | **Phase III STARGLO** | **Phase II** |
| **# of patients** | Part I: 15-60<br>Part II: ~66-104 | N=270 | N=40 |
| **Design** | ▪ **Part I:** Dose-finding for the combination of glofitamab plus G/R-CHOP in r/r indolent NHL<br>▪ **Part II:** Dose expansion glofitamab plus G/R-CHOP or R-CHOP in 1L DLBCL<br>▪ **Part III:** Glofitamab plus R-CHP plus Polivy | ▪ **ARM A:** Glofitamab plus gemcitabine and oxaliplatin, followed by up to 4 cycles of glofitamab monotherapy<br>▪ **ARM B:** Rituxan in combination with gemcitabine and oxaliplatin<br><br>A single dose of Gazyva will be administered 7 days prior to the first dose of glofitamab | ▪ Glofitamab plus R-CHOP (glofitamab is introduced as a consolidation to R-CHOP at cycle 3-8 in patients ctDNA+ at cycle 2) |
| **Primary endpoint** | ▪ Safety | ▪ Overall survival | ▪ EOT PET-CR |
| **Status** | ▪ Part I: FPI Q1 2018<br>▪ Part II: FPI Q1 2021<br>▪ Data presented at ASH 2021 and 2022 | ▪ FPI Q1 2021 | ▪ FPI Q1 2022 |
| **CT Identifier** | NCT03467373 | NCT04408638 | NCT04980222 |

DLBCL=diffuse large B cell lymphoma; SCT=stem cell transplant; CHOP=cyclophosphamide, doxorubicin, vincristine and prednisone; R=Rituxan/MabThera; G=Gazyva; NHL=Non-Hodgkin's lymphoma; r/r=Relapsed or refractory; ctDNA=circulating tumor DNA; ASH=American Society of Hematology; EOT PET-CR=End of treatment PET-complete response rate

# Glofitamab (CD20-TCB, RG6026)

*Bispecific anti-CD20/CD3 antibody engaging T and B cells simultaneously*

| Indication | 2L+ SCT-eligible DLBCL | |
|---|---|---|
| **Phase/study** | **Phase Ib** | **Phase Ib** |
| **# of patients** | N=40 | N=112 |
| **Design** | ▪ Glofitamab plus R-ICE (single-arm study) | ▪ Glofitamab IV plus CELMoD (CC-220 and CC-99282)<br>▪ Lunsumio SC plus CELMoD (CC-220 and CC-99282) |
| **Primary endpoint** | ▪ Objective response rate within 3 cycles | ▪ Safety, DLT, RPTD |
| **Status** | ▪ FPI Q4 2022 | ▪ FPI Q4 2022 |
| **CT Identifier** | NCT05364424 | NCT05169515 |

DLBCL=diffuse large B cell lymphoma; DLT=Dose-limiting toxicity, RPTD=Recommended Phase II Dose; R-ICE= Rituxan plus ifosfamide, carboplatin, and etoposide; IV=Intravenous; SC=Subcutaneous

# Inavolisib (RG6114, GDC-0077)

*A potent, orally available, and selective PI3Kα inhibitor*

| Indication | PIK3CA-mutant HR+ metastatic breast cancer (mBC) | PIK3CA mutant solid tumors and metastatic ER+ HER2-neg breast cancer |
|---|---|---|
| Phase/study | **Phase III INAVO120** | **Phase I** |
| # of patients | N=400 | N=256 |
| Design | ▪ **ARM A:** Inavolisib plus palbociclib plus fulvestrant<br>▪ **ARM B:** Placebo plus palbociclib plus fulvestrant | Monotherapy and in combination with standard of care (letrozole; letrozole plus palbociclib; fulvestrant)<br>▪ **Stage 1:** Dose escalation<br>▪ **Stage 2:** Dose expansion |
| Primary endpoint | ▪ Progression-free survival | ▪ Safety, tolerability and pharmacokinetics |
| Status | ▪ FPI Q1 2020 | ▪ FPI Q4 2016<br>▪ Preclinical/molecule discovery data presented at AACR 2017<br>▪ Data presented at SABCS 2019, 2020 and 2021 |
| CT Identifier | NCT04191499 | NCT03006172 |

ER=Estrogen receptor; HR=Hormon receptor; HER2=Human Epidermal growth factor Receptor 2; PI3K=Phosphoinositide 3-Kinase; AACR=American Association for Cancer Research; SABCS=San Antonio Breast Cancer Symposium

# Giredestrant (SERD (3),RG6171, GDC-9545)

*A selective estrogen receptor degrader or downregulator*

| Indication | ER+ HER2-neg metastatic breast cancer (mBC) | ER+ HER2-neg Stage I-III operable breast cancer (BC) | Neoadjuvant ER+ breast cancer (BC) |
|---|---|---|---|
| **Phase/study** | **Phase I** | **Phase I** | **Phase II coopERA Breast Cancer** |
| **# of patients** | N=181 | N=75 | N=221 |
| **Design** | ▪ Dose escalation and expansion at RPTD<br>▪ Giredestrant monotherapy and in combination with palbociclib and/or LHRH agonist | ▪ Open-label, pre-operative administration<br>▪ Dose escalation | ▪ **ARM A:** Giredestrant followed by giredestrant plus palbociclib<br>▪ **ARM B:** Anastrazole followed by anastrazole plus palbociclib |
| **Primary endpoint** | ▪ Safety | ▪ Safety, tolerability and PK/PD | ▪ Safety, tolerability and PK/PD |
| **Status** | ▪ FPI Q4 2017<br>▪ Data presented at SABCS 2019, ASCO 2020, ASCO 2021 and SABCS 2021 | ▪ FPI Q3 2019<br>▪ Data presented at ASCO 2021 | ▪ FPI Q3 2020<br>▪ Data presented at ESMO and SABCS 2021; ASCO 2022<br>▪ Data (biomarker subgroup analysis) presented at ESMO 2022 |
| **CT Identifier** | NCT03332797 | NCT03916744 | NCT04436744 |

