# Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

# Changes to the development pipeline
## *Q3 2017 update*

### New to phase I

**3 NMEs:**
**RG6160 NME** – multiple myeloma
**RG6147 NME** – geographic atrophy
**RG7945 NME** - glaucoma

### New to phase II

**1 NME transitioned from Ph I:**
**RG6100 Tau MAb** - Alzheimer's disease

**1 AI:**
**RG7388 idasanutlin** - polycythemia vera

### New to phase III

**1 NME transitioned from Ph II:**
**RG6206 anti-myostatin adnectin** – DMD

**1 AI:**
**RG7446 Tecentriq + paclitaxel** – 1L TNBC

### New to registration

**1 AI following filing in US/EU:**
**RG1273 Perjeta + Herceptin** – HER2+ BC adj

**1 AI following filing in US:**
**RG7204 Zelboraf** – Erdheim-Chester disease

### Removed from phase I

**1 AI:**
**RG3616 Erivedge + ruxolitinib** – myelofibrosis

### Removed from phase II

**3 NMEs:**
**RG3637 lebrikizumab** – atopic dermatitis (out-licensed)
**RG7745 Flu A MAb** – influenza A
**RG7221 vanucizumab** - mCRC

### Removed from phase III

**2 AIs:**
**RG1273 Perjeta + Herceptin** - 1L HER2+ gastric cancer
**RG7204 Zelboraf** – BRAFm melanoma adj

### Removed from registration

**1 NME following EU approval:**
**RG7446 Tecentriq** – 2L mUC

**2 AIs following EU approval:**
**RG1569 Actemra** – giant cell arteritis
**RG7446 Tecentriq** – 2L+ NSCLC

**1 CHU following Japan approval:**
**CHU Actemra** – Takayasu arteritis and giant cell arteritis



Status as of October 19, 2017

# Roche Group development pipeline

## Phase I (40 NMEs + 23 AIs)

| | | |
|---|---|---|
| RG6026 | CD20 TCB | heme tumors |
| RG6047 | SERD (2) | ER+ (HER2-neg) mBC |
| RG6058 | TIGIT ± Tecentriq | solid tumors |
| RG6114 | mPI3K alpha inh | HR+ BC |
| RG6146 | BET inh combos | solid + heme tumors |
| RG6160 | - | multiple myeloma |
| RG6180 | personalized cancer vaccine ± T | oncology |
| RG6185 | pan-RAF inh + Cotellic | solid tumors |
| RG7155 | emactuzumab + Tecentriq | solid tumors |
| | emactuzumab + selicrelumab | solid tumors |
| RG7159 | anti-CD20 combos | heme tumors |
| RG7386 | FAP-DR5 biMAb | solid tumors |
| RG7421 | Cotellic + Zelboraf + T | melanoma |
| | Cotellic + T | 2L BRAF WT mM |
| RG7446 | Tecentriq | solid tumors |
| | Tecentriq | NMIBC |
| | T-based Morpheus platform | solid tumors |
| | T + Avastin + Cotellic | 2/3L CRC |
| | T ± Avastin ± chemo | HCC, GC, PaC |
| | T ± Avastin ± chemo | solid tumors |
| | T + Cotellic | solid tumors |
| | T + ipi/IFN | solid tumors |
| | T + Tarceva/Alecensa | NSCLC |
| | T + anti-CD20 combos | heme tumors |
| | T ± lenalidomide ± daratumumab | MM |
| | T + K/HP | HER2+ BC |
| | T + HMA | MDS |
| | T + radium 223 | mCRPC |
| | T + guadecitabine | AML |
| | T + rucaparib | ovarian ca |
| RG7461 | FAP IL2v FP combos | solid tumors |
| RG7601 | Venclexta + Cotellic/idasanutlin | AML |
| | Venclexta ± azacitadine | r/r MDS |
| RG7741 | ChK1 inh | solid tumors |
| RG7802 | CEA TCB ± Tecentriq | solid tumors |
| RG7813 | CEA IL2v FP* + Tecentriq | solid tumors |
| RG7828 | CD20 TDB ± Tecentriq | heme tumors |
| RG7876 | selicrelumab (CD40) + T | solid tumors |
| | selicrelumab + vanucizumab | solid tumors |
| RG7882 | MUC16 ADC | ovarian ca |
| RG7986 | ADC | r/r NHL |
| CHU | Raf/MEK dual inh | solid tumors |
| CHU | glypican-3/CD3 biMAb | solid tumors |
| RG6069 | anti-fibrotic agent | fibrosis |
| RG6107 | C5 inh MAb | PNH |
| RG7835 | - | autoimmune diseases |
| RG7880 | IL-22Fc | inflammatory diseases |
| RG7990 | - | asthma |
| RG6004 | HBV LNA | HBV |
| RG6080 | nacubactam | bact.infections |
| RG7854 | TLR7 agonist (3) | HBV |
| RG7861 | anti-*S. aureus* TAC | infectious diseases |
| RG7907 | HBV Capsid (2) | HBV |
| RG7992 | FGFR1/KLB MAb | metabolic diseases |
| RG6000 | - | ALS |
| RG6029 | Nav1.7 inh (2) | pain |
| RG7203 | PDE10A inh | schizophrenia |
| RG7906 | - | psychiatric disorders |
| IONIS | ASO | Huntington's |
| RG6147 | - | geographic atrophy |
| RG7945 | - | glaucoma |
| CHU | PTH1 recep. ago | hypoparathyroidism |
| CHU | - | hyperphosphatemia |

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

**RG-No** Roche/Genentech
**CHU** Chugai managed
**IONIS** IONIS managed
**PRO** Proximagen managed
**NOV** Novimmune managed

*INN: cergutuzumab amunaleukin
**out-licensed to Galderma and Maruho for atopic dermatitis
§ FPI expected Q4 2017
T=Tecentriq; TCB=T cell bispecific; TDB=T cell dependent bispecific

## Phase II (19 NMEs + 11 AIs)

| | | |
|---|---|---|
| RG3502 | Kadcyla + Tecentriq | 2L HER2+ mBC |
| RG7388 | Idasanutlin § | polycythemia vera |
| RG7421 | Cotellic + Tecentriq ± taxane | TNBC |
| RG7440 | ipatasertib | 1L TNBC |
| | ipatasertib | TNBC neoadj |
| RG7596 | polatuzumab vedotin | DLBCL |
| RG7601 | Venclexta + Rituxan | DLBCL |
| | Venclexta + Rituxan | r/r FL |
| | Venclexta + azacitadine | 1L MDS |
| RG7604 | taselisib + letrozole | (HER2-neg) BC neoadj |
| RG7686 | codrituzumab | liver cancer |
| RG3637 | lebrikizumab ± Esbriet (NME) | IPF |
| RG6125 | Cadherin-11 MAb | RA |
| RG6149 | ST2 MAb | asthma |
| RG7159 | obinutuzumab | lupus |
| RG7625 | Cat-S antag | autoimmune diseases |
| RG7845 | BTK inh | RA, lupus, CSU |
| CHU | nemolizumab** | pruritus in dialysis patients |
| PRO | VAP-1 inh | inflammatory disease |
| NOV | TLR4 MAb | autoimmune diseases |
| RG6152 | CAP endonuclease inh | influenza |
| CHU | URAT1 inh | gout |
| RG1662 | basmisanil | CIAS, post-stroke recovery |
| RG6083 | olesoxime | SMA |
| RG6100 | Tau MAb § | Alzheimer's |
| RG7314 | V1a receptor antag | autism |
| RG7916 | SMN2 splicer(2) | SMA |
| RG7935 | α-synuclein MAb | Parkinson's |
| RG3645 | ranibizumab PDS | wAMD |
| RG7716 | VEGF-ANG2 biMAb | wAMD, DME |



Status as of October 19, 2017

# Roche Group development pipeline

## Phase III (9 NMEs + 30 AIs)

| | | |
|---|---|---|
| RG3502 | Kadcyla | HER2+ BC adj |
| | Kadcyla + Perjeta | HER2+ BC adj |
| RG6013 | emicizumab | hemophilia A w/o FVIII inh |
| | emicizumab | Q4W hemophilia A |
| RG7388 | idasanutlin + chemo | AML |
| RG7440 | ipatasertib + chemo | 1L CRPC |
| RG7421 | Cotellic + Zelboraf + T | BRAFm melanoma |
| RG7446 | Tecentriq | NSCLC adj |
| | Tecentriq | MIBC adj |
| | Tecentriq Dx+ | 1L sq + non-sq SCLC |
| | Tecentriq | RCC adj |
| | T + nab-paclitaxel | 1L non-sq NSCLC |
| | T + chemo+ Avastin | 1L ovarian cancer |
| | T + chemo + Avastin | 1L non-sq NSCLC |
| | T + chemo + pemetrexed | 1L non-sq NSCLC |
| | T + nab-paclitaxel | 1L sq NSCLC |
| | T + paclitaxel | 1L TNBC |
| | T + nab-paclitaxel | 1 LTNBC |
| | T + nab-paclitaxel | TNBC neoadj |
| | T + Avastin | RCC |
| | T + Cotellic | 3L CRC |
| | T ± chemo | 1L mUC |
| | T + chemo | 1L extensive stage SCLC |
| | T + enzalutamide | CRPC |

| | | |
|---|---|---|
| RG7601 | Venclexta + Rituxan | r/r CLL |
| | Venclexta + Gazyva | 1L CLL |
| | Venclexta + bortezomib | MM |
| | Venclexta + HMA | 1L AML |
| RG7604 | taselisib + fulvestrant | ER+(HER2-neg) mBC |
| RG105 | MabThera | pemphigus vulgaris |
| RG1569 | Actemra | systemic sclerosis |
| RG7413 | etrolizumab | ulcerative colitis |
| | etrolizumab | Crohn's |
| RG1450 | gantenerumab | Alzheimer's |
| RG6168 | satralizumab (IL-6R MAb) | NMO |
| RG6206 | anti-myostatin adnectin | DMD |
| RG7412 | crenezumab | Alzheimer's |
| RG7417 | lampalizumab | geographic atrophy |
| RG3645 | Lucentis 0,3mg PFS[1] | DME/DR |

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

**RG-No** Roche/Genentech
**CHU** Chugai managed
**RG1569** Branded as RoActemra (EU)
**RG7159** Branded as Gazyvaro (EU)

T=Tecentriq

## Registration (2 NMEs + 5 AIs)

| | | |
|---|---|---|
| RG435 | Avastin[1] | GBM |
| RG1273 | Perjeta + Herceptin | HER2+ BC adj |
| RG6013 | emicizumab | hemophilia A FVIII inh |
| RG7159 | Gazyva[2] | 1L FL |
| RG7204 | Zelboraf[1] | Erdheim-Chester disease |
| RG7853 | Alecensa | 1L ALK+ NSCLC |
| RG1594 | Ocrevus[3] | PPMS + RMS |

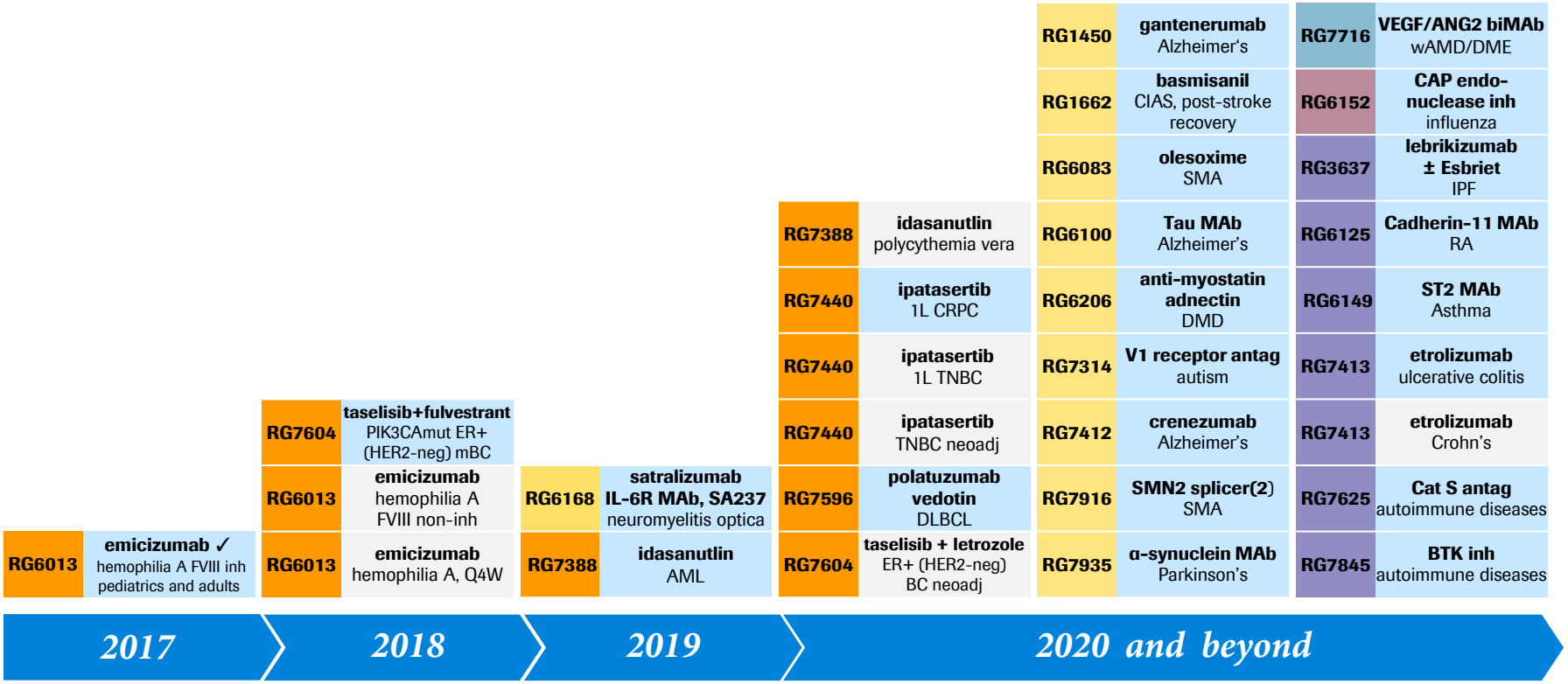
1 US only
2 Approved in EU
3 Approved in US



Status as of October 19, 2017

# NME submissions and their additional indications

## *Projects currently in phase II and III*




✓ Indicates a submission which has occurred with regulatory action pending
Unless stated otherwise submissions are planned to occur in US and EU

New Molecular Entity (NME)
Additional Indication (AI)
Oncology
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Infectious Diseases
CardioMetabolism
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Status as of October 19, 2017

# AI submissions for existing products

## *Projects currently in phase II and III*

| 2017 | | 2018 | | 2019 | | 2020 and beyond | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | RG105 | **MabThera** pemphigus vulgaris | | | | | | |
| | | RG1569 | **Actemra** systemic sclerosis | | | RG3502 | **Kadcyla + Tecentriq** 2L Her2+ mBC | RG3645 | **ranibizumab PDS** wAMD |
| RG3645 | **Lucentis 0.3mg PFS (US)** DME/DR | RG7446 | **Tecentriq + chemo + Avastin** 1L non-sq NSCLC | RG7446 | **Tecentriq + Cotellic** 3L CRC | RG3502 | **Kadcyla + Perjeta** HER2+ BC adj. | RG7159 | **obinutuzumab** lupus nephritis |
| RG435 | **Avastin (US) ✓** GBM | RG7446 | **Tecentriq + nab-paclitaxel** 1L sq NSCLC | RG7421 | **Cotellic + Tecentriq + Zelboraf** BRAFmut melanoma | RG3502 | **Kadcyla** HER2+ BC adj. | RG7446 | **Tecentriq ± chemo** 1L mUC |
| RG1273 | **Perjeta + Herceptin ✓** HER2+ BC adj. | RG7446 | **Tecentriq + nab-paclitaxel** 1L non-sq NSCLC | RG7446 | **Tecentriq** 1L non-sq + sq NSCLC (Dx+) | RG7601 | **Venclexta + Rituxan** r/r FL | RG7446 | **Tecentriq** NSCLC adj |
| RG7159 | **Gazyva (US) ✓** 1L FL | RG7446 | **Tecentriq + chemo + pemetrexed** 1L non-sq NSCLC | RG7446 | **Tecentriq+ nab-paclitaxel** TNBC neoadj | RG7601 | **Venclexta + Rituxan** DLBCL | RG7446 | **Tecentriq** MIBC adj |
| RG7204 | **Zelboraf (US) ✓** Erdheim-Chester disease | RG7446 | **Tecentriq + chemo** 1L extens. stage SCLC | RG7446 | **Tecentriq + paclitaxel** 1L TNBC | RG7601 | **Venclexta + HMA** 1L AML | RG7446 | **Tecentriq + enzalutamide** CRPC |
| RG7601 | **Venclexta + Rituxan** r/r CLL | RG7446 | **Tecentriq + Avastin** RCC | RG7601 | **Venclexta + Gazyva** 1L CLL | RG7601 | **Venclexta + HMA** 1L MDS | RG7446 | **Tecentriq** RCC adj |
| RG7853 | **Alecensa ✓** 1L ALK+ NSCLC | RG7446 | **Tecentriq + nab-paclitaxel** TNBC | RG7601 | **Venclexta + bortezomib** MM | RG7421 | **Cotellic + Tecentriq ± taxane** TNBC | RG7446 | **Tecentriq + chemo + Avastin** 1L ovarian cancer |

✓ Indicates submission to health authorities has occurred
Unless stated otherwise submissions are planned to occur in US and EU

New Molecular Entity (NME)
Additional Indication (AI)
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Status as of October 19, 2017

# Major granted and pending approvals 2017

## *Approved*

| US | | EU | | Japan-Chugai | |
|---|---|---|---|---|---|
| **RG105** | **Rituxan Hycela™** (SC)<br>NHL/CLL<br>June 2017 | **RG435** | **Avastin**<br>chemo backbone extension<br>rel. OC Pt-sensitive<br>June 2017 | **CHU** | **Actemra**<br>Takayasu arteritis and<br>giant cell arteritis<br>August 2017 |
| **RG7446** | **Tecentriq**<br>1L bladder cancer, cis-ineligible<br>April 2017 | **RG7159** | **Gazyva**<br>1L follicular lymphoma<br>September 2017 | | |
| **RG1569** | **Actemra**<br>giant cell arteritis<br>May 2017 | **RG7446** | **Tecentriq**<br>mUC 2L<br>September 2017 | | |
| **RG1569** | **Actemra**<br>CRS<br>August 2017 | **RG7446** | **Tecentriq**<br>2L+ NSCLC<br>September 2017 | | |
| **RG1594** | **Ocrevus**<br>PPMS & RMS<br>March 2017 | **RG7853** | Alecensa<br>2L ALK+ NSCLC<br>February 2017 | | |
| **RG3645** | **Lucentis**<br>mCNV<br>January 2017 | **RG1569** | **Actemra**<br>giant cell arteritis<br>September 2017 | | |
| **RG3645** | **Lucentis**<br>diabetic retinopathy w/o DME<br>April 2017 | | | | |