ER=Estrogen receptor; HER2=Human Epidermal growth factor Receptor; RPTD=Recommended phase II dose; LHRH=Luteinizing hormone–releasing hormone; PK/PD=Pharmacokinetics/Pharmacodynamics; SABCS=San Antonio Breast Cancer Symposium; ASCO=American Society of Clinical Oncology

# Giredestrant (SERD (3),RG6171, GDC-9545)

*A selective estrogen receptor degrader or downregulator*

| Indication | 1L ER+ metastatic breast cancer (mBC) | Adjuvant ER+ breast cancer (BC) |
|---|---|---|
| Phase/study | **Phase III**<br>**persevERA Breast Cancer** | **Phase III**<br>**lidERA Breast Cancer** |
| # of patients | N=978 | N=4,100 |
| Design | ▪ **ARM A:** Giredestrant plus palbociclib<br>▪ **ARM B:** Letrozole plus palbociclib | ▪ **ARM A:** Giredestrant monotherapy<br>▪ **ARM B:** Tamoxifen or aromatase inhibitor |
| Primary endpoint | ▪ Progression-free survival | ▪ Invasive disease-free survival |
| Status | ▪ FPI Q4 2020 | ▪ FPI Q3 2021 |
| CT Identifier | NCT04546009 | NCT04961996 |

ER=Estrogen receptor; HER2=Human Epidermal growth factor Receptor

# Giredestrant (SERD (3),RG6171, GDC-9545)

*A selective estrogen receptor degrader or downregulator*

| Indication | 1L ER+/HER2-positive breast cancer (BC) |
|---|---|
| Phase/study | **Phase III**<br>**heredERA** |
| # of patients | N=812 |
| Design | Induction Phesgo plus taxane followed by maintenance with either:<br>▪ **ARM A:** Giredestrant plus Phesgo<br>▪ **ARM B:** Phesgo |
| Primary endpoint | ▪ Progression-free survival |
| Status | ▪ FPI Q2 2022 |
| CT Identifier | NCT05296798 |

ER=Estrogen receptor; HER2=Human Epidermal growth factor Receptor; Phesgo=FDC of Perjeta and Herceptin for SC administration

# KRAS G12C inhibitor (RG6330, GDC-6036)

*A potent, orally available, and selective inhibitor of the KRAS G12C mutant protein*

| Indication | Advanced or metastatic solid tumors with a KRAS G12C mutation | 2L NSCLC |
|---|---|---|
| Phase/study | **Phase I** | **Phase II/III**<br>**B-FAST*** |
| # of patients | N=438 | Modular design |
| Design | Monotherapy and combinations of GDC-6036 with other anti-cancer therapies | **Cohort G (KRAS G12C)**<br>▪ **ARM A:** GDC-6036<br>▪ **ARM B:** Docetaxel |
| Primary endpoint | ▪ Safety | ▪ Progression-free survival |
| Status | ▪ FPI Q3 2020<br>▪ Data presented at WCLC 2022, ESMO 2022 | ▪ BTD granted by FDA Q3 2022<br>▪ FPI Q4 2022 |
| CT Identifier | NCT04449874 | NCT03178552 |

*Only cohorts with active recruitment shown; NSCLC=Non-small cell lung cancer; WCLC=World Conference on Lung Cancer; ESMO=European Society for Medical Oncology; BTD=Breakthrough therapy designation

# Zinpentraxin alfa (PRM-151, RG6354)

*Recombinant human innate immunity protein pentraxin-2*

| Indication | Idiopathic pulmonary fibrosis (IPF) | | Myelofibrosis |
|---|---|---|---|
| **Phase/study** | **Phase II** | **Phase III STARSCAPE** | **Phase II** |
| **# of patients** | N=117 | N=658 | N=125 |
| **Design** | ▪ **ARM A:** Zinpentraxin alfa at days 1, 3 and 5, then every 4 weeks for 24 weeks plus 4 weeks of follow-up<br>▪ **ARM B**: Placebo | ▪ **ARM A:** Zinpentraxin alfa at days 1, 3 and 5, then every 4 weeks for 52 weeks<br>▪ **ARM B**: Placebo | ▪ Multiple dose study of zinpentraxin alfa |
| **Primary endpoint** | ▪ Least-squares mean change in FVC percentage of predicted value from baseline to week 28 | ▪ Absolute change from baseline to week 52 in FVC | ▪ Bone marrow response rate |
| **Status** | ▪ Study met primary endpoint<br>▪ Data published in JAMA 2018;319(22):2299-2307 and Lancet Respir Med 2019 Aug;7(8):657-664 | ▪ FPI Q1 2021<br>▪ Study stopped per IDMC recommendation at planned futility analysis Q4 2022 as unlikely to meet its primary endpoint | ▪ Study completed Q1 2021 |
| **CT Identifier** | NCT02550873 | NCT04552899 | NCT01981850 |