## *Pending Approval*

| US | | EU | | Japan-Chugai | |
|---|---|---|---|---|---|
| **RG435** | **Avastin**<br>GBM<br>Filed February 2017 | **RG1273** | **Perjeta + Herceptin**<br>HER2+ BC adj<br>Filed August 2017 | **RG6013** | **emicizumab**<br>hemophilia A FVIII inh<br>(pediatrics and adults)<br>Filed July 2017 |
| **RG1273** | **Perjeta + Herceptin**<br>HER2+ BC adj<br>Filed July 2017 | **RG6013** | **emicizumab**<br>hemophilia A FVIII inh<br>(pediatrics and adults)<br>Filed June 2017 | **RG7446** | **Tecentriq**<br>2L+ NSCLC<br>Filed February 2017 |
| **RG6013** | **emicizumab**<br>hemophilia A FVIII inh<br>(pediatrics and adults)<br>Filed June 2017 | **RG7853** | **Alecensa**<br>1L ALK+ NSCLC<br>Filed March 2017 | | |
| **RG7159** | **Gazyva**<br>follicular lymphoma 1L<br>Filed June 2017 | **RG1594** | **Ocrevus**<br>PPMS & RMS<br>Filed April 2016 | | |
| **RG7204** | **Zelboraf**<br>Erdheim-Chester disease<br>Filed June 2017 | | | | |
| **RG7853** | **Alecensa**<br>1L ALK+ NSCLC<br>Filed May 2017 | | | | |

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



Status as of October 19, 2017

# Roche Group development pipeline
## *Combinations*

### Phase I (10 NMEs + 21 AIs)

| | | |
|---|---|---|
| RG6058 | TIGIT ± Tecentriq | solid tumors |
| RG6146 | BET inh combos | solid + heme tumors |
| RG6180 | personalized cancer vaccine ± T | oncology |
| RG6185 | pan-RAF inh + Cotellic | solid tumors |
| RG7155 | emactuzumab + Tecentriq | solid tumors |
| | emactuzumab + selicrelumab | solid tumors |
| RG7159 | anti-CD20 combos | heme tumors |
| RG7421 | Cotellic + Zelboraf + T | melanoma |
| | Cotellic + T | BRAF WT mM2L |
| RG7446 | T-based Morpheus platform | solid tumors |
| | T + Avastin + Cotellic | 2/3L CRC |
| | T ± Avastin ± chemo | HCC, GC, PaC |
| | T ± Avastin ± chemo | solid tumors |
| | T + Cotellic | solid tumors |
| | T + ipi/IFN | solid tumors |
| | T + Tarceva/Alecensa | NSCLC |
| | T + anti-CD20 combos | heme tumors |
| | T ± lenalidomide ± daratumumab | MM |
| | T + K/HP | HER2+ BC |
| | T + HMA | MDS |
| | T + radium 223 | mCRPC |
| | T + guadecitabine | AML |
| | T + rucaparib | ovarian ca |
| RG7461 | FAP IL2v FP combos | solid tumors |
| RG7601 | Venclexta + Cotellic/idasanutlin | AML |
| | Venclexta ± azacitidine | r/r MDS |
| RG7828 | CEA TCB ± Tecentriq | solid tumors |
| RG7813 | CEA IL2v FP* + Tecentriq | solid tumors |
| RG7828 | CD20 TDB ± Tecentriq | heme tumors |
| RG7876 | selicrelumab (CD40) + T | solid tumors |
| | selicrelumab + vanucizumab | solid tumors |

### Phase II (1 NME + 6 AIs)

| | | |
|---|---|---|
| RG3502 | Kadcyla + Tecentriq | 2L HER2+ mBC |
| RG7421 | Cotellic + Tecentriq ± taxane | TNBC |
| RG7601 | Venclexta + Rituxan | DLBCL |
| | Venclexta + Rituxan | r/r FL |
| | Venclexta + azacitidine | 1L MDS |
| RG7604 | taselisib + letrozole | (HER2-) BC neoadj |
| RG3637 | lebrikizumab ± Esbriet | (NME) IPF |

New Molecular Entity (NME)
Additional Indication (AI)
Oncology
Immunology

**RG-No** Roche/Genentech
**CHU** Chugai managed
*INN: cergutuzumab amunaleukin
T=Tecentriq; TCB=T cell bispecific
TDB=T cell dependent bispecific

### Phase III (3 NMEs + 19 AIs)

| | | |
|---|---|---|
| RG3502 | Kadcyla + Perjeta | HER2+ BC adj |
| RG7388 | idasanutlin + chemo | AML |
| RG7440 | ipatasertib + chemo | 1L CRPC |
| RG7421 | Cotellic + Zelboraf + T | BRAFm melanoma |
| RG7446 | T + nab-paclitaxel | 1L non-sq NSCLC |
| | T + chemo + Avastin | 1L ovarian cancer |
| | T + chemo + Avastin | 1L non-sq NSCLC |
| | T + chemo + pemetrexed | 1L non-sq NSCLC |
| | T + nab-paclitaxel | 1L sq NSCLC |
| | T + nab-paclitaxel | 1L TNBC |
| | T + nab-paclitaxel | TNBC neoadj |
| | T + Cotellic | 3L CRC |
| | T + Avastin | RCC |
| | T ± chemo | 1L mUC |
| | T + chemo | 1L extens. stage SCLC |
| | T + enzalutamide | CRPC |
| | T + paclitaxel | 1L TNBC |
| RG7601 | Venclexta + Rituxan | r/r CLL |
| | Venclexta + Gazyva | 1L CLL |
| | Venclexta + bortezomib | MM |
| | Venclexta + HMA | 1L AML |
| RG7604 | taselisib + fulvestrant | ER+ (HER2-neg) mBC |

### Registration (1 AI)

| | | |
|---|---|---|
| RG1273 | Perjeta + Herceptin | HER2+ BC adj |



Status as of October 19, 2017

# Cancer immunotherapy pipeline overview

## Phase I (10 NMEs + 30 AIs)

| | | |
|---|---|---|
| RG6026 | CD20 TCB | hematopoietic tumors |
| RG6058 | TIGIT ± Tecentriq | solid tumors |
| RG6160 | - | multiple myeloma |
| RG6180 | personalized cancer vaccine ± T | oncology |
| RG7155 | emactuzumab + Tecentriq | solid tumors |
| | emactuzumab + selicrezumab | solid tumors |
| RG7421 | Cotellic + Zelboraf + T | melanoma |
| | Cotellic + T | BRAF WT mM2L |
| RG7446 | Tecentriq | solid tumors |
| | Tecentriq | NMIBC |
| | T-based Morpheus platform | pancreatic ca |
| | T + Cotellic ± Avastin | 2/3L CRC |
| | T ± Avastin ± chemo | HCC, GC, PaC |
| | T ± Avastin ± chemo | solid tumors |
| | T + Cotellic | solid tumors |
| | T + ipi/IFN | solid tumors |
| | T + Tarceva/Alecensa | NSCLC |
| | T + anti-CD20 multiple combos | lymphoma |
| | T ± lenalidomide ± daratumumab | MM |
| | T + K/HP | HER2+ BC |
| | T + HMA | MDS |
| | T + radium 223 | mCRPC |
| | T + guadecitabine | AML |
| | T + rucaparib | ovarian ca |
| RG7461 | FAP IL2v FP + Tecentriq ± Avastin | RCC |
| RG7802 | CEA TCB ± Tecentriq | solid tumors |
| RG7813 | CEA IL2v FP* + Tecentriq | solid tumors |
| RG7828 | CD20 TDB ± Tecentriq | solid tumors |
| RG7876 | selicrelumab (CD40) + T | solid tumors |
| | selicrelumab + vanucizumab | solid tumors |

| | | |
|---|---|---|
| AMGN** | Tecentriq + talimogene laherp | TNBC, CRC |
| BLRX** | Tecentriq + BL-8040 | AML, solid tumors |
| CLDX** | Tecentriq + varlilumab | solid tumors |
| CLVS** | Tecentriq + rucaparib | ovarian ca |
| CRVS** | Tecentriq + CPI-444 | solid tumors |
| EPZM** | Tecentriq + tazemetostat | r/r DLBCL |
| HALO** | Tecentriq + PEGPH20 | CCC, GBC |
| INCY** | Tecentriq + epacadostat | solid tumors |
| JNJ** | Tecentriq ± daratumumab | solid tumors |
| KITE** | Tecentriq + KTE-C19 | r/r DLBCL |

## MORPHEUS Platform – Phase Ib/II (2 AIs)

| | | |
|---|---|---|
| RG7446 | T-based Morpheus | pancreatic cancer |
| | T-based Morpheus | gastric cancer |

** External collaborations: HALO – Halozyme PEGPH20; INCY- Incyte IDO inh; CLDX - Celldex CD27 MAb; CRVS – Corvus ADORA2A antag; KITE – Kite KTE-C19; AMGN – Amgen oncolytic virus; JNJ – Janssen CD38 MAb; CLVS – Clovis PARP inh; EPZM – Epizyme EZH2 inh; BLRX - BioLine Rx CXCR4 antag; IMDZ – Immune Design CMB305; SNDX – Syndax HDAC inh

New Molecular Entity (NME)
Additional Indication (AI)
Oncology

**RG-No** Roche/Genentech
*INN: cergutuzumab amunaleukin
T=Tecentriq; TCB=T cell bispecific
TDB=T cell dependent bispecific

## Phase II (4 AIs)

| | | |
|---|---|---|
| RG3502 | Kadcyla + Tecentriq | 2L HER2+ mBC |
| RG7421 | Cotellic + Tecentriq ± taxane | TNBC |
| IMDZ** | Tecentriq + NY-ESO-1 | soft tissue sarcoma |
| SNDX** | Tecentriq + entinostat | TNBC |

## Phase III (18 AIs)

| | | |
|---|---|---|
| RG7421 | Cotellic + Zelboraf + T | BRAFm melanoma |
| RG7446 | Tecentriq | NSCLC adj |
| | Tecentriq | MIBC adj |
| | Tecentriq Dx+ | 1L sq + non-sq SCLC |
| | Tecentriq | RCC adj |
| | T + nab-paclitaxel | 1L non-sq NSCLC |
| | T + chemo + Avastin | 1L ovarian cancer |
| | T + chemo + Avastin | 1L non-sq NSCLC |
| | T + chemo + pemetrexed | 1L non-sq NSCLC |
| | T + nab-paclitaxel | 1L sq NSCLC |
| | T + nab-paclitaxel | 1L TNBC |
| | T + nab-paclitaxel | TNBC neoadj |
| | T + Avastin | RCC |
| | T + Cotellic | 3L CRC |
| | T ± chemo | 1L mUC |
| | T + chemo | 1L extensive stage SCLC |
| | T + enzalutamide | CRPC |
| | T + paclitaxel | 1L TNBC |



Status as of October 19, 2017

Pipeline summary

**Marketed products additional indications**

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

# Alecensa (alectinib, RG7853, AF802)

*New CNS-active inhibitor of anaplastic lymphoma kinase*

| Indication | Treatment-naïve ALK-positive advanced NSCLC | ALK-positive advanced NSCLC in ALK inhibitor-naïve patients who are chemotherapy-naïve or have received one previous line of chemotherapy | ALK-positive crizotinib-naïve advanced NSCLC |
|---|---|---|---|
| **Phase/study** | **Phase III**<br>**ALEX** | **Phase III**<br>**J-ALEX/Japic CTI-132316**<br>Japanese study | **Phase I/II**<br>**AF-001JP**<br>Japanese study |
| **# of patients** | N=286 | N=207 | N=70 |
| **Design** | ▪ **ARM A**: Alecensa 600mg BID<br>▪ **ARM B**: Crizotinib 250mg BID | ▪ **ARM A**: Alecensa 300mg BID<br>▪ **ARM B**: Crizotinib 250mg BID | ▪ **Part 1**: Dose escalation monotherapy<br>▪ **Part 2**: Monotherapy; dose selected based on the results of Part 1 |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Progression-free survival | ▪ Phase I: Determination of recommended dose<br>▪ Phase II: Safety and efficacy |
| **Status** | ▪ Recruitment completed Q3 2015<br>▪ Primary endpoint met Q1 2017<br>▪ Data presented at ASCO 2017<br>▪ Results published in *NEJM* 2017 June; 377:829-838<br>▪ CNS data presented at ESMO 2017 | ▪ Primary analysis positive<br>▪ Data presented at ASCO 2016<br>▪ Breakthrough designation granted by FDA Q3 2016<br>▪ Results published in *Lancet* 2017 Jul; 390(10089):29–39 | ▪ Results published in *Lancet Oncology* 2013 Jun; 14(7):590-8<br>▪ Approved in Japan July 2014 |
| | ▪ Filed in EU Q1 and US Q2 2017<br>▪ Priority review granted by FDA Aug 2017<br>▪ Positive CHMP opinion Oct 2017 | | |
| **CT Identifier** | NCT02075840 | JapicCTI-132316 | JapicCTI-101264 |

In collaboration with Chugai

ASCO=American Society of Clinical Oncology; NSCLC=non-small cell lung cancer

# Alecensa (alectinib, RG7853, AF802)

*New CNS-active inhibitor of anaplastic lymphoma kinase*

| Indication | ALK-positive advanced NSCLC after progression on crizotinib treatment | ALK-positive advanced NSCLC after progression on crizotinib treatment |
|---|---|---|
| Phase/study | **Phase I/II**<br>**AF-002JG/NP28761**<br>US study | **Phase I/II**<br>**ACCALIA/NP28673**<br>Global study |
| # of patients | Phase I: N=36<br>Phase II: N=85 | N=130 |
| Design | ▪ **Part 1**: Dose escalation monotherapy<br>▪ **Part 2**: Monotherapy, dose selected based on results of Part 1 | ▪ **Part 1**: Dose escalation monotherapy<br>▪ **Part 2**: Monotherapy, dose selected based on results of Part 1 |
| Primary endpoint | ▪ Phase I: Determination of recommended dose<br>▪ Phase II: Safety and efficacy | ▪ Phase I: Determination of recommended dose<br>▪ Phase II: Safety and efficacy |
| Status | ▪ Phase I full cohort, including CNS data, published in *Lancet Oncology* 2014 Sep; 15(10):1119-28<br>▪ Primary analysis positive Q1 2015<br>▪ Data presented at ASCO 2015<br>▪ Updated data presented at WCLC 2015 | ▪ Primary analysis positive Q4 2014, updated analysis in Q1 2015<br>▪ Data presented at ASCO 2015<br>▪ Updated data presented at ECC 2015 and ESMO 2016<br>▪ Results published in the *Journal of Clinical Oncology* 2016 Mar; 34(7):661-668 |
| | ▪ Filed Q2 (US) and Q3 (EU) 2015<br>▪ Priority review granted by FDA Q3 2015<br>▪ Breakthrough designation granted by FDA Q2 2013<br>▪ Approved in US Q4 2015 and EU Q1 2017 | |
| CT Identifier | NCT01871805 | NCT01801111 |

In collaboration with Chugai

ASCO=American Society of Clinical Oncology; WCLC=World Conference on Lung Cancer; ECC=European Cancer Congress; ESMO=European Society for Medical Oncology; NSCLC=non-small cell lung cancer

# Avastin

## *Clinical development program*

| Indication | Glioblastoma |
|---|---|
| Phase/study | **Phase III**<br>**AVAglio** |
| # of patients | N=920 |
| Design | ▪ **ARM A:** Concurrent radiation and temozolomide plus placebo; followed by maintenance temozolomide (TMZ) plus placebo for 6 cycles; then placebo until disease progression<br>▪ **ARM B:** Concurrent radiation and TMZ plus Avastin; followed by maintenance TMZ plus Avastin for 6 cycles; then Avastin (15mg/kg q3 weeks) monotherapy until disease progression |
| Avastin dose | ▪ 10 mg/kg q2 weeks or 15 mg/kg q3 weeks |
| Primary endpoint | ▪ Progression-free survival and overall survival |
| Status | ▪ Co-primary endpoint of PFS met Q3 2012<br>▪ Overall survival data presented at ASCO 2013<br>▪ Filed in EU Q1 2013, with negative CHMP opinion Q3 2014<br>▪ Filed in US Q1 2017 |
| CT Identifier | NCT00943826 |

ASCO=American Society of Clinical Oncology

# Cotellic (cobimetinib)

*Selective small molecule inhibitor of MAPK kinase*

| Indication | First-line metastatic triple negative breast cancer | Relapsed or refractory AML not eligible for cytotoxic therapy |
|---|---|---|
| Phase/study | **Phase II COLET** | **Phase I/II** |
| # of patients | N=160 | N=140 |
| Design | ▪ **ARM A:** Cotellic plus paclitaxel<br>▪ **ARM B:** Placebo plus paclitaxel<br>▪ **ARM C:** Cotellic plus Tecentriq plus nab-paclitaxel<br>▪ **ARM D:** Cotellic plus Tecentriq plus paclitaxel | Phase I (dose escalation)<br>▪ **ARM A:** Cotellic plus Venclexta[1]<br>▪ **ARM B:** Idasanutlin plus Venclexta[1]<br><br>Phase II (expansion)<br>▪ **ARM A:** Cotellic plus Venclexta[1]<br>▪ **ARM B:** Idasanutlin plus Venclexta[1] |
| Primary endpoint | ▪ Progression-free survival and safety | ▪ Safety and efficacy |
| Status | ▪ FPI Q1 2015<br>▪ FPI Arms C and D: Q4 2016 | ▪ FPI Q1 2016 |
| CT Identifier | NCT02322814 | NCT02670044 |

In collaboration with Exelixis; [1]Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
AML=acute myeloid leukemia

# Cotellic (cobimetinib)

*Selective small molecule inhibitor of MAPK kinase*

| Indication | First-line BRAFv600 mutation-positive metastatic or unresectable locally advanced melanoma | First-line BRAF-WT metastatic or unresectable locally advanced melanoma | Previously untreated metastatic melanoma BRAF mutation-positive | BRAF-WT metastatic or unresectable locally advanced melanoma after immunotherapy |
|---|---|---|---|---|
| **Phase/study** | **Phase III IMspire150 TRILOGY** | **Phase III IMspire170** | **Phase I** | **Phase Ib** |
| **# of patients** | N=500 | N=500 | N=70 | N=42 |
| **Design** | Double-blind, randomized, placebo-controlled study<br>▪ **ARM A:** Tecentriq plus Cotellic plus Zelboraf[1]<br>▪ **ARM B:** Placebo plus Cotellic plus Zelboraf[1] | ▪ **ARM A:** Cotellic plus Tecentriq<br>▪ **ARM B:** Pembrolizumab | ▪ Dose-finding study of Cotellic plus Tecentriq plus Zelboraf[1] and Tecentriq plus Zelboraf[1] combinations | ▪ Preliminary efficacy of Cotellic plus Tecentriq in patients who have progressed on prior aPD-1 therapy |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Progression-free survival and overall survival | ▪ Safety and PK | ▪ Objective response rate and disease control rate |
| **Status** | ▪ FPI Q1 2017 | ▪ FPI expected Q4 2017 | ▪ FPI Q4 2012<br>▪ Data presented at ESMO 2016 | ▪ FPI Q2 2017 |
| **CT Identifier** | NCT02908672 | NCT03273153 | NCT01656642 | NCT03178851 |

In collaboration with Exelixis

[1]Zelboraf In collaboration with Plexxikon, a member of Daiichi Sankyo Group; ESMO=European Society for Medical Oncology

# Gazyva/Gazyvaro (obinutuzumab)

## *Oncology development program*

| Indication | Diffuse large B-cell lymphoma | Indolent non-Hodgkin's lymphoma MabThera/Rituxan refractory | Front-line indolent non-Hodgkin's lymphoma |
|---|---|---|---|
| **Phase/study** | **Phase III GOYA** | **Phase III GADOLIN** Induction and maintenance study | **Phase III GALLIUM** Induction and maintenance study |
| **# of patients** | N=1,418 | N=411 | N=1,401 |
| **Design** | ▪ **ARM A:** Gazyva 1000mg IV plus CHOP<br>▪ **ARM B:** MabThera/Rituxan plus CHOP | ▪ **ARM A:** Gazyva 1000mg IV plus bendamustine followed by Gazyva maintenance<br>▪ **ARM B:** Bendamustine | ▪ **ARM A:** Gazyva 1000mg IV + chemo followed by Gazyva maintenance<br>▪ **ARM B:** MabThera/Rituxan + chemo followed by MabThera/Rituxan maintenance<br>*Chemotherapy:*<br>▪ For follicular lymphoma (FL): CHOP, CVP or bendamustine<br>▪ For non-FL: physician's choice |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Progression-free survival | ▪ Progression-free survival in FL patients (N=1,202) |
| **Status** | ▪ Final analysis: Primary endpoint not met July 2016<br>▪ Data presented at ASH 2016 | ▪ Trial stopped at interim for efficacy Q1 2015<br>▪ Approved by the FDA Q1 2016 after priority review and by EMA Q2 2016<br>▪ Data presented at ASH 2016<br>▪ Results published in the *Lancet Oncology* 2016 Aug; 17(8):1081-93 | ▪ Trial stopped at interim for efficacy (May 2016)<br>▪ Data presented at ASH 2016<br>▪ Filed in EU Q4 2016, approved in EU Q3 2017<br>▪ Filed in US Q2 2017, priority review granted by FDA<br>▪ Results published in *NEJM* 2017 Oct 5;377(14):1331-1344 |
| **CT Identifier** | NCT01287741 | NCT01059630 | NCT01332968 |

In collaboration with Biogen

ASH=American Society of Hematology; CHOP=cyclophosphamide, doxorubicin, vincristine and prednisone; CVP=cyclophosphamide, vincristine and prednisolone

# Kadcyla

## *First ADC for HER2-positive breast cancer*

| Indication | HER2-positive early breast cancer high-risk patients | Operable HER2-positive early breast cancer | HER2-positive 2L metastatic breast cancer |
|---|---|---|---|
| Phase/study | **Phase III KATHERINE** | **Phase III KAITLIN** | **Phase II KATE2** |
| # of patients | N=1,484 | N=1,850 | N=200 |
| Design | ▪ **ARM A:** Kadcyla 3.6mg/kg Q3W<br>▪ **ARM B:** Herceptin | Following surgery and antracycline-based therapy:<br>▪ **ARM A:** Herceptin 6mg/kg Q3W plus Perjeta 420 mg/kg Q3W plus chemo<br>▪ **ARM B:** Kadcyla 3.6mg/kg Q3W plus Perjeta 420mg/kg Q3W plus chemo | ▪ **ARM A:** Kadcyla plus Tecentriq<br>▪ **ARM B:** Kadcyla plus placebo |
| Primary endpoint | ▪ Invasive disease-free survival | ▪ Invasive disease-free survival | ▪ Progression-free survival |
| Status | ▪ Recruitment complete Q4 2015<br>▪ Data expected in 2018 | ▪ Recruitment complete Q2 2015<br>▪ Data expected in 2019 | ▪ FPI Q3 2016<br>▪ Recruitment completed Q3 2017 |
| CT Identifier | NCT01772472 | NCT01966471 | NCT02924883 |

In collaboration with ImmunoGen, Inc.
ADC=antibody drug conjugate

# Perjeta

## *First-in-class HER2 dimerization inhibitor*

| Indication | Adjuvant HER2-positive breast cancer | Neoadjuvant/adjuvant HER2-positive breast cancer | Advanced HER2-positive gastric cancer |
|---|---|---|---|
| **Phase/study** | **Phase III APHINITY** | **Phase II BERENICE** | **Phase III JACOB** |
| **# of patients** | N=4,803 | N=401 | N=780 |
| **Design** | ▪ **ARM A:** Perjeta (840mg loading, 420 q3w) plus Herceptin for 52 weeks plus chemotherapy (6-8 cycles)<br>▪ **ARM B**: Placebo plus Herceptin (52 weeks) plus chemotherapy (6-8 cycles) | *Neoadjuvant treatment:*<br>▪ **ARM A:** ddAC q2w x4 cycles followed by weekly paclitaxel for 12 weeks, with P+H x4 cycles<br>▪ **ARM B:** FEC plus P+H x4 cycles followed by docetaxel plus P+H x4 cycles<br>*Adjuvant treatment:*<br>▪ P+H q3w to complete 1 year of HER2 therapy<br>▪ Hormonal and radiation therapy as indicated | ▪ **ARM A:** Perjeta (840mg loading, 420mg q3w) plus Herceptin and chemotherapy<br>▪ **ARM B:** Placebo plus Herceptin and chemotherapy |
| **Primary endpoint** | ▪ Invasive disease-free survival (IDFS) | ▪ Safety | ▪ Overall survival |
| **Status** | ▪ Recruitment completed Q3 2013<br>▪ Primary endpoint met Q1 2017<br>▪ Data presented at ASCO 2017<br>▪ Results published in *NEJM* 2017 Jul 13; 377(2):122-131<br>▪ Filed in the US and EU Q3 2017; priority review granted by FDA | ▪ Recruitment completed Q3 2015<br>▪ Data in-house<br>▪ Data presented at SABCS 2016 | ▪ Recruitment completed Q1 2016<br>▪ Data presented at ESMO 2017<br>▪ Study did not meet primary endpoint |
| **CT Identifier** | NCT01358877 | NCT02132949 | NCT01774786 |

ddAC=dose-dense doxorubicin plus cyclophosphamide; FEC=fluorouracil, epirubicin and cyclophosphamide; ASCO=American Society of Clinical Oncology; SABCS=San Antonio Breast Cancer Symposium

# Tecentriq (atezolizumab, RG7446)

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

| Indication | 1L non-squamous and squamous NSCLC PD-L1-selected patients | 1L non-squamous NSCLC | 1L non-squamous NSCLC | 1L non-squamous NSCLC |
|---|---|---|---|---|
| Phase/study | **Phase III IMpower110** | **Phase III IMpower150** | **Phase III IMpower130** | **Phase III IMpower132** |
| # of patients | N=570 | N=1,200 | N=650 | N=568 |
| Design | ▪ **ARM A:** Tecentriq monotherapy<br>▪ **ARM B**: *NSq*: carboplatin or cisplatin plus pemetrexed *Sq:* carboplatin or cisplatin plus gemcitabine | ▪ **ARM A:** Tecentriq plus paclitaxel plus carboplatin<br>▪ **ARM B**: Tecentriq plus Avastin plus paclitaxel plus carboplatin<br>▪ **ARM C**: Avastin plus paclitaxel plus carboplatin | ▪ **ARM A:** Tecentriq plus nab-paclitaxel plus carboplatin<br>▪ **ARM B**: Nab-paclitaxel plus carboplatin | ▪ **ARM A:** Tecentriq plus carboplatin or cisplatin plus pemetrexed<br>▪ **ARM B**: Carboplatin or cisplatin plus pemetrexed |
| Primary endpoint | ▪ Overall survival | ▪ Progression-free survival and overall survival | ▪ Progression-free survival and overall survival | ▪ Progression-free survival and overall survival |
| Status | ▪ FPI Q3 2015<br>▪ IMpower111 consolidated into IMpower110 Q3 2016 | ▪ FPI Q2 2015<br>▪ Recruitment completed Q4 2016 | ▪ FPI Q1 2015<br>▪ Recruitment completed Q1 2017 | ▪ FPI Q2 2016<br>▪ Recruitment completed Q2 2017 |
| CT Identifier | NCT02409342 | NCT02366143 | NCT02367781 | NCT02657434 |

NSCLC=non-small cell lung cancer; NSq=non-squamous; Sq=squamous

# Tecentriq (atezolizumab, RG7446)

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

| Indication | Adjuvant NSCLC | 1L squamous NSCLC | 1L extensive-stage SCLC |
|---|---|---|---|
| Phase/study | **Phase III IMpower010** | **Phase III IMpower131** | **Phase III IMpower133** |
| # of patients | N=1,127 | N=1,025 | N=400 |
| Design | Following adjuvant cisplatin-based chemotherapy<br>▪ **ARM A:** Tecentriq<br>▪ **ARM B**: Best supportive care | ▪ **ARM A:** Tecentriq plus paclitaxel plus carboplatin<br>▪ **ARM B**: Tecentriq plus nab-paclitaxel plus carboplatin<br>▪ **ARM C**: Nab-paclitaxel plus carboplatin | ▪ **ARM A:** Tecentriq plus carboplatin plus etoposide<br>▪ **ARM B**: Placebo plus carboplatin plus etoposide |
| Primary endpoint | ▪ Disease-free survival | ▪ Progression-free survival and overall survival | ▪ Progression-free survival and overall survival |
| Status | ▪ FPI Q3 2015<br>▪ Trial amended from PD-L1-selected patients to all-comers<br>▪ FPI for all-comer population Q4 2016 | ▪ FPI Q2 2015<br>▪ Recruitment completed Q1 2017 | ▪ FPI Q2 2016<br>▪ Orphan drug designation granted by FDA October 2016<br>▪ Recruitment completed Q2 2017 |
| CT Identifier | NCT02486718 | NCT02367794 | NCT02763579 |

NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer

# Tecentriq (atezolizumab, RG7446)

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

| Indication | Metastatic NSCLC 2L | Locally advanced or metastatic NSCLC (2L/3L) | Locally advanced or metastatic NSCLC PD-L1 positive | Locally advanced or metastatic NSCLC PD-L1 positive |
|---|---|---|---|---|
| **Phase/study** | **Phase III OAK** | **Phase II POPLAR** | **Phase II BIRCH** | **Phase II FIR** |
| **# of patients** | N=1,225 | N=287 | N=667 | N=130 |
| **Design** | ▪ **ARM A:** Tecentriq 1200mg q3w<br>▪ **ARM B:** Docetaxel | ▪ **ARM A**: Tecentriq 1200mg q3w<br>▪ **ARM B**: Docetaxel | Single arm study:<br>▪ Tecentriq 1200mg q3w | Single arm study:<br>▪ Tecentriq 1200mg q3w |
| **Primary endpoint** | ▪ Overall survival | ▪ Overall survival | ▪ Objective response rate | ▪ Objective response rate |
| **Status** | ▪ Recruitment completed Q2 2015<br>▪ Data presented at ESMO 2016<br>▪ Data filed with FDA Q3 2016<br>▪ Results published in *Lancet* 2017 Jan; 389(10066):255–265<br>▪ Data presented at ASCO 2017 | ▪ Recruitment completed Q2 2014<br>▪ Data presented at ASCO 2015 (interim) and ECC 2015 (primary)<br>▪ Results published in *Lancet* 2017 Apr 30; 387 (10030):1837-46<br>▪ Updated data presented at ASCO 2016 | ▪ Recruitment completed Q4 2014<br>▪ Primary analysis presented at ECC 2015 | ▪ Recruitment completed Q2 2014<br>▪ Data presented at ASCO 2015 |
| | ▪ Filed with the FDA and priority review granted Q1 2016, approved in US Q4 2016 | | | |
| | ▪ Approved in EU Q3 2017 | | | |
| **CT Identifier** | NCT02008227 | NCT01903993 | NCT02031458 | NCT01846416 |

NSCLC=non-small cell lung cancer; ASCO=American Society of Clinical Oncology; ESMO=European Society for Medical Oncology; ECC=European Cancer Congress

# Tecentriq (atezolizumab, RG7446)

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

| Indication | Extensive-stage small cell lung cancer 1L |
|---|---|
| Phase/study | **Phase I** |
| # of patients | N=53 |
| Design | ▪ Tecentriq plus Tarceva[1] or Alecensa |
| Primary endpoint | ▪ Safety |
| Status | ▪ FPI Q1 2014<br>▪ FPI in Alecensa arm Q3 2015<br>▪ Recruitment completed in Tarceva arm Q3 2015<br>▪ Data from Tarceva presented at WCLC and ESMO Asia 2016 |
| CT Identifier | NCT02013219 |

[1] Tarceva is a registered trademark of OSI Pharmaceuticals, LLC, a subsidiary of Astellas US, LLC
ESMO=European Society for Medical Oncology; WCLC=World Conference on Lung Cancer

# Tecentriq (atezolizumab, RG7446)

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

| Indication | Locally advanced or metastatic urothelial bladder cancer | |
|---|---|---|
| **Phase/study** | **Phase III**<br>**IMvigor211** | **Phase II**<br>**IMvigor210** |
| **# of patients** | N=932 | N=439 |
| **Design** | Patients who progressed on at least one platinum-containing regimen will receive:<br>▪ **ARM A:** Tecentriq 1200mg q3w<br>▪ **ARM B:** Chemotherapy (vinflunine, paclitaxel or docetaxel) | ▪ **Cohort 1**: Treatment-naive and cisplatin-ineligible patients<br>▪ **Cohort 2**: Patients with disease progression following or during platinum-containing treatment |
| **Primary endpoint** | ▪ Overall survival | ▪ Objective response rate |
| **Status** | ▪ Recruitment completed Q1 2016<br>▪ Data presented at EACR-AACR-SIC Special Conference 2017 | ▪ Cohort 2: US accelerated approval Q2 2016; filed in EU Q2 2016<br>▪ Cohort 2 results published in *Lancet* May 2016; 387(10031):p1909–1920<br>▪ Updated data (Cohorts 1 and 2) presented at ESMO 2016<br>▪ Cohort 1: Data filed with FDA Q4 2016, priority review granted, accelerated approval granted by FDA Q2 2017 |
| | ▪ Approved in EU Q3 2017 | |
| **CT Identifier** | NCT02302807 | NCT02951767 (Cohort 1), NCT02108652 (Cohort 2) |

UC=urothelial carcinoma; ESMO=European Society for Medical Oncology; EACR-AACR-SIC=European Association for Cancer Research - American Association for Cancer Research - Italian Cancer Society

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – UC*

| Indication | Adjuvant high-risk muscle-invasive urothelial cancer PD-L1-positive patients | 1L metastatic urothelial carcinoma | High-risk non-muscle-invasive bladder cancer |
|---|---|---|---|
| **Phase/study** | **Phase III IMvigor010** | **Phase III IMvigor130** | **Phase Ib/II** |
| **# of patients** | N=800 | N=1,200 | N=70 |
| **Design** | After cystectomy:<br>▪ **ARM A:** Tecentriq monotherapy<br>▪ **ARM B**: Observation | ▪ **ARM A:** Tecentriq plus gemcitabine and carboplatin or cisplatin<br>▪ **ARM B**: Placebo plus gemcitabine and carboplatin or cisplatin<br>▪ **ARM C**: Tecentriq monotherapy | ▪ **Cohort 1a:** Tecentriq (BCG-unresponsive NMIBC)<br>▪ **Cohort 1b:** Tecentriq + BCG (BCG-unresponsive NMIBC)<br>▪ **Cohort 2:** Tecentriq + BCG (BCG-relapsing NMIBC)<br>▪ **Cohort 3:** Tecentriq + BCG (BCG-naive NMIBC) |
| **Primary endpoint** | ▪ Disease-free survival | ▪ Progression-free survival, overall survival and safety | ▪ Safety and objective response rate |
| **Status** | ▪ FPI October 2015 | ▪ FPI Q3 2016<br>▪ FPI for Arm C (amended study) Q1 2017 | ▪ FPI Q2 2016 |
| **CT Identifier** | NCT02450331 | NCT02807636 | NCT02792192 |

UC=urothelial carcinoma; BCG=Bacille Calmette-Guérin; NMIBC=non-muscle invasive bladder cancer

# Tecentriq (atezolizumab, RG7446)

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

| Indication | Adjuvant renal cell carcinoma | Untreated advanced renal cell carcinoma | |
|---|---|---|---|
| **Phase/study** | **Phase III IMmotion010** | **Phase III IMmotion151** | **Phase II IMmotion150** |
| **# of patients** | N=664 | N=900 | N=305 |
| **Design** | ▪ **ARM A:** Tecentriq monotherapy<br>▪ **ARM B:** Observation | ▪ **ARM A**: Tecentriq plus Avastin<br>▪ **ARM B**: Sunitinib | ▪ **ARM A**: Tecentriq plus Avastin<br>▪ **ARM B**: Tecentriq; following PD: Tecentriq plus Avastin<br>▪ **ARM C**: Sunitinib; following PD: Tecentriq plus Avastin |
| **Primary endpoint** | ▪ Disease-free survival | ▪ Progression-free survival and overall survival (co-primary endpoint) | ▪ Progression-free survival |
| **Status** | ▪ FPI Q1 2017 | ▪ FPI Q2 2015<br>▪ Recruitment completed Q4 2016 | ▪ Recruitment completed Q1 2015<br>▪ Presented at ASCO GU and AACR 2017<br>▪ Updated data presented at ASCO 2017 |
| **CT Identifier** | NCT03024996 | NCT02420821 | NCT01984242 |

ASCO GU=American Society of Clinical Oncology Genitourinary Cancers; AACR=American Association for Cancer Research; PD=progressive disease

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – prostate cancer*

| Indication | Metastatic castration-resistant prostate cancer | Metastatic castration-resistant prostate cancer |
|---|---|---|
| **Phase/study** | **Phase Ib** | **Phase III**<br>**IMbassador250** |
| **# of patients** | N=45 | N=558 |
| **Design** | ▪ Tecentriq plus radium-223 dichloride | ▪ **ARM A:** Tecentriq plus enzalutamide<br>▪ **ARM B:** Enzalutamide |
| **Primary endpoint** | ▪ Safety and tolerability | ▪ Overall survival |
| **Status** | ▪ FPI Q3 2016 | ▪ FPI Q1 2017 |
| **CT Identifier** | NCT02814669 | NCT03016312 |

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – colorectal cancer*

| Indication | Third-line advanced or metastatic colorectal cancer | 2/3L metastatic colorectal cancer |
|---|---|---|
| Phase/study | **Phase III**<br>**IMblaze370** | **Phase I** |
| # of patients | N=360 | N=84 |
| Design | ▪ **ARM A**: Tecentriq plus Cotellic[1]<br>▪ **ARM B**: Tecentriq<br>▪ **ARM C**: Regorafenib | Open-label, single-arm, two-stage study with Cotellic[1] plus Tecentriq plus Avastin<br>▪ **Stage 1:** Safety run-in<br>▪ **Stage 2:** Dose-expansion with two cohorts;<br>– Expansion<br>– Biopsy |
| Primary endpoint | ▪ Overall survival | ▪ Safety |
| Status | ▪ FPI Q2 2016<br>▪ Recruitment completed Q1 2017 | ▪ FPI Q3 2016 |
| CT Identifier | NCT02788279 | NCT02876224 |