FVC=Forced vital capacity, JAMA=Journal of the American Medical Association

# Crovalimab (RG6107, SKY59)

*A humanized monoclonal antibody against complement C5*

| Indication | Paroxysmal nocturnal hemoglobinuria (PNH) | Paroxysmal nocturnal hemoglobinuria (PNH) patients switching from a C5 inhibitor |
|---|---|---|
| **Phase/study** | **Phase I/II**<br>**COMPOSER** | **Phase III**<br>**COMMODORE 1** |
| **# of patients** | N=59 | N=250 |
| **Design** | Healthy volunteers and treatment naïve and pretreated patients with PNH:<br>▪ **Part I:** Single ascending dose study in healthy subjects<br>▪ **Part II:** Intra-patient single ascending dose study in PNH patients<br>▪ **Part III:** Multiple-dose study in PNH patients<br>▪ **Part IV:** Dose confirmation in PNH patients | ▪ **ARM A:** Crovalimab<br>▪ **ARM B:** Eculizumab<br>▪ **ARM C:** Patients switching to crovalimab from ravulizumab, higher than labeled doses of eculizumab & C5 SNP patients (descriptive-arm) |
| **Primary endpoint** | ▪ Safety, PK, PD | ▪ Safety |
| **Status** | ▪ Nonclinical data published in Scientific Reports 2017 Apr; 7(1):1080<br>▪ Data presented for Part 2 and 3 at ASH 2018 and 2019 | ▪ FPI Q3 2020 |
| **CT Identifier** | NCT03157635 | NCT04432584 |

In collaboration with Chugai

ASH=American Society of Hematology; PNH=Paroxysmal nocturnal hemoglobinuria; PK/PD=Pharmacokinetics/Pharmacodynamics

# Crovalimab (RG6107, SKY59)

*A humanized monoclonal antibody against complement C5*

| Indication | Paroxysmal nocturnal hemoglobinuria (PNH)<br>C5 inhibitor naive patients | Paroxysmal nocturnal hemoglobinuria (PNH)<br>C5 inhibitor naive patients (China only) |
|---|---|---|
| Phase/study | **Phase III**<br>**COMMODORE 2** | **Phase III**<br>**COMMODORE 3** |
| # of patients | N=200 | N=51 |
| Design | ▪ **ARM A:** Crovalimab<br>▪ **ARM B:** Eculizumab | ▪ Crovalimab loading dose IV on Day 1, followed by weekly crovalimab SC doses for 4 weeks |
| Primary endpoint | ▪ Non-inferiority of crovalimab compared to eculizumab:<br>▪ % patients with transfusion avoidance from baseline through week 25<br>▪ % patients with haemolysis control, as measured by LDH <=1.5ULN from week 5-25 | ▪ Percentage of patients with transfusion avoidance from baseline through week 25<br>▪ Mean percentage of participants with hemolysis control (week 5 through week 25) |
| Status | ▪ FPI Q4 2020<br>▪ Recruitment completed Q2 2022 | ▪ FPI Q1 2021; Recruitment completed Q3 2021<br>▪ Study met its co-primary endpoints Q1 2022<br>▪ Filed in China (priority review) Q3 2022<br>▪ Data presented at ASH 2022 |
| CT Identifier | NCT04434092 | NCT04654468 |

In collaboration with Chugai

LDH=Lactate Dehydrogenase; ULN=Upper Limit of Normal; IV=Intravenous; SC=Subcutaneous

# Crovalimab (RG6107, SKY59)

*A humanized monoclonal antibody against complement C5*

| Indication | Atypical hemolytic uremic syndrome (aHUS) study 1 - adults | Atypical hemolytic uremic syndrome (aHUS) study 2 - paediatrics |
|---|---|---|
| **Phase/study** | **Phase III COMMUTE-a** | **Phase III COMMUTE-p** |
| **# of patients** | N=90 | N=35 |
| **Design** | Single-arm study of aHUS patients<br>▪ **Cohort 1**: not previously treated with C5i<br>▪ **Cohort 2:** switching from C5i<br>▪ **Cohort 3:** known C5 polymorphism | Single-arm study of aHUS patients<br>▪ **Cohort 1:** not previously treated with C5i<br>▪ **Cohort 2:** switching from C5i ≤18y/o |
| **Primary endpoint** | ▪ Cohort 1+3: proportion of patients with complete TMA response anytime between baseline and week 25<br>▪ Cohort 2: proportion of patients with maintained TMA control from baseline through week 25 | ▪ Cohort 1: proportion of patients with complete TMA response anytime between baseline and week 25<br>▪ Cohort 2: proportion of patients with maintained TMA control from baseline through week 25 |
| **Status** | ▪ FPI Q4 2021 | ▪ FPI Q4 2021 |
| **CT Identifier** | NCT04861259 | NCT04958265 |

In collaboration with Chugai

aHUS=Atypical Hemolytic Uremic Syndrome; C5i=C5 inhibitor; TMA=thrombotic microangiopathy