[1] Cotellic in collaboration with Exelixis

# Tecentriq (atezolizumab, RG7446)

## *Anti-PD-L1 cancer immunotherapy – solid tumors*

| Indication | Solid tumors | Solid tumors | Solid tumors |
|---|---|---|---|
| **Phase/study** | **Phase I** | **Phase I** | **Phase I** |
| **# of patients** | N=291 | N=225 | N=151 |
| **Design** | ▪ **ARM A**: HCC: Tecentriq + Avastin<br>▪ **ARM B**: HER2-neg. GC: Tecentriq + Avastin + oxaliplatin + leucovorin + 5-FU<br>▪ **ARM C:** PaC: Tecentriq + nab-paclitaxel + gemcitabine<br>▪ **ARM D:** HCC: Tecentriq + vanucizumab or Tecentriq + Avastin<br>▪ **ARM E:** Squamous cell mEC: Tecentriq + 5FU-Cis and Tecentriq + FOLFOX; adenocarcinoma mEC: Tecentriq + FOLFOX | ▪ **ARM A**: Tecentriq + Avastin<br>▪ **ARM B**: Tecentriq + Avastin + FOLFOX<br>▪ **ARM C**: Tecentriq + carboplatin + paclitaxel<br>▪ **ARM D**: Tecentriq + carboplatin+ pemetrexed<br>▪ **ARM E**: Tecentriq + carboplatin+ nab-paclitaxel<br>▪ **ARM F**: Tecentriq + nab-paclitaxel | ▪ **ARM A:** Dose-finding Tecentriq plus Cotellic[1]<br>▪ **ARM B:** Dose-expansion Tecentriq plus Cotellic[1] |
| **Primary endpoint** | ▪ Safety | ▪ Safety and PK | ▪ Safety |
| **Status** | ▪ FPI April 2016<br>▪ ARM D on hold<br>▪ FPI Arm E Q1 2017 | ▪ FPI Q2 2012<br>▪ Updated data presented at AACR 2016 (CRC) and ASCO 2016 (TNBC, Arm F) | ▪ FPI Q4 2013<br>▪ CRC cohort data presented at ASCO 2016 and ESMO 2016 |
| **CT Identifier** | NCT02715531 | NCT01633970 | NCT01988896 |

[1] Cotellic in collaboration with Exelixis

AACR=American Association for Cancer Research; ASCO=American Society of Clinical Oncology; ESMO=European Society for Medical Oncology; HCC=hepatocellular carcinoma; GC=gastric cancer; PaC=pancreatic cancer; mEC=metastatic esophageal cancer; CRC=colorectal cancer; TNBC=triple-negative breast cancer

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – solid tumors*

| Indication | Locally advanced or metastatic solid tumors | Locally advanced or metastatic solid tumors |
|---|---|---|
| **Phase/study** | **Phase I** | **Phase I** |
| **# of patients** | N=200 | N=660 |
| **Design** | ▪ **ARM A:** Tecentriq plus ipilimumab<br>▪ **ARM B:** Tecentriq plus interferon alpha-2b<br>▪ **ARM C:** Tecentriq plus PEG-interferon alfa-2a<br>▪ **ARM D:** Tecentriq plus PEG-interferon alfa-2a plus Avastin<br>▪ **ARM E:** Tecentriq plus Gazyva | ▪ Dose escalation study |
| **Primary endpoint** | ▪ Safety | ▪ Safety and PK |
| **Status** | ▪ FPI Q3 2014 | ▪ FPI Q2 2011<br>▪ Initial efficacy data presented at ASCO 2013<br>▪ Data from bladder cohort presented at ASCO and ESMO 2014; TNBC cohort presented at AACR 2015; updated lung and bladder data presented at ASCO 2015; GBM data presented at SNO 2015; SCCHN data presented at ESMO 2017 |
| **CT Identifier** | NCT02174172 | NCT01375842 |

ASCO=American Society of Clinical Oncology; ESMO=European Society for Medical Oncology; AACR=American Association for Cancer Research; SNO=Society for Neuro-Oncology; GBM=glioblastoma multiforme

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – breast*

| Indication | Previously untreated metastatic triple negative breast cancer | Previously untreated metastatic triple negative breast cancer |
|---|---|---|
| Phase/study | **Phase III IMpassion130** | **Phase III IMpassion131** |
| # of patients | N=900 | N=540 |
| Design | ▪ **ARM A**: Tecentriq plus nab-paclitaxel<br>▪ **ARM B**: Placebo plus nab-paclitaxel | ▪ **ARM A**: Tecentriq plus paclitaxel<br>▪ **ARM B**: Placebo plus paclitaxel |
| Primary endpoint | ▪ Progression-free survival and overall survival (co-primary endpoint) | ▪ Progression-free survival and overall survival (co-primary endpoint) |
| Status | ▪ FPI Q3 2015<br>▪ Recruitment completed Q2 2017 | ▪ FPI Q3 2017 |
| CT Identifier | NCT02425891 | NCT03125902 |

# Tecentriq (atezolizumab, RG7446)

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

| Indication | Neoadjuvant triple negative breast cancer | Metastatic breast cancer and locally advanced early breast cancer HER2-positive |
|---|---|---|
| Phase/study | **Phase III**<br>**IMpassion031** | **Phase I** |
| # of patients | N=204 | N=76 |
| Design | ▪ **ARM A**: Tecentriq plus nab-paclitaxel<br>▪ **ARM B**: Placebo plus nab-paclitaxel | ▪ **Cohort 1A** (mBC): Tecentriq plus Perjeta plus Herceptin<br>▪ **Cohort 1B** (mBC): Tecentriq plus Kadcyla[1]<br>▪ **Cohort 1F** (mBC): Tecentriq plus Perjeta plus Herceptin plus docetaxel<br>▪ **Cohort 2A** (eBC): Tecentriq plus Perjeta plus Herceptin<br>▪ **Cohort 2B** (eBC): Tecentriq plus Kadcyla[1]<br>▪ **Cohort 2C** (expansion on cohort 1B): Tecentriq plus Kadcyla[1] |
| Primary endpoint | ▪ Percentage of participants with pathologic complete response (pCR) | ▪ Safety |
| Status | ▪ FPI Q3 2017 | ▪ FPI Q4 2015 |
| CT Identifier | NCT03197935 | NCT02605915 |

[1] In collaboration with ImmunoGen, Inc.

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – ovarian*

| Indication | Front-line ovarian cancer | Advanced gynecological cancers and platinum-sensitive ovarian cancer |
|---|---|---|
| Phase/study | **Phase III IMaGYN050** | **Phase Ib** |
| # of patients | N=1,300 | N=48 |
| Design | ▪ **ARM A:** Tecentriq plus carboplatin plus paclitaxel plus Avastin<br>▪ **ARM B:** Carboplatin plus paclitaxel plus Avastin | ▪ **Part 1**: Dose finding Tecentriq plus rucaparib (CO-338)[1]<br>▪ **Part 2:** Expansion Tecentriq plus rucaparib (CO-338)[1] |
| Primary endpoint | ▪ Progression-free survival and overall survival (co-primary endpoint) | ▪ Safety |
| Status | ▪ FPI Q1 2017 | ▪ FPI Q2 2017 |
| CT Identifier | NCT03038100 | NCT03101280 |

[1] Rucaparib in collaboration with Clovis

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – hematology*

| Indication | Multiple myeloma | Myelodysplastic syndromes | Acute myeloid leukemia |
|---|---|---|---|
| **Phase/study** | **Phase I** | **Phase I** | **Phase Ib** |
| **# of patients** | N≈214 | N=46 | N=40 |
| **Design** | ▪ Tecentriq monotherapy<br>▪ Tecentriq plus lenalidomide<br>▪ Tecentriq plus daratumumab[1]<br>▪ Tecentriq plus lenalidomide plus daratumumab[1] | ▪ Tecentriq monotherapy and azacitidine combination cohorts | ▪ Tecentriq plus guadecitabine (SGI-110)[2] |
| **Primary endpoint** | ▪ Safety | ▪ Safety | ▪ Safety and efficacy |
| **Status** | ▪ FPI Q3 2015<br>▪ FPI daratumumab[1] cohorts Q3 2016<br>▪ Study on partial clinical hold | ▪ FPI Q3 2015 | ▪ FPI Q4 2016 |
| **CT Identifier** | NCT02431208 | NCT02508870 | NCT02892318 |

[1] Daratumumab cohorts in collaboration with Janssen; [2] SGI-110 in collaboration with Astex

# Tecentriq (atezolizumab, RG7446)

*Anti-PD-L1 cancer immunotherapy – hematology*

| Indication | 1L FL and 1L DLBCL | Relapsed or refractory FL | Relapsed or refractory FL and DLBCL | Relapsed or refractory FL or DLBCL |
|---|---|---|---|---|
| **Phase/study** | **Phase I** | **Phase I** | **Phase I** | **Phase I/II** |
| **# of patients** | N=92 | N=46 | N=46 | N=86 |
| **Design** | ▪ Tecentriq plus Gazyva plus bendamustine<br>▪ Tecentriq plus Gazyva plus CHOP | ▪ Tecentriq plus Gazyva plus lenalidomide | ▪ **Stage 1:** Safety evaluation Tecentriq plus Gazyva<br>▪ **Stage 2:** Expansion Tecentriq plus Gazyva<br>▪ **Stage 3:** New cohort Tecentriq plus tazemetostat[1] | ▪ **Dose escalation:** Tecentriq plus Gazyva/Rituxan plus polatuzumab vedotin[2]<br>▪ **Expansion:** Tecentriq plus Gazyva/Rituxan plus polatuzumab vedotin[2] |
| **Primary endpoint** | ▪ Safety and efficacy | ▪ Safety and efficacy | ▪ Safety | ▪ Safety and efficacy |
| **Status** | ▪ FPI Q4 2015 | ▪ FPI Q4 2015<br>▪ Study on partial clinical hold | ▪ FPI Q4 2014<br>▪ FPI Stage 3 Q1 2017 | ▪ FPI FL Q4 2016<br>▪ Study amended to change from Gazyva to Rituxan for DLBCL<br>▪ FPI DLBCL Q1 2017 |
| **CT Identifier** | NCT02596971 | NCT02631577 | NCT02220842 | NCT02729896 |

[1] Tazemetostat tested for r/r DLBCL in collaboration with Epizyme; [2] Polatuzumab vedotin in collaboration with Seattle Genetics;
FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma

# Venclexta (venetoclax, RG7601, ABT-199)

*Novel small molecule Bcl-2 selective inhibitor – CLL*

| Indication | Untreated CLL patients with coexisting medical conditions | Relapsed or refractory CLL | Relapsed or refractory CLL with 17p deletion |
|---|---|---|---|
| **Phase/study** | **Phase III CLL14** | **Phase III MURANO** | **Phase II** |
| **# of patients** | N=432 | N=391 | N=100 |
| **Design** | ▪ **ARM A**: Venclexta plus Gazyva<br>▪ **ARM B**: Chlorambucil plus Gazyva | ▪ **ARM A**: Venclexta plus Rituxan<br>▪ **ARM B**: Rituxan plus bendamustine | ▪ Single-agent Venclexta |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Progression-free survival | ▪ Safety and maximum tolerated dose (MTD) |
| **Status** | ▪ FPI Q4 2014<br>▪ Recruitment completed Q3 2016 | ▪ Recruitment completed Q3 2015<br>▪ Study met primary endpoint at interim analysis | ▪ Breakthrough designation granted by FDA Q2 2015, priority review granted, US approval Q2 2016<br>▪ Approved in EU Q4 2016 |
| **CT Identifier** | NCT02242942 | NCT02005471 | NCT01889186 |

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
CLL=chronic lymphocytic leukemia

# Venclexta (venetoclax, RG7601, ABT-199)

*Novel small molecule Bcl-2 selective inhibitor – CLL*

| Indication | Relapsed or refractory CLL | Relapsed CLL and SLL | Relapsed or refractory or previously untreated CLL | Relapsed or refractory or previously untreated CLL |
|---|---|---|---|---|
| **Phase/study** | **Phase II** | **Phase Ib** | **Phase Ib** | **Phase Ib** |
| **# of patients** | N=120 | N=50 | N=100 | N=90 |
| **Design** | ▪ Venclexta after ibrutinib therapy<br>▪ Venclexta after idelalisib therapy | ▪ Dose-escalation study in combination with MabThera/Rituxan | ▪ Venclexta in combination with MabThera/Rituxan and bendamustine | ▪ Venclexta in combination with Gazyva |
| **Primary endpoint** | ▪ Overall response rate | ▪ Safety and maximum tolerated dose | ▪ Safety and maximum tolerated dose | ▪ Safety and maximum tolerated dose |
| **Status** | ▪ FPI Q3 2014<br>▪ Data presented at ASH 2015<br>▪ Updated data presented at ASCO 2016 | ▪ Recruitment completed Q1 2015<br>▪ Data presented at ASCO 2014 and EHA 2015<br>▪ Updated data presented at ASH 2015 and ASCO 2016<br>▪ Breakthrough designation granted by FDA Q1 2016 | ▪ FPI Q2 2013<br>▪ Data presented at ASH 2015 | ▪ FPI Q1 2014<br>▪ Data presented at ASH 2015 |
| **CT Identifier** | NCT02141282 | NCT01682616 | NCT01671904 | NCT01685892 |

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
CLL=chronic lymphocytic leukemia; SLL=small lymphocytic lymphoma
ASH=American Society of Hematology; ASCO=American Society of Clinical Oncology; EHA=European hematology association

# Venclexta (venetoclax, RG7601, ABT-199)

*Novel small molecule Bcl-2 selective inhibitor – NHL*

| Indication | Relapsed or refractory FL | B cell NHL and front-line DLBCL |
|---|---|---|
| Phase/study | **Phase II**<br>**CONTRALTO** | **Phase I/II**<br>**CAVALLI** |
| # of patients | N=165 | N=248 |
| Design | ▪ **ARM A:** Venclexta plus Rituxan<br>▪ **ARM B:** Venclexta plus Rituxan plus bendamustine<br>▪ **ARM C:** Rituxan plus bendamustine | Phase I (dose finding, patients with B cell NHL):<br>▪ **ARM A:** Venclexta plus R-CHOP<br>▪ **ARM B:** Venclexta plus G-CHOP<br>Phase II (expansion, patients with 1L DLBCL):<br>▪ Venclexta plus R-CHOP |
| Primary endpoint | ▪ Overall response rate | ▪ Safety and efficacy |
| Status | ▪ FPI Q4 2014<br>▪ Data presented at ASH 2016 | ▪ FPI Q2 2014<br>▪ Data presented at ASCO 2016 and ASH 2016 |
| CT Identifier | NCT02187861 | NCT02055820 |

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

FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma; NHL=non-Hodgkin's lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine and prednisone; R=Rituxan/MabThera; G=Gazyva; ASH=American Society of Hematology; ASCO=American Society of Clinical Oncology

# Venclexta (venetoclax, RG7601, ABT-199)

*Novel small molecule Bcl-2 selective inhibitor – MM*

| Indication | Relapsed or refractory multiple myeloma | | |
|---|---|---|---|
| **Phase/study** | **Phase III BELLINI** | **Phase I** | **Phase I** |
| **# of patients** | N=240 | N=66 | N=84 |
| **Design** | ▪ **ARM A**: Venclexta plus bortezomib plus dexamethasone<br>▪ **ARM B**: Placebo plus bortezomib plus dexamethasone | Patients receiving bortezomib and dexamethasone as standard therapy:<br>▪ **Dose escalation cohort:** Venclexta plus bortezomib plus dexamethasone<br>▪ **Safety expansion cohort:** Venclexta plus bortezomib plus dexamethasone | ▪ **Dose escalation cohort:** Venclexta dose escalation<br>▪ **Safety expansion cohort:** Venclexta expansion<br>▪ **Combination:** Venclexta plus dexamethasone |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Safety and maximum tolerated dose | ▪ Safety and maximum tolerated dose |
| **Status** | ▪ FPI Q3 2016 | ▪ FPI Q4 2012<br>▪ Data presented at ASCO 2015<br>▪ Updated data presented at ASCO 2016 and ASH 2016 | ▪ FPI Q4 2012<br>▪ Data presented at ASCO 2015<br>▪ Updated data presented at ASCO 2016 and ASH 2016 |
| **CT Identifier** | NCT02755597 | NCT01794507 | NCT01794520 |

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

MM=multiple myeloma; ASCO=American Society of Clinical Oncology; ASH=American Society of Hematology

# Venclexta (venetoclax, RG7601, ABT-199)

*Novel small molecule Bcl-2 selective inhibitor – AML*

| Indication | AML | Relapsed or refractory AML not eligible for cytotoxic therapy |
|---|---|---|
| Phase/study | **Phase II** | **Phase Ib/II** |
| # of patients | N=32 | N=140 |
| Design | ▪ Dose escalation of Venclexta | Phase I (dose escalation):<br>▪ **ARM A:** Cotellic[1] plus Venclexta<br>▪ **ARM B:** Idasanutlin plus Venclexta<br>Phase II (expansion):<br>▪ **ARM A:** Cotellic[1] plus Venclexta<br>▪ **ARM B:** Idasanutlin plus Venclexta |
| Primary endpoint | ▪ Overall response rate | ▪ Safety and efficacy |
| Status | ▪ FPI Q4 2013<br>▪ Data presented at ASH 2014<br>▪ Updated data presented at ASCO 2016 | ▪ FPI Q1 2016 |
| CT Identifier | NCT01994837 | NCT02670044 |

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute; [1] Cotellic in collaboration with Exelixis
AML=acute myelogenous leukemia; ASH=American Society of Hematology; ASCO=American Society of Clinical Oncology

# Venclexta (venetoclax, RG7601, ABT-199)

*Novel small molecule Bcl-2 selective inhibitor – AML*

| Indication | Treatment-naïve AML not eligible for standard induction therapy | | |
|---|---|---|---|
| **Phase/study** | **Phase Ib** | **Phase I/II** | **Phase III** |
| **# of patients** | N=160 | N=65 | N=400 |
| **Design** | ▪ Venclexta (dose escalation) plus decitabine<br>▪ Venclexta (dose escalation) plus azacitidine<br>▪ Venclexta (dose escalation) plus decitabine plus posaconazole | ▪ Venclexta (dose escalation) plus low-dose cytarabine | ▪ **ARM A:** Venclexta plus azacitidine<br>▪ **ARM B:** Azacitidine |
| **Primary endpoint** | ▪ Safety | ▪ Safety, PK, PD and efficacy | ▪ Percentage of participants with CR, Overall survival |
| **Status** | ▪ FPI Q4 2014<br>▪ Data presented at ASH 2015<br>▪ Breakthrough designation granted by FDA Q1 2016<br>▪ Updated data presented at ASCO 2016 | ▪ FPI Q1 2015<br>▪ Initial data presented at ASCO 2016<br>▪ Updated data presented at ASH 2016 | ▪ FPI Q1 2017 |
| **CT Identifier** | NCT02203773 | NCT02287233 | NCT02993523 |

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

AML=acute myelogenous leukemia; ASH=American Society of Hematology; ASCO=American Society of Clinical Oncology

# Venclexta (venetoclax, RG7601, ABT-199)

*Novel small molecule Bcl-2 selective inhibitor – MDS*

| Indication | Myelodysplastic syndromes after azacitidine failure | Treatment-naive myelodysplastic syndromes |
|---|---|---|
| **Phase/study** | **Phase Ib** | **Phase II** |
| **# of patients** | N=66 | N=90 |
| **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 | ▪ **ARM A:** Venclexta 400 mg plus azacitidine<br>▪ **ARM B:** Venclexta 800 mg plus azacitidine<br>▪ **ARM C:** Azacitidine |
| **Primary endpoint** | ▪ Safety, PK/PD, efficacy | ▪ Overall response rate |
| **Status** | ▪ FPI Q1 2017 | ▪ FPI Q1 2017 |
| **CT Identifier** | NCT02966782 | NCT02942290 |

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
MDS=myelodysplastic syndromes

# Zelboraf

*Selective small molecule inhibitor of mutant BRAF*

| Indication | Adjuvant therapy in patients with resected cutaneous BRAF mutation positive melanoma |
|---|---|
| Phase/study | **Phase III**<br>**BRIM8** |
| # of patients | N=475 |
| Design | 52-week treatment<br>▪ **ARM A:** Zelboraf 960mg bid<br>▪ **ARM B:** Placebo |
| Primary endpoint | ▪ Disease-free survival |
| Status | ▪ Recruitment completed Q2 2015<br>▪ Study did not meet primary endpoint |
| CT Identifier | NCT01667419 |

In collaboration with Plexxikon, a member of Daiichi Sankyo Group
See also combinations with Cotellic (MEK inhibitor) and Tecentriq (aPD-L1 MAb)

# OCREVUS (ocrelizumab, RG1594)

## *Humanized mAb 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:** Ocrelizumab 2x 300 mg iv followed by 600 mg iv every 24 weeks<br>▪ **ARM B:** Interferon β-1a | 96-week treatment period:<br>▪ **ARM A:** Ocrelizumab 2x 300 mg iv followed by 600 mg iv every 24 weeks<br>▪ **ARM B:** Interferon β-1a | 120-week treatment period:<br>▪ **ARM A:** Ocrelizumab 2x 300 mg iv every 24 weeks<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 Expanded Disability Status Scale (EDSS) |
| **Status** | ▪ Primary endpoint met Q2 2015<br>▪ Data presented at ECTRIMS 2015<br>▪ Updated data presented at AAN 2017 | ▪ Primary endpoint met Q2 2015<br>▪ Data presented at ECTRIMS 2015<br>▪ Updated data presented at AAN 2017 | ▪ Primary endpoint met Q3 2015<br>▪ Data presented at ECTRIMS 2015<br>▪ Updated data presented at AAN 2017 |
| | ▪ Results published in *NEJM*, 2017 Jan 19;376(3):221-234 | | ▪ Results published in *NEJM*, 2017 Jan 19;376(3):209-220 |
| | ▪ Filed globally in 2016<br>▪ Approved in US Q1 2017 | | |
| **CT Identifier** | NCT01247324 | NCT01412333 | NCT01194570 |

ECTRIMS=European Committee for Treatment and Research in Multiple Sclerosis; AAN=Annual Meeting of the American Academy of Neurology

# Actemra/RoActemra

*Interleukin-6 receptor inhibitor*

| Indication | Systemic sclerosis | Giant cell arteritis |
|---|---|---|
| Phase/study | **Phase III**<br>**focuSSced** | **Phase III**<br>**GiACTA** |
| # of patients | N=210 | N=250 |
| Design | Blinded 48-week treatment with weekly dosing:<br>▪ **ARM A:** Actemra SC 162mg<br>▪ **ARM B:** Placebo SC<br>Open-label weekly dosing at weeks 49 to 96:<br>▪ Actemra SC 162mg | Part 1: 52-week blinded period<br>▪ **ARM A:** Actemra SC 162mg qw plus 26 weeks prednisone taper<br>▪ **ARM B:** Actemra SC 162mg q2w plus 26 weeks prednisone taper<br>▪ **ARM C:** Placebo plus 26 weeks prednisone taper<br>▪ **ARM D:** Placebo plus 52 weeks prednisone taper<br>Part II:<br>▪ 104-wk open label extension: patients in remission followed off of the study drug; Patients with active disease receive open label Actemra SC 162mg qw |
| Primary endpoint | ▪ Change in modified Rodnan skin score (mRSS) at week 48 | ▪ Proportion of patients in sustained remission at week 52 |
| Status | ▪ FPI Q4 2015<br>▪ Breakthrough designation granted by FDA Q1 2015<br>▪ Recruitment completed Q1 2017 | ▪ Recruitment completed Q2 2015<br>▪ Primary and key secondary endpoints met Q2 2016<br>▪ Breakthrough designation granted by FDA Q3 2016<br>▪ Data presented at ACR 2016<br>▪ Filed globally Q4 2016; approved in US Q2 2017; approved in EU Q3 2017<br>▪ Results published in *NEJM*, 2017 Jul 27;377(4):317-328 |
| CT Identifier | NCT02453256 | NCT01791153 |

In collaboration with Chugai

ACR=American College of Rheumatology; BTD=Breakthrough Therapy Designation

# MabThera/Rituxan

## *Immunology development program*

| Indication | Moderate to severely active pemphigus vulgaris |
|---|---|
| Phase/study | **Phase III**<br>**PEMPHIX** |
| # of patients | N=132 |
| Design | ▪ **ARM A:** Rituxan<br>▪ **ARM B:** Mycophenolate mofetil |
| Primary endpoint | ▪ Proportion of patients who achieve sustained complete remission |
| Status | ▪ FPI Q2 2015<br>▪ Results published in *Lancet* 2017 Mar; 389(10083): p2031–2040 |
| CT Identifier | NCT02383589 |

# Obinutuzumab (GA101, RG7159)

*Immunology development program*

| Indication | Lupus nephritis |
|---|---|
| Phase/study | **Phase II**<br>**NOBILITY** |
| # of patients | N=120 |
| Design | ▪ **ARM A:** Obinutuzumab 1000mg IV plus mycophenolate mofetil<br>▪ **ARM B:** Placebo IV plus mycophenolate mofetil |
| Primary endpoint | ▪ Percentage of participants who achieve complete renal response (CRR) |
| Status | ▪ FPI Q4 2015 |
| CT Identifier | NCT02550652 |

In collaboration with Biogen

# Xolair

*Humanized mAb that selectively binds to IgE*

| Indication | Chronic rhinosinusitis with nasal polyps | |
|---|---|---|
| Phase/study | **Phase III**<br>**POLYP 1** | **Phase III**<br>**POLYP 2** |
| # of patients | N=120 | N=120 |
| Design | Placebo-controlled study of Xolair in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) who have had an inadequate response to standard-of-care treatments:<br>▪ **ARM A:** Xolair every 2 weeks or every 4 weeks<br>▪ **ARM B:** Placebo | Placebo-controlled study of Xolair in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) who have had an inadequate response to standard-of-care treatments:<br>▪ **ARM A:** Xolair every 2 weeks or every 4 weeks<br>▪ **ARM B:** Placebo |
| Primary endpoint | ▪ Change from baseline in average daily nasal congestion score (NCS) at week 24<br>▪ Change from baseline in nasal polyp score (NPS) to week 24 | ▪ Change from baseline in average daily nasal congestion score (NCS) at week 24<br>▪ Change from baseline in nasal polyp score (NPS) to week 24 |
| Status | ▪ FPI expected Q4 2017 | ▪ FPI expected Q4 2017 |
| CT Identifier | NCT03280550 | NCT03280537 |

In collaboration with Novartis

# Lucentis

*Anti-VEGF antibody fragment for ocular diseases*

| Indication | AMD port delivery device (Ranibizumab Port Delivery System) |
|---|---|
| Phase/study | **Phase II LADDER** |
| # of patients | N=220 |
| Design | ▪ Four-arm study: Lucentis monthly intravitreal control vs three ranibizumab formulations delivered via implant |
| Primary endpoint | ▪ Time to first refill |
| Status | ▪ FPI Q3 2015<br>▪ Recruitment completed Q3 2017 |
| CT Identifier | NCT02510794 |

In collaboration with Forsight and Novartis
AMD=age-related macular degeneration

Pipeline summary

Marketed products additional indications

**Global Development late-stage trials**

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

# Emicizumab (RG6013, ACE910)

*Factor VIII mimetic for treatment of hemophilia A*

| Indication | Hemophilia A | | |
|---|---|---|---|
| **Phase/study** | **Phase I**<br>Study in Japan | **Phase I/II**<br>Study in Japan | **Non-Interventional study** |
| **# of patients** | N=82 | N=18 | N>90 |
| **Design** | ▪ Enrolled 64 healthy volunteers and 18 patients | ▪ Extension study in patients from phase 1 | ▪ A single arm, multicenter, non-interventional study evaluating bleeding incidence, health-related quality of life and safety in patients with hemophilia A and inhibitors to factor VIII under standard-of-care treatment |
| **Primary endpoint** | ▪ Exploratory safety and efficacy | ▪ Exploratory safety and efficacy | ▪ Number of bleeds over time, sites of bleed, type of bleed |
| **Status** | ▪ Recruitment completed Q2 2014<br>▪ Data presented at ASH 2014 | ▪ Recruitment completed Q4 2014<br>▪ Data presented at ISTH 2015<br>▪ Extension data presented at WFH 2016 | ▪ Inhibitor cohort closed Q4 2015, except China<br>▪ FPI in non-inhibitor and pediatric subjects in Q1 2016<br>▪ Initial data presented at ASH 2016 |
| | ▪ Breakthrough Therapy Designation granted by FDA Q3 2015 | | |
| **CT Identifier** | JapicCTI-121934 | JapicCTI-132195 | NCT02476942 |

In collaboration with Chugai

ASH=American Society of Hematology; ISTH=International Society on Thrombosis and Haemostasis; WFH=World Federation of Hemophilia

# Emicizumab (RG6013, ACE910)

*Factor VIII mimetic for treatment of hemophilia A*

| Indication | Hemophilia A patients with inhibitors to factor VIII | Hemophilia A pediatric patients with inhibitors to factor VIII |
|---|---|---|
| Phase/study | **Phase III**<br>**HAVEN 1** | **Phase III**<br>**HAVEN 2** |
| # of patients | N=118 | N=60 |
| Design | Patients on episodic treatment prior to study entry:<br>▪ **Arm A:** Episodic treatment + emicizumab prophylaxis<br>▪ **Arm B:** Episodic treatment (no prophylaxis)<br>Patients on prophylaxis prior to study entry:<br>▪ **Arm C:** Emicizumab prophylaxis + episodic treatment<br>Patients on episodic treatment previously on non-interventional study:<br>▪ **Arm D:** Emicizumab prophylaxis + episodic treatment | Patients on prophylactic or episodic treatment prior to study entry:<br>▪ Emicizumab prophylaxis |
| Primary endpoint | ▪ Number of bleeds over 24 weeks | ▪ Number of bleeds over 52 weeks |
| Status | ▪ FPI Q4 2015<br>▪ Recruitment completed in Arms A and B Q2 2016<br>▪ Primary and all secondary endpoints met Q4 2016<br>▪ Results published in *NEJM* 2017 Aug 31;377(9):809-818 | ▪ FPI Q3 2016<br>▪ Positive interim results in Q2 2017<br>▪ Recruitment completed Q2 2017 |
| | ▪ Data presented at ISTH 2017<br>▪ Filed in US and EU in Q2 2017; granted accelerated assessment (EMA) and priority review (FDA) | |
| CT Identifier | NCT02622321 | NCT02795767 |

In collaboration with Chugai
ISTH=International Society on Thrombosis and Haemostasis

# Emicizumab (RG6013, ACE910)

*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**: Emicizumab prophylaxis qw<br>▪ **Arm B**: Emicizumab prophylaxis q2w<br>▪ **Arm C**: Episodic FVIII treatment; switch to emicizumab prophylaxis possible after 24 weeks<br>Patients on FVIII prophylaxis prior to study entry:<br>▪ **Arm D**: Emicizumab prophylaxis qw | Multicenter, open-label, non-randomized study to assess the efficacy, safety, pharmacokinetics, and pharmacodynamics of emicizumab administered every 4 weeks.<br>▪ **Part 1:** Pharmacokinetic (PK) run-in part (N=6)<br>▪ **Part 2:** Expansion part (N=40) |
| Primary endpoint | ▪ Number of bleeds over 24 weeks | ▪ Number of bleeds over 24 weeks |
| Status | ▪ FPI Q3 2016<br>▪ Recruitment completed Q2 2017 | ▪ FPI Q1 2017<br>▪ Recruitment completed Q2 2017 |
| CT Identifier | NCT02847637 | NCT03020160 |

In collaboration with Chugai

# Ipatasertib (RG7440, GDC-0068)

*Highly selective small molecule inhibitor of Akt*

| Indication | 1L castration-resistant prostate cancer | 2L castration-resistant prostate cancer | 1L metastatic gastric or gastroesophageal junction adenocarcinoma |
|---|---|---|---|
| **Phase/study** | **Phase III**<br>**IPATential150** | **Phase II**<br>**A.MARTIN** | **Phase II**<br>**JAGUAR** |
| **# of patients** | N=850 | N=262 | N=153 |
| **Design** | ▪ **ARM A:** Ipatasertib plus abiraterone<br>▪ **ARM B:** Placebo plus abiraterone | ▪ **ARM A:** Ipatasertib 400 mg plus abiraterone<br>▪ **ARM B:** Ipatasertib 200 mg plus abiraterone<br>▪ **ARM C:** Placebo plus abiraterone | ▪ **ARM A:** Ipatasertib plus mFOLFOX6<br>▪ **ARM B:** Placebo plus mFOLFOX6 |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Progression-free survival | ▪ Progression-free survival |
| **Status** | ▪ FPI Q2 2017 | ▪ Recruitment completed Q4 2014<br>▪ Data in-house<br>▪ ITT data presented at ASCO 2016<br>▪ Biomarker data at ESMO 2016 | ▪ Recruitment completed Q4 2014<br>▪ Data showed no benefit in treated vs control group Q2 2016 |
| **CT Identifier** | NCT03072238 | NCT01485861 | NCT01896531 |

In collaboration with Array BioPharma

ASCO=American Society of Clinical Oncology; ESMO=European Society for Medical Oncology; mFOLFOX6=modified FOLFOX (folinic acid, fluorouracil, oxaliplatin); ITT=intention to treat

# Ipatasertib (RG7440, GDC-0068)

*Highly selective small molecule inhibitor of Akt*

| Indication | 1L triple-negative breast cancer | | Neoadjuvant TNBC |
|---|---|---|---|
| **Phase/study** | **Phase III**<br>**IPATunity130** | **Phase II**<br>**LOTUS** | **Phase II**<br>**FAIRLANE** |
| **# of patients** | N=450 | N=120 | N=150 |
| **Design** | Cohort 1: Dx+ 1L TNBC (N=249)<br>▪ **Arm A:** Ipatasertib plus paclitaxel<br>▪ **Arm B:** Placebo plus paclitaxel<br>Cohort 2: Dx+ HR+ mBC (N=201)<br>▪ **Arm A:** Ipatasertib plus paclitaxel<br>▪ **Arm B:** Placebo plus paclitaxel | ▪ **ARM A:** Ipatasertib plus paclitaxel<br>▪ **ARM B:** Placebo plus paclitaxel | ▪ **ARM A:** Ipatasertib plus paclitaxel<br>▪ **ARM B:** Placebo plus paclitaxel |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Progression-free survival | ▪ Pathologic complete response (pCR) |
| **Status** | ▪ FPI expected Q4 2017 | ▪ Recruitment completed Q1 2016<br>▪ Data presented at ASCO 2017<br>▪ Data published in *Lancet Oncology* 2017 Aug 8. pii: S1470-2045(17)30450-3 | ▪ FPI Q1 2015<br>▪ Recruitment completed Q2 2017 |
| **CT Identifier** | | NCT02162719 | NCT02301988 |

In collaboration with Array BioPharma

ASCO=American Society of Clinical Oncology; TNBC=triple-negative breast cancer

# Polatuzumab vedotin (RG7596)

*ADC targeting CD79b to treat B cell malignancies*

| Indication | Non-Hodgkin's lymphoma | Non-Hodgkin's lymphoma<br>1L DLBCL |
|---|---|---|
| Phase/study | **Phase II**<br>**ROMULUS** | **Phase Ib/II** |
| # of patients | N=246 | N=110 |
| Design | ▪ **Arm A:** Pinatuzumab vedotin plus Rituxan<br>▪ **Arm B:** Polatuzumab vedotin plus Rituxan<br>▪ **Arm C:** Polatuzumab vedotin plus Rituxan<br>▪ **Arms E, G, H:** Polatuzumab vedotin plus Gazyva | ▪ **PhIb:** Dose escalation<br>▪ **PhII:** Polatuzumab vedotin in combination with Rituxan or Gazyva and CHP non-randomized |
| Primary endpoint | ▪ Safety and anti-tumor activity | ▪ Safety and response by PET/CT |
| Status | ▪ FPI in Gazyva arms Q1 2015<br>▪ Recruitment completed Q3 2016<br>▪ Updated data presented at ASCO, ICML and EHA 2015<br>▪ Updated data presented at ASH 2016 | ▪ FPI Q4 2013<br>▪ Recruitment completed Q3 2016<br>▪ Initial data presented at ASH 2015<br>▪ Updated data presented at ASH 2016, ICML and EHA 2017 |
| CT Identifier | NCT01691898 | NCT01992653 |

In collaboration with Seattle Genetics

ADC=antibody–drug conjugate; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; ASCO=American Society of Clinical Oncology; ICML=international Conference on Malignant Lymphoma; EHA=European Hematology Association; ASH=American Society of Hematology; BR=bendamustine and Rituxan; CHP=cyclophosphamide, hydroxydoxorubicin, prednisone

# Polatuzumab vedotin (RG7596)

*ADC targeting CD79b to treat B cell malignancies*

| Indication | Relapsed or refractory FL and DLBCL | 1L DLBCL |
|---|---|---|
| Phase/study | **Phase Ib/II** | **Phase III POLARIX** |
| # of patients | N=224 | N=875 |
| Design | ▪ **PIb:** Dose escalation<br>▪ **PhII:** Polatuzumab vedotin plus BR vs. BR<br>▪ **PhII expansion:** Polatuzumab vedotin plus Gazyva, non-randomized | ▪ **ARM A:** Polatuzumab vedotin plus R-CHP<br>▪ **ARM B:** R-CHOP |
| Primary endpoint | ▪ Safety and response by PET/CT | ▪ Progression-free survival |
| Status | ▪ FPI Q4 2014<br>▪ Recruitment completed Q3 2016<br>▪ Updated data presented at ASH 2016, ICML and EHA 2017<br>▪ PRIME designation (Q2 2017) and Breakthrough Therapy Designation granted (Q3 2017) for r/r DLBCL | ▪ FPI expected Q4 2017 |
| CT Identifier | NCT02257567 | NCT03274492 |

In collaboration with Seattle Genetics

ADC=antibody–drug conjugate; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; ASH=American Society of Hematology; ICML=international Conference on Malignant Lymphoma; EHA=European Hematology Association; BR=bendamustine and Rituxan; R-CHP=Rituxan, cyclophosphamide, hydroxydoxorubicin, prednisone; R-CHOP=Rituxan, cyclophosphamide, doxorubicin, vincristine, and prednisone