# Crovalimab (RG6107, SKY59)

*A humanized monoclonal antibody against complement C5*

| Indication | Sickle cell disease (SCD) acute treatment | Sickle cell disease (SCD) chronic VOC prevention |
|---|---|---|
| Phase/study | **Phase Ib CROSSWALK-a** | **Phase IIa CROSSWALK-c** |
| # of patients | N=30 | N=90 |
| Design | ▪ **ARM A:** Crovalimab<br>▪ **ARM B:** Placebo | ▪ **ARM A:** Crovalimab<br>▪ **ARM B:** Placebo |
| Primary endpoint | ▪ Safety | ▪ VOC rate, up to 48 weeks |
| Status | ▪ FPI Q1 2022 | ▪ FPI Q1 2022 |
| CT Identifier | NCT04912869 | NCT05075824 |

SCD=Sickle Cell Disease; VOC=Vaso-occlusive crises

# Crenezumab (RG7412)

*Humanized monoclonal antibody targeting all forms of Aß*

| Indication | Alzheimer's prevention initiative (API) Colombia |
|---|---|
| Phase/study | **Phase II**<br>Cognition study |
| # of patients | N=252 |
| Design | ▪ **ARM A:** PSEN1 E280A mutation carriers receive crenezumab SC or IV<br>▪ **ARM B:** PSEN1 E280A mutation carriers receive placebo<br>▪ **ARM C:** non-mutation carriers receive placebo |
| Primary endpoint | ▪ Change on Alzheimer's Prevention Initiative (API) Composite Cognitive Test total score at 260 weeks treatment<br>▪ Annualized rate of change in an Episodic Memory Measure: Free and Cued Selective Reminding Task (FCSRT) |
| Status | ▪ Study did not meet its co-primary endpoints Q2 2022<br>▪ Data presented at AAIC 2022 |
| CT Identifier | NCT01998841 |

In collaboration with AC Immune

Ab=amyloid-beta; SC=Subcutaneous; IV=Intravenous

# Gantenerumab (RG1450)

*Fully human monoclonal antibody binding aggregated forms of Aß*

| Indication | Prodromal to mild Alzheimer's disease | | |
|---|---|---|---|
| **Phase/study** | **Phase III GRADUATE 1** | **Phase III GRADUATE 2** | **Phase II GRADUATION** |
| **# of patients** | N=1,016 | N=1,016 | N=192 |
| **Design** | 104-week SC treatment period:<br>▪ **ARM A:** Gantenerumab<br>▪ **ARM B:** Placebo | 104-week SC treatment period:<br>▪ **ARM A:** Gantenerumab<br>▪ **ARM B:** Placebo | 104-week SC treatment period:<br>▪ Gantenerumab SC treatment q1w dosing regimen |
| **Primary endpoint** | ▪ Change in CDR-SOB at 27 months | ▪ Change in CDR-SOB at 27 months | ▪ Change from baseline in deposited amyloid (PET centiloid levels) |
| **Status** | ▪ FPI Q2 2018<br>▪ Recruitment completed Q2 2020 | ▪ FPI Q3 2018<br>▪ Recruitment completed Q2 2020 | ▪ FPI Q4 2020<br>▪ Recruitment completed Q3 2021<br>▪ Study closed due to GRADUATE results Q4 2022 |
| | ▪ Studies did not meet their primary endpoint Q4 2022<br>▪ Data presented at CTAD 2022 | | |
| **CT Identifier** | NCT03443973 | NCT03444870 | NCT04592341 |

In collaboration with MorphoSys AG

Aß=amyloid-beta; CDR-SOB=Clinical Dementia Rating Scale Sum of Boxes; SC=Subcutaneous; BTD=Breakthrough Therapy Designation; PET= positron emission tomography

# Gantenerumab (RG1450)

*Fully human monoclonal antibody binding aggregated forms of Aß*

| Indication | Prodromal Alzheimer's disease | Mild Alzheimer's disease | Cognitively unimpaired participants at risk for or at the earliest stages of Alzheimer's disease |
|---|---|---|---|
| **Phase/study** | **Phase II/III**<br>**SCarlet RoAD[1]** | **Phase III**<br>**Marguerite RoAD[1]** | **Phase III**<br>**SKYLINE[2]** |
| **# of patients** | N=799 | N=389 | N=1,200 |
| **Design** | 104-week SC treatment period:<br>▪ **ARM A:** Gantenerumab (225 mg)<br>▪ **ARM B:** Gantenerumab (105 mg)<br>▪ **ARM C:** Placebo | 104-week SC treatment period:<br>▪ **ARM A:** Gantenerumab<br>▪ **ARM B:** Placebo | ▪ **ARM A:** Gantenerumab q1w or q2w (patient preference)<br>▪ **ARM B:** Placebo |
| **Primary endpoint** | ▪ Change in CDR-SOB at 2 years<br>▪ Sub-study: change in brain amyloid by PET at 2 years | ▪ Change in ADAS-Cog and CDR-SOB at 2 years (co-primary) | ▪ Cognitive composite (PACC5) |
| **Status** | ▪ Phase I PET data: *Archives of Neurology*, 2012 Feb;69(2):198-207<br>▪ Recruitment completed Q4 2013<br>▪ Dosing stopped due to futility Q4 2014<br>▪ FPI in open label extension study Q4 2015<br>▪ Published in *Alzheimers Res Ther* 2017 Dec 8;9(1):95 | ▪ FPI Q1 2014<br>▪ Recruitment stopped Q4 2015<br>▪ FPI Q1 2016 for open label extension | ▪ FPI Q2 2022<br>▪ Study closed due to GRADUATE results Q4 2022 |
| | ▪ 36 OLE data published in J Prev Alzheimers Dis 2021;8(1):3-6 | | |
| **CT Identifier** | NCT01224106 | NCT02051608 | NCT05256134 |