# Polatuzumab vedotin (RG7596)

*ADC targeting CD79b to treat B cell malignancies*

| Indication | Relapsed or refractory FL or DLBCL | | |
|---|---|---|---|
| **Phase/study** | **Phase I/II** | **Phase I/II** | **Phase I/II** |
| **# of patients** | N=116 | N=116 | N=86 |
| **Design** | ▪ **Dose escalation cohort:** Polatuzumab vedotin plus Gazyva plus Venclexta[1]<br>▪ **Expansion cohort DLBCL:** Polatuzumab vedotin plus Rituxan plus Venclexta[1]<br>▪ **Expansion cohort FL:** Polatuzumab vedotin plus Gazyva plus Venclexta[1] | ▪ **Dose escalation cohort:** Polatuzumab vedotin plus Gazyva plus lenalidomide<br>▪ **Expansion cohort DLBCL:** Polatuzumab vedotin plus Rituxan plus lenalidomide<br>▪ **Expansion cohort FL:** Polatuzumab vedotin plus Gazyva plus lenalidomide | ▪ **Dose escalation cohort:** Polatuzumab vedotin plus Gazyva plus Tecentriq<br>▪ **Expansion cohort DLBCL:** Polatuzumab vedotin plus Rituxan plus Tecentriq<br>▪ **Expansion cohort FL:** Polatuzumab vedotin plus Gazyva plus Tecentriq |
| **Primary endpoint** | ▪ Percentage of participants with CR | ▪ Percentage of participants with CR | ▪ Percentage of participants with CR |
| **Status** | ▪ FPI Q1 2016 | ▪ FPI Q1 2016 | ▪ FPI Q4 2016 |
| **CT Identifier** | NCT02611323 | NCT02600897 | NCT02729896 |

In collaboration with Seattle Genetics; [1]Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
ADC=antibody–drug conjugate; FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma; CR=complete response

# Taselisib (RG7604, GDC-0032)

*Mutant-selective PI3 kinase inhibitor*

| Indication | HER2-negative ER-positive metastatic breast caner patients who progressed after aromatase inhibitor therapy | Neoadjuvant HER2-negative ER-positive breast cancer | Solid tumors and HER2-negative HR-positive breast cancer |
|---|---|---|---|
| **Phase/study** | **Phase III SANDPIPER** | **Phase II LORELEI** | **Phase I/II** |
| **# of patients** | N=600 | N=330 | N=724 |
| **Design** | ▪ **ARM A**: Taselisib plus fulvestrant<br>▪ **ARM B:** Placebo plus fulvestrant | ▪ **ARM A**: Taselisib plus letrozole<br>▪ **ARM B:** Placebo plus letozole | **Phase I:**<br>▪ Taselisib<br>▪ Taselisib plus letrozole or fulvestrant<br>**Phase II:**<br>▪ Taselisib (multiple doses) plus letrozole or fulvestrant |
| **Primary endpoint** | ▪ Progression-free survival | ▪ Response rate and pCR | ▪ Safety, PK and efficacy |
| **Status** | ▪ FPI Q2 2015<br>▪ Recruitment completed Q3 2017 | ▪ Recruitment completed Q3 2016<br>▪ Study met co-primary endpoint of ORR<br>▪ Data presented at ESMO 2017 | ▪ Recruitment completed Q2 2014<br>▪ Updated data presented at SABCS 2014 |
| **CT Identifier** | NCT02340221 | NCT02273973 | NCT01296555 |

SABCS=San Antonio Breast Cancer Symposium; pCR=pathologic complete response; ER=estrogen receptor; HR=hormone receptor

# Crenezumab (RG7412)

## *Humanized mAb targeting all forms of Aβ*

| Indication | Prodromal to mild Alzheimer's disease | |
|---|---|---|
| Phase/study | **Phase III CREAD 1** | **Phase III CREAD 2** |
| # of patients | N=750 | N=750 |
| Design | ▪ **ARM A:** Crenezumab IV 60mg/kg q4w<br>▪ **ARM B:** Placebo IV q4w | ▪ **ARM A:** Crenezumab IV 60mg/kg q4w<br>▪ **ARM B:** Placebo IV q4w |
| Primary endpoint | ▪ CDR-SB at 105 weeks | ▪ CDR-SB at 105 weeks |
| Status | ▪ FPI Q1 2016 | ▪ FPI Q1 2017 |
| CT Identifier | NCT02670083 | NCT03114657 |

In collaboration with AC Immune

Aβ=amyloid-beta; CDR-SB=Clinical Dementia Rating, Sum of Boxes

# Crenezumab (RG7412)

## *Humanized mAb targeting all forms of Aβ*

| Indication | Alzheimer's disease | |
|---|---|---|
| Phase/study | **Phase II**<br>**ABBY**<br>Cognition study | **Phase II**<br>**BLAZE**<br>Biomarker study |
| # of patients | N=446 | N=91 |
| Design | ▪ **ARM A**: Crenezumab SC<br>▪ **ARM B**: Crenezumab IV<br>▪ **ARM C:** Placebo | ▪ **ARM A**: Crenezumab SC<br>▪ **ARM B**: Crenezumab IV<br>▪ **ARM C:** Placebo |
| Primary endpoint | ▪ Change in cognition (ADAS-cog) and Clinical Dementia Rating, Sum of Boxes (CDR-SB) score from baseline to week 73 | ▪ Change in brain amyloid load from baseline to week 69 |
| Status | ▪ Recruitment completed Q3 2012<br>▪ Positive trend in cognition was observed in higher dose for people with milder disease consistently across both studies (ABBY/BLAZE) and across endpoint<br>▪ Data presented at AAIC 2014 | ▪ Recruitment completed Q3 2012<br>▪ Cognition data presented at AAIC 2014<br>▪ Exploratory amyloid PET analysis suggests reduced amyloid accumulation in ARM B<br>▪ Biomarker data presented at CTAD 2014 |
| CT Identifier | NCT01343966 | NCT01397578 |

In collaboration with AC Immune

Aβ=amyloid-beta; ADAS-cog=Alzheimer's Disease Assessment Scale cognitive subscale; CDR-SB=Clinical Dementia Rating, Sum of Boxes; AAIC=Alzheimer's Association International Conference; CTAD=Clinical Trials on Alzheimer's Disease

# Crenezumab (RG7412)

## *Humanized mAb targeting all forms of Aβ*

| Indication | Mild to moderate Alzheimer's disease | Alzheimer's Prevention Initiative (API) Colombia |
|---|---|---|
| **Phase/study** | **Phase I** | **Phase II**<br>Cognition study |
| **# of patients** | N=72 | N=300 |
| **Design** | ▪ **ARM A/B**: Crenezumab dose level I & placebo<br>▪ **ARM C/D**: Crenezumab dose level II & placebo<br>▪ **ARM E/F**: Crenezumab dose level III & placebo | ▪ **ARM A**: 100 carriers receive crenezumab SC<br>▪ **ARM B**: 100 carriers receive placebo<br>▪ **ARM C:** 100 non-carriers receive placebo |
| **Primary endpoint** | ▪ Safety (incidence and nature of MRI safety findings) and PK | ▪ Change on Alzheimer's Prevention Initiative (API) Composite Cognitive Test total score |
| **Status** | ▪ FPI Q1 2015<br>▪ Recruitment completed Q3 2016<br>▪ Interim data presented at CTAD 2016<br>▪ Data presented at AD/PD and AAN 2017 | ▪ FPI Q4 2013<br>▪ Recruitment completed Q1 2017 |
| **CT Identifier** | NCT02353598 | NCT01998841 |

In collaboration with AC Immune

Aβ=amyloid-beta; CTAD= Clinical Trials on Alzheimer's Disease; AD/PD=Alzheimer's & Parkinson's Diseases Congress

# Gantenerumab (RG1450)

## *Fully human mAb binding aggregated forms of Aβ*

| Indication | Prodromal Alzheimer's disease | Mild Alzheimer's disease |
|---|---|---|
| **Phase/study** | **Phase II/III**<br>**SCarlet RoAD** | **Phase III**<br>**Marguerite RoAD** |
| **# of patients** | N=799 | N=1,000 |
| **Design** | 104-week subcutaneous treatment period<br>▪ **ARM A:** Gantenerumab (225 mg)<br>▪ **ARM B:** Gantenerumab (105 mg)<br>▪ **ARM C:** Placebo | 104-week subcutaneous treatment period<br>▪ **ARM A:** Gantenerumab<br>▪ **ARM B:** Placebo |
| **Primary endpoint** | ▪ Change in CDR-SB at 2 years<br>▪ Sub-study: change in brain amyloid by PET at 2 years | ▪ Change in ADAS-Cog and CDR-SB at 2 years (co-primary) |
| **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>▪ Data presented at AAIC 2015<br>▪ FPI in open label extension study Q4 2015 | ▪ FPI Q1 2014<br>▪ Recruitment stopped Q4 2015<br>▪ FPI Q1 2016 for open label extension |
| **CT Identifier** | NCT01224106 | NCT02051608 |

In collaboration with MorphoSys AG

Aβ=amyloid-beta; CDR-SB=Clinical Dementia Rating, Sum of Boxes; ADAS-cog=Alzheimer's Disease Assessment Scale cognitive subscale; AAIC=Alzheimer's Association International Conference

# Olesoxime (RG6083)

*Mitochondrial-targeted neuroprotective small molecule*

| Indication | Spinal muscular atrophy<br>Type 2 and 3 | |
|---|---|---|
| **Phase/study** | **Phase II**<br>Registrational study | **Phase II**<br>**OLEOS** |
| **# of patients** | N=165 | N=165 |
| **Design** | ▪ **ARM A:** Olesoxime<br>▪ **ARM B:** Placebo | ▪ Open-label, single arm study to evaluate long-term safety, tolerability, and effectiveness of 10 mg/kg olesoxime in patients with SMA |
| **Primary endpoint** | ▪ Motor function measure | ▪ Safety |
| **Status** | ▪ Study completed Q4 2013<br>▪ Presented at AAN 2014<br>▪ Published in *Lancet Neurology* 2017 Jul; 16(7):513-522 | ▪ FPI Q4 2015<br>▪ Recruitment completed Q1 2017 |
| **Collaborator** | Trophos acquisition | |
| **CT Identifier** | NCT01302600 | NCT02628743 |

AAN=Annual Meeting of the American Academy of Neurology

# RG6206

*Myostatin-inhibiting adnectin fusion protein*

| Indication | Duchenne Muscular Dystrophy |
|---|---|
| Phase/study | **Phase II/III** |
| # of patients | N=159 |
| Design | Randomized, double blind, placebo-controlled study in ambulatory boys age 6-11 years with duchenne muscular dystrophy<br>▪ **ARM A:** RG6206 low dose<br>▪ **ARM B:** RG6206 high dose<br>▪ **ARM C:** Placebo |
| Primary endpoint | ▪ Change from baseline in the 4 stair climb velocity after 48 weeks |
| Status | ▪ FPI Q3 2017 |
| CT Identifier | NCT03039686 |

In collaboration with Bristol-Myers Squibb

# Etrolizumab (RG7413)

*Humanized mAb against beta 7 integrin*

| Indication | Ulcerative colitis patients who are TNF-naïve | | |
|---|---|---|---|
| **Phase/study** | **Phase III**<br>**HIBISCUS I**<br>Induction study | **Phase III**<br>**HIBISCUS II**<br>Induction study | **Phase III**<br>**GARDENIA**<br>Sustained remission study |
| **# of patients** | N=350 | N=350 | N=720 |
| **Design** | ▪ **ARM A**: Etrolizumab 105mg SC q4w plus adalimumab placebo SC<br>▪ **ARM B**: Etrolizumab placebo SC plus adalimumab SC<br>▪ **ARM C**: Etrolizumab placebo SC plus adalimumab placebo SC | ▪ **ARM A**: Etrolizumab 105mg SC q4w plus adalimumab placebo SC<br>▪ **ARM B**: Etrolizumab placebo SC plus adalimumab SC<br>▪ **ARM C**: Etrolizumab placebo SC plus adalimumab placebo SC | Time on treatment 54 weeks<br>▪ **ARM A**: Etrolizumab 105mg SC q4w plus placebo IV<br>▪ **ARM B**: Placebo SC q4w plus inflixumab IV |
| **Primary endpoint** | ▪ Induction of remission compared with placebo as determined by the Mayo Clinic Score (MCS) at week 10 | ▪ Induction of remission compared with placebo as determined by the Mayo Clinic Score (MCS) at week 10 | ▪ Proportion of patients in sustained clinical remission as determined by Mayo Clinic Score (MCS) at weeks 10, 30 and 54 |
| **Status** | ▪ FPI Q4 2014 | ▪ FPI Q4 2014 | ▪ FPI Q4 2014 |
| **CT Identifier** | NCT02163759 | NCT02171429 | NCT02136069 |

# Etrolizumab (RG7413)

*Humanized mAb against beta 7 integrin*

| Indication | Ulcerative colitis patients who are TNF-naïve and refractory or intolerant to immunosuppressant and/or corticosteroid treatment | Ulcerative colitis patients who are refractory or intolerant of TNF inhibitors | Moderate to severe ulcerative colitis patients |
|---|---|---|---|
| **Phase/study** | **Phase III**<br>**LAUREL**<br>Maintenance study | **Phase III**<br>**HICKORY**<br>Induction and maintenance study | **Phase III**<br>**COTTONWOOD**<br>Open label extension study |
| **# of patients** | N=350 | N=800 | N=2,625 |
| **Design** | Induction phase:<br>▪ **ARM A:** Open label etrolizumab 105mg SC q4w<br>Maintenance study:<br>▪ **ARM B:** Etrolizumab 105mg SC q4w<br>▪ **ARM C:** Placebo | Cohort 1 (open-label):<br>▪ **ARM A:** Etrolizumab induction + placebo maintenance<br>▪ **ARM B:** Etrolizumab induction + maintenance<br>Cohort 2 (blinded):<br>▪ **ARM A:** Etrolizumab induction + maintenance<br>▪ **ARM B:** Placebo induction + maintenance | ▪ Patients who were previously enrolled in etrolizumab phase II and phase III studies and meet recruitment criteria will receive etrolizumab 105 SC q4w |
| **Primary endpoint** | ▪ Maintenance of remission (at week 62) among randomized patients in remission at Week 10 as determined by the Mayo Clinic Score (MCS) | ▪ Clinical Remission (Mayo Clinic Score, MCS) at Week 14<br>▪ Remission maintenance (by MCS, at Week 66) among patients with remission at Week 14 | ▪ Long-term efficacy as determined by partial Mayo Clinic Score (pMCS), incidence of adverse events |
| **Status** | ▪ FPI Q3 2014 | ▪ FPI Q2 2014<br>▪ First data presented at ECCO 2017<br>▪ Open label induction and endoscopy data to be presented at UEGW 2017 | ▪ FPI Q3 2014 |
| **CT Identifier** | NCT02165215 | NCT02100696 | NCT02118584 |

ECCO=European Crohn's and Colitis Organisation; MCS=Mayo Clinic Score

# Etrolizumab (RG7413)

*Humanized mAb against beta 7 integrin*

| Indication | Moderately to severely active Crohn's disease | Moderately to severely active Crohn's disease |
|---|---|---|
| Phase/study | **Phase III**<br>**BERGAMOT** | **Phase III**<br>**JUNIPER**<br>Open label extension study for BERGAMOT |
| # of patients | N=1,250 | N=900 |
| Design | ▪ **ARM A**: Etrolizumab SC 210 mg (induction only)<br>▪ **ARM B**: Etrolizumab SC 105 mg and maintenance<br>▪ **ARM C**: Placebo | ▪ Etrolizumab SC 105mg q4w |
| Primary endpoint | ▪ Induction and maintenance of clinical remission | ▪ Safety |
| Status | ▪ FPI Q1 2015<br>▪ Cohort 1 data to be presented at UEGW 2017 | ▪ FPI Q2 2015 |
| CT Identifier | NCT02394028 | NCT02403323 |

UEGW=United European Gastroenterology Week

# Lebrikizumab (RG3637)

*Humanized mAb binding specifically to IL-13*

| Indication | Idiopathic pulmonary fibrosis |
|---|---|
| Phase/study | **Phase II**<br>**RIFF** |
| # of patients | N=507 |
| Design | ▪ **ARM A:** Lebrikizumab SC q4w<br>▪ **ARM B:** Placebo<br>▪ **ARM C:** Lebrikizumab SC q4w + Esbriet<br>▪ **ARM D:** Esbriet |
| Primary endpoint | ▪ Change in FVC at week 52 |
| Status | ▪ FPI Q4 2013 (arms A&B)<br>▪ Data in-house for Arms A&B<br>▪ FPI in arms C and D in Q3 2015<br>▪ Recruitment completed in arms C and D in Q3 2016 |
| CT Identifier | NCT01872689 |

COPD=chronic obstructive pulmonary disease; SOC=standard of care; TCS=Topical corticosteroids; EADV=European Academy of Dermatology and Venereology Congress

# Lampalizumab (RG7417)

*Selective anti-complement factor D mAb fragment*

| Indication | Geographic atrophy secondary to age-related macular degeneration | | | |
|---|---|---|---|---|
| **Phase/study** | **Phase III CHROMA** | **Phase III SPECTRI** | **Phase II** | **Phase III OMASPECT** |
| **# of patients** | N=936 | N=936 | N=90 | N=1,800 |
| **Design** | ▪ **ARM A:** Lampalizumab 10mg q4w<br>▪ **ARM B:** Lampalizumab 10mg q6w<br>▪ **ARM C:** Placebo | ▪ **ARM A:** Lampalizumab 10mg q4w<br>▪ **ARM B:** Lampalizumab 10mg q6w<br>▪ **ARM C:** Placebo | ▪ **ARM A:** Lampalizumab 10mg q2w<br>▪ **ARM B:** Lampalizumab 10mg q4w<br>▪ **ARM C:** Placebo | ▪ Open-label extension study to assess the long-term safety profile of lampalizumab. Enrolls participants from phase III studies CHROMA and SPECTRI |
| **Primary endpoint** | ▪ Primary: change in GA area<br>▪ Secondary: change in BCVA and in additional measures of visual function | ▪ Primary: change in GA area<br>▪ Secondary: change in BCVA and in additional measures of visual function | ▪ Change in GA area | ▪ Safety |
| **Status** | ▪ FPI Q3 2014<br>▪ Fast track designation received Q4 2014<br>▪ Recruitment completed | ▪ FPI Q3 2014<br>▪ Fast track designation received Q4 2014<br>▪ Recruitment completed<br>▪ Study did not meet primary endpoint Q3 2017 | ▪ FPI Q4 2014<br>▪ Recruitment completed | ▪ FPI Q3 2016 |
| **CT Identifier** | NCT02247479 | NCT02247531 | NCT02288559 | NCT02745119 |

GA=Geographic atrophy; BCVA=best corrected visual acuity

Pipeline summary

Marketed products additional indications

Global Development late-stage trials

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**pRED (Roche Pharma Research & Early Development)**

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gRED (Genentech Research & Early Development)

# Oncology development programs
## *Small molecules*

| Molecule | Idasanutlin (MDM2 antagonist, RG7388) | |
|---|---|---|
| **Indication** | **Relapsed/refractory AML MIRROS** | **Refractory AML not eligible for cytotoxic therapy** |
| **Phase/study** | **Phase III** | **Phase I** |
| **# of patients** | N=440 | N=140 |
| **Design** | ▪ **ARM A:** Idasanutlin plus cytarabine<br>▪ **ARM B:** Placebo plus cytarabine | Phase I (dose escalation)<br>▪ **ARM A:** Cotellic[1] plus Venclexta[2]<br>▪ **ARM B:** Idasanutlin plus Venclexta[2]<br>Phase II (expansion)<br>▪ **ARM A:** Cotellic[1] plus Venclexta[2]<br>▪ **ARM B:** Idasanutlin plus Venclexta[2] |
| **Primary endpoint** | ▪ Overall survival | ▪ Safety and efficacy |
| **Status** | ▪ FPI Q4 2015 | ▪ FPI Q1 2016 |
| **CT Identifier** | NCT02545283 | NCT02670044 |

[1] Cotellic in collaboration with Exelixis; [2] Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
AML=acute myeloid leukemia; ASCO=American Society of Clinical Oncology; ECC=European Cancer Congress; ESMO=European Society for Medical Oncology

# Oncology development programs
## *Small molecules*

| Molecule | Idasanutlin (MDM2 antagonist, RG7388) | | |
|---|---|---|---|
| **Indication** | **Relapsed/refractory FL and DLBCL** | | **Polycythemia vera** |
| **Phase/study** | **Phase Ib/II** | **Phase Ib/II** | **Phase II** |
| **# of patients** | N=120 | N=140 | N=20 |
| **Design** | Dose escalation of idasanutlin plus Gazyva/Rituxan<br>▪ **ARM A:** Dose expansion of idasanutlin plus Gazyva in FL<br>▪ **ARM B:** Dose expansion of idasanutlin plus Rituxan in DLBCL | Dose escalation of idasanutlin plus Venclexta plus Gazyva/Rituxan<br>▪ **ARM A:** Dose expansion of idasanutlin plus Venclexta plus Gazyva in FL<br>▪ **ARM B:** Dose expansion of idasanutlin plus Venclexta plus Rituxan in DLBCL | Single-arm study of idasanutlin monotherapy in participants with hydroxyurea (HU)-resistant/intolerant Polycythemia vera (PV) |
| **Primary endpoint** | ▪ Safety and efficacy | ▪ Safety and efficacy | ▪ Composite response at week 32 for participants with splenomegaly at baseline<br>▪ Hematocrit (Hct) control without phlebotomy at week 32 for participants without splenomegaly at baseline |
| **Status** | ▪ FPI Q4 2015 | ▪ FPI Q3 2017 | ▪ FPI expected Q4 2017 |
| **CT Identifier** | NCT02624986 | NCT03135262 | NCT03287245 |

FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma

# Oncology development programs
## *Small molecules*

| Molecule | BET inhibitor (RG6146, TEN-010) | | | |
|---|---|---|---|---|
| **Indication** | **Solid tumors** | **Relapsed/refractory AML** | **Relapsed/refractory MM** | **Relapsed/refractory DLBCL** |
| **Phase/study** | **Phase I** | **Phase I** | **Phase Ib** | **Phase Ib** |
| **# of patients** | N=100 | N=36 | N=86 | N=94 |
| **Design** | ▪ Dose escalation and expansion study | ▪ Dose escalation and cohort expansion study | Dose escalation and cohort expansion study:<br>▪ **Part 1:** RG6146 monotherapy<br>▪ **Part 2:** RG6146 in combination with daratumumab | ▪ Dose escalation and cohort expansion study of the doublet or triplet combination with RG6146 plus Venclexta[1] ±Rituxan |
| **Primary endpoint** | ▪ Safety and efficacy | ▪ Safety and efficacy | ▪ Safety and efficacy | ▪ Safety and efficacy |
| **Status** | ▪ FPI Q4 2013 | ▪ FPI Q4 2014 | ▪ FPI Q2 2017 | ▪ FPI Q3 2017 |
| **CT Identifier** | NCT01987362 | NCT02308761 | NCT03068351 | NCT03255096 |
| **Collaborator** | Tensha acquisition | | | |

[1] Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
AML=acute myeloid leukemia; MM=multiple myeloma; DLBCL=diffuse large B cell lymphoma

# Oncology development programs
## *Monoclonal antibodies*

| Molecule | Codrituzumab (Glypican-3 MAb GC33, RG7686) | | |
|---|---|---|---|
| **Indication** | **Metastatic liver cancer (hepatocellular carcinoma)** | **2L metastatic liver cancer (hepatocellular carcinoma)** | **Metastatic liver cancer (hepatocellular carcinoma)** |
| **Phase/study** | Phase Ib | Phase II | Phase Ib |
| **# of patients** | N=40-50 | N=185 | N=20 |
| **Design** | ▪ Study US Monotherapy<br>▪ Study Japan Monotherapy<br>▪ Dose escalation study in combo with SOC | ▪ Adaptive design study Double blind randomized 2:1, RG7686:placebo<br>▪ Patients are stratified according to the level of GPC-3 expression in tumor | ▪ Dose escalation and expansion study in combination with Tecentriq |
| **Primary endpoint** | ▪ Safety and tolerability | ▪ Progression-free survival | ▪ Safety and tolerability |
| **Status** | ▪ Recruitment completed Q4 2013<br>▪ Data presented at ASCO 2014<br>▪ Further steps under evaluation | ▪ Recruitment completed Q1 2013<br>▪ Data presented at ASCO 2014<br>▪ Further steps under evaluation | ▪ Recruitment completed Q3 2017 (Japan and Taiwan) |
| | Monotherapy development on hold | | |
| **CT Identifier** | NCT00746317, NCT00976170 | NCT01507168 | JapicCTI-163325 |
| **Collaborator** | Chugai | | |

ASCO=American Society of Clinical Oncology

# Oncology development programs
## *Monoclonal antibodies*

| Molecule | **Vanucizumab**<br>(ANG2-VEGF biMAb, RG7221) |
|---|---|
| **Indication** | **Solid tumors** |
| **Phase/study** | **Phase I** |
| **# of patients** | N≈132 |
| **Design** | ▪ Multiple ascending dose study with extension cohorts in solid tumors to assess the PD effects and platinum-resistant ovarian cancer<br>▪ Dose escalation of vanucizumab plus Tecentriq |
| **Primary endpoint** | ▪ Safety and PK |
| **Status** | ▪ FPI Q4 2012<br>▪ Data presented at ASCO 2014 (Dose escalation), ASCO 2015 (ovarian cancer cohort), ECC 2015 (biomarker/imaging)<br>▪ FPI in combination arm Q2 2016 |
| **CT Identifier** | NCT01688206 |

ASCO=American Society of Clinical Oncology; ECC=European Cancer Congress;

# Oncology development programs

*Monoclonal antibodies*

| Molecule | **Emactuzumab** (CSF-1R MAb, RG7155) | |
|---|---|---|
| **Indication** | **Solid tumors** | |
| **Phase/study** | **Phase I** | **Phase I** |
| **# of patients** | N=310 | N=146 |
| **Design** | Emactuzumab in combination with Tecentriq<br>▪ **Part 1:** Dose escalation<br>▪ **Part 2:** Expansion | Emactuzumab in combination with selicrelumab (CD40 MAb)<br>▪ **Part 1:** Dose escalation<br>▪ **Part 2:** Expansion |
| **Primary endpoint** | ▪ Safety | ▪ Safety, PK and PD |
| **Status** | ▪ FPI Q1 2015 | ▪ FPI Q2 2016 |
| **CT Identifier** | NCT02323191 | NCT02760797 |

# Oncology development programs
## *Monoclonal antibodies*

| Molecule | FAP-IL2v FP (RG7461) | |
|---|---|---|
| **Indication** | **Solid tumors** | **1L Renal call carcinoma** |
| **Phase/study** | **Phase I** | **Phase Ib** |
| **# of patients** | N=60 | N=110 |
| **Design** | ▪ **Part A:** Dose escalation study (monotherapy)<br>▪ **Part B:** Dose escalation and extension in combination with trastuzumab (HER2+ breast cancer)<br>▪ **Part C:** Dose escalation and extension in combination with cetuximab (head & neck cancer) | **Part I:** Dose escalation<br>▪ Arm A: FAP-IL2v plus Tecentriq;<br>▪ Arm B: FAP-IL2v plus Tecentriq plus Avastin<br>**Part II:** Dose expansion<br>▪ Arm A: FAP-IL2v plus Tecentriq;<br>▪ Arm B: FAP-IL2v plus Tecentriq plus Avastin |
| **Primary endpoint** | ▪ Safety, PK/PD and efficacy (Part B/C only) | ▪ Safety, PD and efficacy |
| **Status** | ▪ FPI Q4 2015<br>▪ FPI Part B/C expected Q4 2017 | ▪ FPI Q1 2017 |
| **CT Identifier** | NCT02627274 | NCT03063762 |

# Oncology development programs
## *Monoclonal antibodies*

| Molecule | Cergutuzumab amunaleukin (CEA-IL2v, RG7813) | |
|---|---|---|
| **Indication** | **Solid tumors** | |
| **Phase/study** | **Phase I** | **Phase Ib** |
| **# of patients** | N=113 | N=75 |
| **Design** | ▪ Single and multiple dose escalation study with extension cohorts | ▪ **Part 1:** Dose escalation of RG7813 in combination with Tecentriq<br>▪ **Part 2:** Dose expansion RG7813 in combination with Tecentriq |
| **Primary endpoint** | ▪ Safety, PK and PD | ▪ Safety, efficacy, PK and PD |
| **Status** | ▪ Recruitment completed Q1 2016<br>▪ Imaging data presented at ASCO 2015<br>▪ Biomarker/imaging data presented at ECC 2015<br>▪ Final imaging data presented at ESMO 2016<br>▪ PD data presented at ESMO 2017 | ▪ FPI in Q2 2015 |
| **CT Identifier** | NCT02004106 | NCT02350673 |

ASCO=American Society of Clinical Oncology; ECC=European Cancer Congress; ESMO=European Society for Medical Oncology

# Oncology development programs
## *Monoclonal antibodies*

| Molecule | CEA TCB (RG7802) | |
|---|---|---|
| **Indication** | **CEA-positive solid tumors** | |
| **Phase/study** | **Phase Ia** | **Phase Ib** |
| **# of patients** | N≈286 (DE & DF) | N=410 |
| **Design** | ▪ **Part I:** Dose escalation of RG7802<br>▪ **Part II:** Dosing strategy<br>▪ **Part III**: Assessment of schedule<br>▪ **Part IV:** Dose and schedule expansion | ▪ **Part I:** RG7802 dose escalation plus Tecentriq<br>▪ **Part II**: Expansion at defined dose and schedule |
| **Primary endpoint** | ▪ Safety, Efficacy, PK and PD | ▪ Safety, Efficacy, PK and PD |
| **Status** | ▪ FPI Q4 2014<br>▪ Data presented at ASCO 2017 | ▪ FPI Q1 2016<br>▪ Data presented at ASCO 2017 |
| **CT Identifier** | NCT02324257 | NCT02650713 |

ASCO=American Society of Clinical Oncology

# Oncology development programs
## *Monoclonal antibodies*

| Molecule | CD20 TCB (RG6026) | FAP-DR5 biMAB (RG7386) |
|---|---|---|
| Indication | Relapsed or refractory B cell non-Hodgkin's lymphoma | Solid tumors |
| Phase/study | Phase I | Phase I |
| # of patients | N≈30 (+40+20) | N=120 |
| Design | First-in-man single-agent dose escalation study<br>▪ Initial dose escalation (N≈30)<br>▪ Expansion cohort in r/r DLBCL (N=40)<br>▪ Expansion cohort in r/r FL (N=20)<br><br>All patients will receive pretreatment with a single dose of Gazyva (1000mg) | ▪ **Part I:** Dose escalation<br>▪ **Part II:** Tumor biopsy and imaging evaluation for assessment of treatment-induced pharmacodynamic (PD) effects<br>▪ **Part III:** Evaluation of antitumor activity of single-agent RG7386 in patients with histologically confirmed recurrent or metastatic, non-resectable FAP+ sarcomas with two or fewer prior regimens for advanced disease |
| Primary endpoint | ▪ Safety | ▪ Parts I and II – safety and tolerability<br>▪ Part III – antitumor activity |
| Status | ▪ FPI Q1 2017 | ▪ FPI Q3 2015 |
| CT Identifier | NCT03075696 | NCT02558140 |

# Oncology development programs

## *Monoclonal antibodies*

| Molecule | Selicrelumab (CD40 MAb, RG7876) | |
|---|---|---|
| **Indication** | **Solid tumors** | **Solid tumors** |
| **Phase/study** | **Phase Ib** | **Phase Ib** |
| **# of patients** | N=160 | N=170 |
| **Design** | ▪ **Part I:** Selicrelumab single dose escalation in combination with Tecentriq<br>▪ **Part II:** Selicrelumab multiple doses, in combination with Tecentriq<br>▪ **Part III:** Indication specific extension | ▪ Selicrelumab dose escalation in combination with vanucizumab (ANG2-VEGF biMAb) |
| **Primary endpoint** | ▪ Safety, PD and efficacy | ▪ Safety, PD and efficacy |
| **Status** | ▪ FPI Q4 2014 | ▪ FPI Q1 2016 |
| **CT Identifier** | NCT02304393 | NCT02665416 |

# Neuroscience development programs

Roche pRED

| Molecule | Basmisanil (GABRA5 NAM, RG1662) | |
|---|---|---|
| **Indication** | **Cognitive impairment associated with schizophrenia** | **Stroke recovery** |
| **Phase/study** | **Phase II** | **Phase II STROBE** |
| **# of patients** | N=180 | N=95 |
| **Design** | For 24 weeks patients will receive:<br>▪ **ARM A**: RG1662 80mg twice daily<br>▪ **ARM B**: RG1662 240mg twice daily<br>▪ **ARM C**: Placebo | Starting on day 5-7 post-stroke, patients will receive treatment for 90 days.<br>▪ **ARM A**: RG1662 240mg twice daily<br>▪ **ARM B**: Placebo |
| **Primary endpoint** | ▪ Efficacy (cognitive function), PK, safety and tolerability | ▪ PK, PD, safety and tolerability |
| **Status** | ▪ FPI Q4 2016 | ▪ FPI Q1 2017 |
| **CT Identifier** | NCT02953639 | NCT02928393 |

# Neuroscience development programs

Roche pRED

| Molecule | NME (RG7906) | PDE10A inhibitor (RG7203) |
|---|---|---|
| Indication | Psychiatric disorders | Schizophrenia |
| Phase/study | Phase I | Phase I |
| # of patients | N=164 | N=48 |
| Design | ▪ **Part 1:** Adaptive single ascending dose in healthy volunteers. Single-center, randomized, placebo-controlled, parallel study<br>▪ **Part 2:** Adaptive multiple ascending dose in healthy volunteers. Single-center, randomized, double-blind, placebo-controlled, parallel study | ▪ Multicenter, randomized, double-blind, placebo-controlled, crossover study to evaluate the effects of RG7203 in participants with mild to moderate negative symptoms of schizophrenia treated with antipsychotics. |
| Primary endpoint | ▪ Safety, tolerability, PK and PD | ▪ Safety, tolerability, PK and PD |
| Status | ▪ FPI Q1 2016<br>▪ Part 1 completed, Part 2 completed | ▪ FPI Q2 2016<br>▪ Study completed |
| CT Identifier | NCT02699372 | NCT02824055 |

# Neuroscience development programs

## *Spinal muscular atrophy*

| | | |
|---|---|---|
| **Molecule** | **SMN2 splicing modifier (2)** (RG7916) | |
| **Indication** | **Spinal muscular atrophy** | |
| **Phase/study** | **Phase I** | **Phase II SUNFISH** |
| **# of patients** | N=33 | N=186 |
| **Design** | ▪ Randomized, double-blind, adaptive single ascending dose (SAD), placebo-controlled study in healthy volunteers | Randomized, double-blind, placebo- controlled study in adult and pediatric patients with type 2 or type 3 spinal muscular atrophy<br>▪ **Part 1** (dose-finding): At least 12 weeks<br>▪ **Part 2** (confirmatory): 24 months |
| **Primary endpoint** | ▪ Safety and tolerability | ▪ Safety, tolerability, PK, PD and efficacy |
| **Status** | ▪ FPI Q1 2016<br>▪ Study completed Q3 2016<br>▪ Data presented at Child Neurology Society conference 2016 | ▪ FPI Q4 2016<br>▪ FPI Part 2 Oct 2017<br>▪ Data of Part 1 presented at CureSMA and WMS 2017 |
| | Orphan drug designation granted by FDA Q1 2017 | |
| **CT Identifier** | NCT02633709 | NCT02908685 |
| **Collaborator** | PTC Therapeutics, SMA Foundation | |

# Neuroscience development programs

## *Spinal muscular atrophy*

| | | |
|---|---|---|
| **Molecule** | **SMN2 splicing modifier (2)** (RG7916) | |
| **Indication** | **Spinal muscular atrophy** | |
| **Phase/study** | **Phase II FIREFISH** | **Phase II JEWELFISH** |
| **# of patients** | N=48 | N=24 |
| **Design** | Open-label study in infants with type 1 spinal muscular atrophy<br>▪ **Part 1** (dose-finding): At least 4 weeks<br>▪ **Part 2** (confirmatory): 24 months | ▪ Open-label single arm study in adolescents and adults (12–60 yrs) with spinal muscular atrophy type 2/3 previously treated with SMN2 targeting therapy. |
| **Primary endpoint** | ▪ Safety, tolerability, PK, PD and efficacy | ▪ Safety, tolerability and PK |
| **Status** | ▪ FPI Q4 2016 | ▪ FPI Q1 2017 |
| | Orphan drug designation granted by FDA Q1 2017 | |
| **CT Identifier** | NCT02913482 | NCT03032172 |
| **Collaborator** | PTC Therapeutics, SMA Foundation | |

# Neuroscience development programs

## *Autism*

| Molecule | V1a receptor antagonist (RG7314) | |
|---|---|---|
| Indication | Autism | |
| Phase/study | **Phase II VANILLA** | **Phase II aV1ation** |
| # of patients | N=223 | N=300 |
| Design | ▪ Multicenter, randomized, double-blind, placebo-controlled proof-of-concept study in individuals with autism spectrum disorder | ▪ Multicenter, randomized, double-blind, placebo-controlled proof-of-concept study in pediatrics (5–17 yrs) with autism spectrum disorder |
| Primary endpoint | ▪ Safety and efficacy | ▪ Safety and efficacy |
| Status | ▪ FPI Q3 2013<br>▪ Data presented at IMFAR 2017 | ▪ FPI Q4 2016 |
| CT Identifier | NCT01793441 | NCT02901431 |

IMFAR=International Meeting for Autism Research

# Neuroscience development programs

*Parkinson's disease*

| | |
|---|---|
| **Molecule** | **Anti-αSynuclein**<br>(RG7935, PRX002) |
| **Indication** | **Parkinson's disease** |
| **Phase/study** | **Phase II**<br>**PASADENA** |
| **# of patients** | N=300 |
| **Design** | ▪ Randomized, double-blind, placebo-controlled study to evaluate the efficacy of RO7046015 (RG7935, PRX002) in participants with early Parkinson's disease |
| **Primary endpoint** | ▪ Change from baseline in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) |
| **Status** | ▪ FPI Q2 2017 |
| **CT Identifier** | NCT03100149 |
| **Collaborator** | Prothena |