[1]In collaboration with MorphoSys AG; [2]In collaboration with Banner Alzheimer's Institute

Aß=amyloid-beta; CDR-SOB=Clinical Dementia Rating Scale Sum of Boxes; PET= positron emission tomography; ADAS-cog=Alzheimer's Disease Assessment Scale cognitive subscale; SC=Subcutaneous; OLE=Open Label Extension; PACC5=Preclinical Alzheimer's Cognitive Composite

# Tominersen (RG6042, HTT ASO)

*Antisense oligonucleotide (ASO) targeting human HTT mRNA*

| Indication | Huntington's disease |
|---|---|
| Phase/study | **Phase II**<br>**GENERATION HD2** |
| # of patients | N=360 |
| Design | Patients aged 25 to 50 years with prodromal (very early subtle signs of HD) or early manifest HD<br>▪ **ARM A:** Tominersen 60mg q16w via a lumbar puncture<br>▪ **ARM B:** Tominersen 100mg q16w via a lumbar puncture<br>▪ **ARM C:** Placebo q16w via a lumbar puncture |
| Primary endpoint | ▪ Safety, biomarkers and efficacy |
| Status | ▪ FPI expected H1 2023 |
| CT Identifier | NCT05686551 |

In collaboration with Ionis Pharmaceuticals
HD=Huntington's Disease; HTT=Huntingtin

# Fenebrutinib (RG7845, GCD-0853)

*Highly selective and reversible (noncovalent) bruton tyrosine kinase*

| Indication | Primary progressive multiple sclerosis (PPMS) | Relapsing multiple sclerosis (RMS) | |
|---|---|---|---|
| **Phase/study** | **Phase III FENtrepid** | **Phase III FENhance 1** | **Phase III FENhance 2** |
| **# of patients** | N=946 | N=736 | N=736 |
| **Design** | ▪ **ARM A:** Fenebrutinib twice daily oral<br>▪ **ARM B:** Ocrevus 2x300mg IV q24w | ▪ **ARM A:** Fenebrutinib twice daily oral<br>▪ **ARM B:** Teriflunomide once daily oral | ▪ **ARM A:** Fenebrutinib twice daily oral<br>▪ **ARM B:** Teriflunomide once daily oral |
| **Primary endpoint** | ▪ Time to onset of cCDP12 | ▪ Time to onset of cCDP12 and annualized relapse rate | ▪ Time to onset of cCDP12 and annualized relapse rate |
| **Status** | ▪ FPI Q4 2020 | ▪ FPI Q1 2021 | ▪ FPI Q1 2021 |
| **CT Identifier** | NCT04544449 | NCT04586023 | NCT04586010 |

IV=Intravenous; cCDP12=Composite 12-week confirmed disability progression

# Balovaptan (RG7314)

*Small molecule antagonist of the V1A vasopressin receptor*

| Indication | Post-traumatic stress disorder (PTSD) |
|---|---|
| Phase/study | **Phase II** |
| # of patients | N=252 |
| Design | ▪ **ARM A:** Balovaptan IV once a day for 12 weeks<br>▪ **ARM B:** Placebo |
| Primary endpoint | ▪ Change from baseline in the Clinician-Administered PTSD Total Symptom Severity Score |
| Status | ▪ FPI Q3 2022 |
| CT Identifier | NCT05401565 |

PTSD=Post-traumatic stress disorder

# TNKase (RG3625, tenecteplase)

*Small molecule tissue plasminogen activator*

| Indication | Stroke patients between 4.5 and 24 hours |
|---|---|
| Phase/study | **Phase III**<br>TIMELESS |
| # of patients | N=456 |
| Design | ▪ **ARM A:** Tenecteplase (0.25 mg/kg, maximum 25 mg) single bolus injection<br>▪ **ARM B:** Placebo |
| Primary endpoint | ▪ Ordinal modified Rankin scale (mRS) score after 90 days |
| Status | ▪ FPI Q1 2019<br>▪ Recruitment completed Q4 2022 |
| CT Identifier | NCT03785678 |

# Anti-IL-6 (RG6179)

*A monoclonal antibody that potently binds interleukin-6 (IL-6) cytokine*

| Indication | Diabetic macular edema (DME) and Uveitic macular edema (UME) | Diabetic macular edema (DME) | |
|---|---|---|---|
| **Phase/study** | **Phase I**<br>**DOVETAIL** | **Phase II**<br>**BARDENAS** | **Phase II**<br>**ALLUVIUM** |
| **# of patients** | N=90 | N=210-230 | N=360-400 |
| **Design** | ▪ Part I: Multiple ascending dose study of intravitreal monotherapy<br>▪ Part II: monotherapy and in combination with anti-VEGF | ▪ **ARM A:** Anti-IL-6 plus ranibizumab<br>▪ **ARM B:** Ranibizumab plus sham control | ▪ **Arm A:** 0.25 mg anti-IL-6 Q8W<br>▪ **Arm B:** 1.0 mg anti-IL-6 Q8W<br>▪ **Arm C:** 1.0 mg anti-IL-6 Q4W<br>▪ **Arm D**: 0.5 mg ranibizumab Q4W |
| **Primary endpoint** | ▪ Safety, tolerability, PK | ▪ Mean change from baseline in BCVA averaged over week 44 and week 48 | ▪ Mean change from baseline in BCVA averaged over week 44 and week 48 |
| **Status** | ▪ FPI Q3 2019 | ▪ FPI Q4 2021 | ▪ FPI Q4 2021 |
| **CT Identifier** | | NCT05151744 | NCT05151731 |

PK=Pharmacokinetics; BCVA=Best corrected visual acuity

# Anti-IL-6 (RG6179)

*A monoclonal antibody that potently binds interleukin-6 (IL-6) cytokine*

| Indication | Uveitic macular edema (UME) | |
|---|---|---|
| **Phase/study** | **Phase III<br>MEERKAT** | **Phase III<br>SANDCAT** |
| **# of patients** | N=225 | N=225 |
| **Design** | ▪ **ARM A:** Anti-IL-6 low-dose q4w to week 12, followed by PRN<br>▪ **ARM B:** Anti-IL-6 high-dose q4w to week 12, followed by PRN<br>▪ **ARM C:** Sham control q4w to week 12,followed by PRN | ▪ **ARM A:** Anti-IL-6 low-dose q4w to week 12, followed by PRN<br>▪ **ARM B:** Anti-IL-6 high-dose q4w to week 12, followed by PRN<br>▪ **ARM C:** Sham control q4w to week 12,followed by PRN |
| **Primary endpoint** | ▪ Proportion of participants with ≥ 15 letter improvement from baseline in BCVA at week 16 | ▪ Proportion of participants with ≥ 15 letter improvement from baseline in BCVA at week 16 |
| **Status** | ▪ FPI Jan 2023 | ▪ FPI expected Q1 2023 |
| **CT Identifier** | NCT05642312 | NCT05642325 |

BCVA=Best corrected visual acuity; PRN= Pro re nata

Roche Group development pipeline

Marketed products development programmes

Roche Pharma global development programmes

Roche Pharma research and early development (pRED)

Genentech research and early development (gRED)

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# pRED oncology development programs -1

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Oncology** | | | | | |
| **FAP-4-1BBL (RG7827)** | Solid tumors | I | ~150 | FPI Q2 2018<br>Data presented at ESMO 2020<br>Recruitment completed Q2 2021 | |
| | 3L+ MSS mCRC | Ib | 80 | FPI Q3 2021<br>Combination study with cibisatamab | NCT04826003 |
| **CD19-4-1BBL (RG6076)** | R/R B cell non-Hodgkin's lymphoma | I | 362 | Part I: FPI Q3 2019<br>Part II: FPI Q3 2020<br>Data presented at ASH 2022 | NCT04077723 |
| **PD1-IL2v (RG6279)** | Solid tumors | I | 348 | Part I: FPI Q2 2020; recruitment completed Q4 2021<br>Part II: FPI Q1 2022 | NCT04303858 |
| **cibisatamab (CEA x CD3, RG7802)** | CEA-positive solid tumors | Ia | 149 | FPI Q4 2014<br>Data presented at ASCO 2017 | NCT02324257 |
| | | Ib | 228 | FPI Q1 2016<br>Data presented at ASCO 2017 | NCT02650713 |
| | 3L+ MSS mCRC | Ib | 46 | FPI Q1 2019 | NCT03866239 |
| **PD1-LAG3 (RG6139)** | Solid tumors | I | 320 | FPI Q4 2019<br>Data presented at ESMO 2022<br>Recruitment completed Q4 2022 | NCT04140500 |
| | Solid tumors | II | 210 | FPI Q2 2021<br>Randomized trial, compared with nivolumab | NCT04785820<br>TALIOS |
| | Untreated unresectable or metastatic melanoma | II | 80 | FPI Q3 2022 | NCT05419388 |

# pRED oncology development programs -2

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Oncology** | | | | | |
| **CD25 (RG6292)** | Solid tumors | I | 110 | FPI Q4 2019 | NCT04158583 |
| | Advanced and metastatic solid tumors | I | 160 | Part I: FPI Q1 2021<br>Part II: FPI Q4 2021 | NCT04642365 |
| **forimtamig (Anti-GPRC5D, RG6234)** | Multiple myeloma | I | 240 | FPI Q4 2020<br>Data presented at EHA 2022<br>Data presented at ASH 2022 | NCT04557150 |
| **HLA-A2-WT1 x CD3 (RG6007)** | AML | I | 220 | FPI Q4 2020 | NCT04580121 |
| **FAP-CD40 (RG6189)** | Solid tumors | I | 280 | FPI Q2 2021 | NCT04857138 |
| **HLA-A2-MAGE-A4 x CD3 (RG6129)** | Solid tumors | I | 260 | FPI Q1 2022 | NCT05129280 |
| **BRAFi (3) (RG6344)** | Solid tumors | I | 292 | FPI Q1 2022 | ISRCTN13713551 |
| **CD19xCD28 (RG6333)** | R/R B cell non-Hodgkin's lymphoma | I | ~200 | FPI Q1 2022<br>Combination study with glofitamab | NCT05219513 |
| **EGFRvIIIxCD3 (RG6156)** | Glioblastoma | I | ~200 | FPI Q2 2022 | NCT05187624 |
| **NME (RG6524)** | Solid tumors | I | 168 | FPI Jan 2023 | NCT05619744 |

# pRED neuroscience development programs -1

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Neuroscience** | | | | | |
| **trontinemab (BS-gantenerumab, RG6102)** | Alzheimer's disease | IIa | ~120 | FPI Q1 2021 | NCT04639050 |
| **Brain Shuttle-CD20 (BS-CD20, RG6035)** | Multiple sclerosis | I | 30 | FPI Q3 2021 | ISRCTN16295177 |
| **ralmitaront (partial TAAR1 agonist, RG7906)** | Schizophrenia | II | 36 | FPI Q4 2018<br>Recruitment completed Q3 2019 | |
| | | II | 247 | FPI Q4 2019 | NCT03669640 (TWAIN I) |
| **prasinezumab[1] (anti-αSynuclein, RG7935, PRX002)** | Parkinson's disease | II | 316 | The study did not meet its primary endpoint, but showed a reduced clinical decline of core motor signs (MDS UPDRS partIII). Data presented at MDS & ADPD 2020-22. The Open Label Extension is ongoing. | NCT03100149 (PASADENA) |
| | | IIb | 575 | FPI Q2 2021 | NCT04777331 (PADOVA) |
| **alogabat (GABA-Aa5 PAM, RG7816)** | Autism spectrum disorder | II | 105 | FPI Q1 2021 | NCT04299464 (Aurora) |
| **NME (RG7637)** | Psychiatric disorders | I | 80 | FPI Q3 2020 | NCT04475848 |
| **rugonersen (UBE3A LNA, RG6091)** | Angelman syndrome | I | 66 | FPI Q3 2020 | NCT04428281 |
| **NME (RG6182)** | Neurodegenerative disorder | I | 30 | FPI Q4 2020 | |

Partner: [1]Prothena
BS=Brain Shuttle

# pRED neuroscience development programs -2

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Neuroscience** | | | | | |
| **NME (RG6289)** | Alzheimer's disease | I | 138 | FPI Q4 2021 | |
| **NME (RG6163)** | Psychiatric disorders | I | 84 | FPI Q1 2022 | |
| **selnoflast* (NLRP3i, RG6418)** | Parkinson's disease | Ib | 48 | FPI Q3 2022 | |
| **basmisanil (GABA-Aa5 NAM, RG1662)** | Dup15q syndrome | II | 90 | FPI Q4 2022 | NCT05307679 |

*molecule also in gRED development: Phase Ic in coronary artery disease with FPI Q4 2022

# pRED immunology and ophthalmology development programs

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Immunology** | | | | | |
| **selnoflast* (NLRP3i, RG6418)** | Chronic obstructive pulmonary disease | Ib | 102 | FPI Q2 2022<br>Study closed Q3 2022 | |
| **Ophthalmology** | | | | | |
| **VEGF-Ang2 DutaFab (RG6120)** | nAMD | I | 200 | FPI Q4 2020 | NCT04567303 |
| **vicasinabin (CB2 receptor agonist, RG7774)** | DR | II | 135 | FPI Q2 2020 | NCT04265261 (CANBERRA) |
| **NME (RG6209)** | retinal disease | I | ~70 (Part I) | FPI Q4 2022 | |

*molecule also in gRED development: Phase Ic in coronary artery disease with FPI Q4 2022

# pRED infectious diseases development programs

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Infectious Diseases** | | | | | |
| **ruzotolimod (TLR7 agonist (3) RG7854)** | Chronic hepatitis B | I | 150 | FPI Q4 2016<br>Data presented at APASL 2019 | NCT02956850 |
| **ruzotolimod/ xalnesiran/ PDL1 LNA (RG7854/RG6346/RG6084)** | Chronic hepatitis B | II | 275 | FPI Q3 2020 | NCT04225715 (PIRANGA) |
| **PDL1 LNA (RG6084)** | Chronic hepatitis B | I | 35 | FPI Q1 2019<br>Part Ia: completed<br>Part Ib: initiated | |
| **Abx MCP (RG6006)** | A. baumannii infections | I | 204 | FPI Q4 2020 | NCT04605718 |

Abx MCP=antibiotic macrocyclic peptide

Roche Group development pipeline

Marketed products development programmes

Roche Pharma global development programmes

Roche Pharma research and early development (pRED)

Genentech research and early development (gRED)

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# gRED oncology development programs -1

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Oncology** | | | | | |
| **cevostamab (anti-FcRH5 x CD3; RG6160)** | R/R multiple myeloma | I | 300 | FPI Q3 2017<br>Data presented at ASH 2020, 2021 & 2022 | NCT03275103 |
| | R/R multiple myeloma | I | 120 | FPI Q2 2021 | NCT04910568 |
| | BCMA-experienced R/R MM | I/II | 140 | FPI Q4 2022 | NCT05535244 |
| **runimotamab (HER2 x CD3, RG6194)** | Metastatic HER2-expressing cancers | I | 440 | FPI Q2 2018 | NCT03448042 |
| **NME (RG6286)** | Locally advanced or metastatic colorectal cancer | I | 67 | FPI Q3 2020 | NCT04468607 |
| **IL15/IL15Ra-Fc (RG6323)[1]** | Solid tumors | Ia/Ib | 250 | FPI Q1 2020 | NCT04250155 |
| | R/R multiple myeloma | I | 60 | FPI Q2 2022 | NCT05243342 |
| | R/R multiple myeloma | I | 90 | FPI Jan 2023<br>Combination study with cevostamab | NCT05646836 |
| **autogene cevumeran (Individualized Neoantigen-Specific Therapy (iNeST); RG6180)[2]** | Solid tumors | Ia/IIb | 271 | FPI Q4 2017<br>Data presented at AACR 2020<br>Recruitment completed Q1 2022 | NCT03289962 |
| | 1L advanced melanoma | II | 132 | FPI Q1 2019 | NCT03815058 (IMcode001) |

Partner: [1]Xencor, [2]BioNTech

# gRED oncology development programs -2

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Oncology** | | | | | |
| **SHP2i (RG6344)[1]** | Solid tumors | Ia | ~50 | FPI Q1 2020 | NCT04252339 |
| | Solid tumors | Ib | ~125 | FPI Q3 2022 | NCT05487235 |
| **belvarafenib (RG6185)[2]** | nRASmt CPI-experienced melanoma | Ib | 83 | FPI Q2 2021<br>Data presented at ESMO 2021 | NCT04835805 |
| **NME (RG6392)** | Oncology | I | 60 | FPI Q4 2021 | ISRCTN92655801 |
| **NME (RG6411)** | Solid tumors | I | 110 | FPI Q4 2022 | NCT05581004 |

Partner: [1]Relay, [2]Hanmi

# gRED immunology and ophthalmology development programs

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Immunology** | | | | | |
| **NME (RG6287, GDC-8264)** | Inflammatory bowel disease | I | 68 | FPI Q1 2020<br>Recruitment completed Q3 2021 | EUDRACT2019-002613-19 |
| | Inflammatory diseases | I | 16 | FPI Q4 2021 | |
| **NME (RG6315, MTBT1466A)** | Immunologic disorders | I | ~24 | FPI Q3 2020 | |
| **astegolimab (Anti-ST2, (RG6149, AMG 282, MSTT1041A)[1]** | Chronic obstructive pulmonary disease | IIb | 930 | FPI Q4 2021 | NCT05037929 |
| **NME (RG6341, GDC-6599)** | Asthma | Ia/Ib | 84 | FPI Q4 2021 | |
| **TMEM16A potentiator (RG6421, GDC-6988)** | Cystic fibrosis | Ib | 30 | FPI Q3 2022 | ISRCTN15406513 |
| **Ophthalmology** | | | | | |
| **NME (RG6312)** | Geographic atrophy | Ia | 63 | FPI Q4 2022 | NCT04615325 |
| **NME (RG6351)** | Retinal disease | I | 42-78 | FPI Q2 2022 | |

Partner: [1]Amgen

# gRED neuroscience and infectious diseases development programs

| Molecule | Indication | Phase | # of patients | Status | CT Identifier |
|---|---|---|---|---|---|
| **Neuroscience** | | | | | |
| **semorinemab (RG6100)[1]** | Prodromal to mild Alzheimer's disease | II | 457 | FPI Q4 2017<br>Primary endpoint not met Q3 2020<br>Data presented at CTAD 2020 | NCT03289143 (TAURIEL) |
| | Mild-to-moderate Alzheimer's disease | II | 272 | FPI Q1 2019<br>One of two co-primary endpoints met Q3 2021<br>Data presented at CTAD 2021<br>The Open Label Extension is ongoing | NCT03828747 (LAURIET) |
| **Infectious Diseases** | | | | | |
| **LepB inhibitor (RG6319)** | Complicated urinary tract infection | I | 56 | FPI Q1 2022 | |

Partner: [1]AC Immune

Roche Group development pipeline

Marketed products development programmes

Roche Pharma global development programmes

Roche Pharma research and early development (pRED)

Genentech research and early development (gRED)

Spark

# Hemophilia A

*Unique gene therapy platform*

| Molecule | SPK-8011 (RG6357) | | SPK-8016 (RG6358) |
|---|---|---|---|
| **Indication** | **Hemophilia A** | | **Hemophilia A with inhibitors to Factor VIII** |
| **Phase/study** | **Phase I** | **Phase I/II** | **Phase I/II** |
| **# of patients** | N=100 | N=30 | N=30 |
| **Design** | ▪ Long term follow up study of patients who have received SPK-8011 in any prior Spark-sponsored SPK-8011 study | ▪ Gene transfer, dose-finding safety, tolerability, and efficacy study of SPK-8011 | ▪ Gene transfer, dose-finding safety, tolerability, and efficacy study of SPK-8016 in individuals with FVIII inhibitors |
| **Primary endpoint** | ▪ Safety | ▪ Safety and changes from baseline in FVIII activity levels at week 52 | ▪ Safety; peak and steady state FVIII activity levels at week 52 |
| **Status** | ▪ Ongoing | ▪ Updated data presented at ISTH 2020 and 2021<br>▪ Recruitment completed Q1 2021<br>▪ Data published in *NEJM* 2021; 385:1961-1973<br>▪ 5-year data published at ASH 2022 | ▪ FPI Q1 2019 |
| **CT Identifier** | NCT03432520 | NCT03003533 | NCT03734588 |

ISTH=International Society on Thrombosis and Haemostasis; NEJM=New England Journal of Medicine

# Pompe disease

*Unique gene therapy platform*

| | |
|---|---|
| **Molecule** | **SPK-3006 (RG6359)** |
| **Indication** | **Pompe disease** |
| **Phase/study** | **Phase I/II RESOLUTE** |
| **# of patients** | N=20 |
| **Design** | ▪ Gene transfer study for late-onset Pompe disease |
| **Primary endpoint** | ▪ Safety |
| **Status** | ▪ FPI Q4 2020<br>▪ Recruitment completed Q2 2022 |
| **CT Identifier** | NCT04093349 |

# Doing now what patients need next