# Infectious diseases development programs

Roche pRED

| Molecule | Nacubactam (DBO beta lactamase inhibitor, RG6080, OP0595) | | | |
|---|---|---|---|---|
| **Indication** | **Infectious diseases** | | **Bronchoalveolar lavage** | **Complicated urinary tract infection** |
| **Phase/study** | **Phase I** | **Phase I** | **Phase I** | **Phase I** |
| **# of patients** | N=56 | N=32 | N=20 | N=20 |
| **Design** | ▪ Randomized, double-blind, placebo-controlled, multiple-ascending dose (MAD) study in healthy volunteers with nacubactam monotherapy and in combination with meropenem | ▪ **Part 1:** Adults with stable mild, moderate or severe renal impairment and a control group of participants with normal renal function<br>▪ **Part 2:** Adults with stable end-stage renal disease undergoing hemodialysis | ▪ Open label, one treatment, one group study to investigate intrapulmonary lung penetration of nacubactam in healthy volunteers | ▪ Open label, one treatment, one group study, to investigate the PK of nacubactam and meropenem in patients with cUTI |
| **Primary endpoint** | ▪ Safety, PK | ▪ Safety, PK | ▪ Intrapulmonary penetration | ▪ PK |
| **Status** | ▪ FPI Q4 2016<br>▪ Study completed | ▪ FPI Q4 2016 | ▪ FPI Q2 2017 | ▪ FPI Q3 2017 |
| **CT Identifier** | NCT02972255 | NCT02975388 | NCT03182504 | NCT03174795 |
| **Collaborator** | Meiji and Fedora | | | |

cUTI=complicated urinary tract infection

# Infectious diseases development programs

## *Chronic hepatitis B*

| Molecule | TLR7 agonist (3) (RG7854) | HBV LNA (RG6004) | Capsid inhibitor CAPi (2) (RG7907) |
|---|---|---|---|
| Indication | Chronic hepatitis B | Chronic hepatitis B | Chronic hepatitis B |
| Phase/study | Phase I | Phase I | Phase I |
| # of patients | N=110 | N=110 | N=128 |
| Design | ▪ Healthy volunteer and chronic hepatitis B patient study | ▪ Healthy volunteer and chronic hepatitis B patient study | ▪ Healthy volunteer and chronic hepatitis B patient study |
| Primary endpoint | ▪ Safety, PK and PD | ▪ Safety, PK and PD | ▪ Safety, PK and PD |
| Status | ▪ FPI Q4 2016 | ▪ FPI Q1 2017 | ▪ FPI Q4 2016 |
| CT Identifier | NCT02956850 | NCT03038113 | NCT02952924 |

TLR7=toll-like receptor 7; LNA=locked nucleic acid

# Ophthalmology development programs

| Molecule | VEGF-Ang2 biMAb (VA2) (RG7716) | | |
|---|---|---|---|
| **Indication** | **Wet age-related macular degeneration** | | **Center-involving diabetic macular edema (CI-DME)** |
| **Phase/study** | **Phase II AVENUE** | **Phase II STAIRWAY** | **Phase II BOULEVARD** |
| **# of patients** | N=271 | N=75 | N=210 |
| **Design** | ▪ **ARM A:** SoC (Lucentis), q4w<br>▪ **ARM B:** 1.5 mg VA2, q4w<br>▪ **ARM C:** 6mg VA2, q4w<br>▪ **ARM D:** 6mg VA2, q4w / q8w<br>▪ **ARM E:** SoC q4w x 3 doses, switch group to 6 mg VA2 q4w | ▪ **ARM A:** SoC (Lucentis), q4w<br>▪ **ARM B:** 6mg VA2, q>8w (short interval duration)<br>▪ **ARM C:** 6mg VA2, q>8w (long interval duration) | ▪ **ARM A:** SoC (Lucentis), 0.3 mg q4w<br>▪ **ARM B:** 1.5mg VA2, q4w<br>▪ **ARM C:** 6mg VA2, q4w |
| **Primary endpoint** | ▪ Change from baseline BCVA after 32 weeks | ▪ Change from baseline BCVA at Week 40 | ▪ Mean change from baseline BCVA at week 24 |
| **Status** | ▪ FPI Q3 2015<br>▪ Recruitment completed Q1 2017 | ▪ FPI Q1 2017<br>▪ Recruitment completed Q1 2017 | ▪ FPI Q2 2016<br>▪ Recruitment completed Q1 2017 |
| **CT Identifier** | NCT02484690 | NCT03038880 | NCT02699450 |

BCVA=best corrected visual acuity; SoC=standard of care

# Ophthalmology development programs

| | |
|---|---|
| **Molecule** | **NME**<br>(RG7945) |
| **Indication** | **Primary open angle glaucoma (POAG) or ocular hypertension (OHT)** |
| **Phase/study** | **Phase I** |
| **# of patients** | N=52 |
| **Design** | ▪ **Part A:** Placebo-controlled parallel multiple-ascending dose study<br>▪ **Part B:** Extension including up to two selected doses from Part A and latanoprost 0.005% as active comparator |
| **Primary endpoint** | ▪ Safety/tolerability and efficacy (change from baseline in mean intraocular pressure (IOP)) after 7 days of RG7945 administration |
| **Status** | ▪ FPI Oct 2017 |
| **CT Identifier** | NCT03293992 |

# Immunology development programs

Roche pRED

| Molecule | Cathepsin S inhibitor (CAT-S inh) (RG7625) | Cadherin 11 MAb (RG6125) |
|---|---|---|
| Indication | Primary Sjögren's syndrome | Rheumatoid Arthritis |
| Phase/study | **Phase II** | **Phase IIa/b** |
| # of patients | N=75 | N≈250 |
| Design | ▪ **ARM A**: RG7625<br>▪ **ARM B**: Placebo | Phase IIa (PoC)<br>▪ **ARM A:** RG6125<br>▪ **ARM B:** Placebo<br>Phase IIb (DRF)<br>▪ **ARM A, B, C:** RG6125<br>▪ **ARM D:** Placebo |
| Primary endpoint | ▪ Percentage of participants with a clinically relevant decrease in European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI) Score | ▪ Primary Endpoint at Week 12: proportion of patients achieving an American College of Rheumatology (ACR) 50 response at week 12 using RG6125 as adjunct therapy |
| Status | ▪ FPI Q3 2016<br>▪ Recruitment completed Q1 2017 | ▪ FPI Q4 2016 |
| CT Identifier | NCT02701985 | NCT03001219 |

PoC=proof of concept; DRF=dose range finding

# Immunology development programs

| Molecule | C5 inh MAb (RG6107, SKY59) | NME (RG7835) |
|---|---|---|
| Indication | Paroxysmal nocturnal hemoglobinuria | Autoimmune diseases |
| Phase/study | **Phase I/II COMPOSER** | **Phase I** |
| # of patients | N=49 | N=40 |
| Design | Healthy volunteers and treatment naïve/pretreated patients with PNH<br>▪ **Part 1:** Single ascending dose study in healthy subjects<br>▪ **Part 2:** Intra-patient single ascending dose study in PNH patients<br>▪ **Part 3**: Multiple-dose study in PNH patients | ▪ A randomized, adaptive, investigator/subject blind, single ascending dose, placebo-controlled study of subcutaneously administered RO7049665 (RG7835) in healthy volunteers |
| Primary endpoint | ▪ Safety, PK and PD | ▪ Safety, PK and PD |
| Status | ▪ Part 1: FPI Q4 2016<br>▪ Part 2/3: FPI Q2 2017<br>▪ Nonclinical data published in *Scientific Reports* 2017 Apr; 7(1):1080 | ▪ FPI Q3 2017 |
| CT Identifier | NCT03157635 | NCT03221179 |
| Collaborator | Chugai | |

PNH=paroxysmal nocturnal hemoglobinuria

# Other development programs

| | |
|---|---|
| **Molecule** | **Bitopertin** (RG1678) |
| **Indication** | **Beta thalassemia** |
| **Phase/study** | **Phase II** |
| **# of patients** | N=24 |
| **Design** | ▪ Single arm, multi center, proof-of-mechanism study of multiple oral doses of bitopertin in adults with nontransfusion-dependent β-thalassemia |
| **Primary endpoint** | ▪ Safety and efficacy (Change in total Hb level from baseline to the end of the 16-week treatment interval) |
| **Status** | ▪ FPI expected Q4 2017 |
| **CT Identifier** | NCT03271541 |

Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

**gRED (Genentech Research & Early Development)**

# Oncology development programs
## *Monoclonal antibodies*

gRED Genentech Research & Early Development

| Molecule | CD20 TDB (RG7828) | Anti-TIGIT MAb (RG6058, MTIG7192A) | NME (RG6160) |
|---|---|---|---|
| **Indication** | **Hematologic tumors** | **Solid tumors** | **Relapsed/refractory multiple myeloma** |
| **Phase/study** | **Phase I** | **Phase I** | **Phase I** |
| **# of patients** | N=390 | N=300 | N=80 |
| **Design** | ▪ Dose escalation study of RG7828 as single agent and in combination with Tecentriq<br>▪ Expansion cohorts for r/r FL, r/r DLBCL and r/r MCL | ▪ **Phase 1a:** Dose escalation and expansion MTIG7192A/RG6058<br>▪ **Phase 1b**: Dose escalation and expansion Tecentriq plus MTIG7192A/RG6058 | ▪ Dose escalation and expansion of single agent |
| **Primary endpoint** | ▪ Safety/tolerability, dose/schedule, PK, and response rates | ▪ Safety/tolerability, PK variability and preliminary efficacy | ▪ Safety/tolerability |
| **Status** | ▪ FPI Q3 2015 | ▪ FPI Q2 2016 | ▪ FPI Q3 2017 |
| **CT Identifier** | NCT02500407 | NCT02794571 | NCT03275103 |

TDB=T cell dependent bispecific; FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma; MCL=mantle cell lymphoma; r/r=relapsed/refractory

# Oncology development programs
## *Antibody–drug conjugates*

gRED Genentech Research & Early Development

| Molecule | Anti-MUC16 TDC (RG7882) | NME ADC (RG7986) |
|---|---|---|
| **Indication** | **Platinum-resistant ovarian cancer or unresectable pancreatic cancer** | **Relapsed or refractory B cell non-Hodgkin's lymphoma** |
| **Phase/study** | **Phase I** | **Phase I** |
| **# of patients** | N=95 | N=80 |
| **Design** | ▪ Dose escalation and expansion | ▪ Dose escalation and expansion |
| **Primary endpoint** | ▪ Safety and PK | ▪ Safety and PK |
| **Status** | ▪ FPI Q2 2014<br>▪ Data presented at AACR 2017 | ▪ FPI Q3 2015 |
| **CT Identifier** | NCT02146313 | NCT02453087 |
| **Collaborator** | Seattle Genetics | |

TDC=thiomab drug conjugate; MUC16=Mucin-16; ADC=antibody–drug conjugate; AACR=American Association for Cancer Research

# Oncology development programs
*Small molecules*

gRED Genentech Research & Early Development

| Molecule | ChK1 inhibitor (RG7741, GDC-0575) | SERD (2) (RG6047, GDC-0927/SRN-927) | PI3K inhibitor (RG6114, GDC-0077) |
|---|---|---|---|
| Indication | Solid tumors | Metastatic ER+ HER2-neg. breast cancer | PIK3CA mutant solid tumors and metastatic ER+ HER2- breast cancer |
| Phase/study | Phase I | Phase I | Phase I |
| # of patients | N=112 | N=90 | N=156 |
| Design | ▪ **Stage 1:** Dose escalation<br>▪ **Stage 2:** Cohort expansion | ▪ Dose escalation and expansion at recommended phase II dose (RP2D) | Monotherapy and in combination with SoC (letrozole; letrozole plus palbociclib; fulvestrant)<br>▪ **Stage 1:** Dose escalation<br>▪ **Stage 2:** Expansion |
| Primary endpoint | ▪ Safety and PK | ▪ Safety | ▪ Safety, tolerability and PK |
| Status | ▪ FPI Q2 2012 | ▪ FPI Q1 2015 | ▪ FPI Q4 2016<br>▪ Preclinical/molecule discovery data presented at AACR 2017 |
| CT Identifier | NCT01564251 | NCT02316509 | NCT03006172 |
| Collaborator | Array BioPharma | Seragon acquisition | |

AACR=American Association for Cancer Research; SoC=standard of care
SERD=selective estrogen receptor degrader

# Oncology development programs

## *Cancer vaccines*

Genentech Research & Early Development

| | |
|---|---|
| **Molecule** | **Personalized Cancer Vaccine (PCV)** (RG6180) |
| **Indication** | **Locally advanced or metastatic solid tumors** |
| **Phase/study** | **Phase Ia/Ib** |
| **# of patients** | N=572 |
| **Design** | Open-label, multicenter, global study<br>▪ **Phase 1a:** Dose escalation of RG6180 as single agent<br>▪ **Phase 1b:** Dose escalation, exploration and expansion trial of RG6180 in combination with Tecentriq |
| **Primary endpoint** | ▪ Safety/tolerability, PK and immune response |
| **Status** | ▪ FPI expected Q4 2017 |
| **CT Identifier** | NCT03289962 |
| **Collaborator** | BioNTech |

# Neuroscience development programs

gRED Genentech Research & Early Development

| Molecule | Nav1.7 (2) (RG6029, GDC-0310) | DLK inhibitor (RG6000, GDC-0134) |
|---|---|---|
| Indication | Pain | Amyotrophic lateral sclerosis |
| Phase/study | Phase I | Phase I |
| # of patients | N=95 | N=72 |
| Design | ▪ Randomized, placebo-controlled, double-blind study in healthy volunteers | ▪ Randomized, double-blind, placebo-controlled, multicenter, single and multiple ascending dose study |
| Primary endpoint | ▪ Safety, tolerability and PK of single and multiple doses | ▪ Safety, tolerability, and PK of single and multiple doses |
| Status | ▪ FPI Q3 2015 | ▪ FPI Q2 2016 |
| CT Identifier | NCT02742779 | NCT02655614 |
| Collaborator | Xenon Pharmaceuticals Inc. | |

# Neuroscience development programs

*Alzheimer's disease*

gRED Genentech Research & Early Development

| Molecule | Anti-Tau (RG6100) | |
|---|---|---|
| **Indication** | **Prodromal to mild Alzheimer's disease** | |
| **Phase/study** | **Phase I** | **Phase II** |
| **# of patients** | N=71 | N=360 |
| **Design** | ▪ Randomized, double-blind, placebo-controlled, single-center single ascending dose (healthy volunteers) and multiple dose study (healthy volunteers and Alzheimer's patients) | ▪ Randomized, double-blind, placebo-controlled, multi-center efficacy and safety study |
| **Primary endpoint** | ▪ Safety, tolerability and PK of single doses and multiple doses | ▪ Safety, CDR-SB score from baseline to week 72 |
| **Status** | ▪ FPI Q2 2016 | ▪ FPI expected Oct 2017 |
| **CT Identifier** | NCT02820896 | NCT03289143 |
| **Collaborator** | AC Immune | |

# Immunology development programs

gRED Genentech Research & Early Development

| Molecule | IL-22Fc (RG7880) | |
|---|---|---|
| **Indication** | **Inflammatory diseases** | **Diabetic foot ulcer** |
| **Phase/study** | **Phase Ib** | **Phase Ib** |
| **# of patients** | N=48 | N=72 |
| **Design** | ▪ Multiple ascending dose study with healthy volunteer and patient cohorts | ▪ Repeat dose study in patients with neuropathic diabetic foot ulcers that do not respond adequately to standard wound care |
| **Primary endpoint** | ▪ Safety and tolerability | ▪ Safety and tolerability |
| **Status** | ▪ FPI Q2 2016 | ▪ FPI Q4 2016 |
| **CT Identifier** | NCT02749630 | NCT02833389 |

# Immunology development programs

gRED Genentech Research & Early Development

| Molecule | ST2 MAb (RG6149, AMG 282, MSTT1041A) | NME (RG7990, BITS7201A) | NME (RG6069, GDC-3280) |
|---|---|---|---|
| **Indication** | **Asthma** | **Mild atopic asthma** | **Interstitial lung disease** |
| **Phase/study** | **Phase IIb ZENYATTA** | **Phase I** | **Phase I** |
| **# of patients** | N=500 | N=80 | N=80 |
| **Design** | Add-on therapy for the treatment of high-need, uncontrolled asthma in adults (50-week subcutaneous treatment period):<br>▪ **ARM A:** RG6149 (70 mg)<br>▪ **ARM B:** RG6149 (210mg)<br>▪ **ARM C:** RG6149 (490mg)<br>▪ **ARM D:** Placebo | ▪ Single and multiple ascending dose study with healthy volunteer and patient cohorts | ▪ Randomized, double-blind, placebo-controlled, ascending, single and multiple oral dose study |
| **Primary endpoint** | ▪ Percentage of participants with asthma exacerbations | ▪ Safety and tolerability | ▪ Safety, tolerability, and PK |
| **Status** | ▪ FPI Q3 2016<br>▪ Phase II trial enrolling | ▪ FPI Q2 2016 | ▪ Study completed Q1 2016 |
| **CT Identifier** | NCT02918019 | NCT02748642 | NCT02471859 |
| **Collaborator** | Amgen | Novimmune SA | |

# Immunology development programs

gRED Genentech Research & Early Development

| Molecule | BTK inhibitor (RG7845, GDC-0853) | | |
|---|---|---|---|
| **Indication** | **Rheumatoid arthritis** | **Moderate to severe active systemic lupus erythematosus** | **Chronic spontaneous urticaria** |
| **Phase/study** | **Phase II** | **Phase II** | **Phase IIa** |
| **# of patients** | N=580 | N=240 | N=45 |
| **Design** | Randomized, double-blind, parallel group study in rheumatoid arthritis patients<br>▪ **Cohort 1:** RG7845 vs adalimumab in patients with inadequate response to previous MTX<br>▪ **Cohort 2:** RG7845 vs placebo in patients with inadequate response to previous TNF | Randomized, double-blind, placebo-controlled study in active systemic lupus erythematosus patients<br>▪ **ARM A:** GDC-0853 (high dose)<br>▪ **ARM B:** GDC-0853 (low dose)<br>▪ **ARM C:** Placebo | Randomized, double-blind, placebo-controlled study in patients with CSU refractory to H1 anti-histamines<br>▪ **ARM A:** GDC-0853<br>▪ **ARM B:** Placebo |
| **Primary endpoint** | ▪ ACR 50 and safety | ▪ Systemic Lupus Erythematosus Responder Index (SRI)-4 response at Week 48 | ▪ Change from Baseline in the Urticaria Activity Score over 7 days (UAS7) at Day 57 |
| **Status** | ▪ FPI Q3 2016 | ▪ FPI Q1 2017 | ▪ FPI Q2 2017 |
| **CT Identifier** | NCT02833350 | NCT02908100 | NCT03137069 |

CSU=chronic spontaneous urticaria; MTX=methotrexate

# Infectious diseases development programs

gRED Genentech Research & Early Development

| | |
|---|---|
| **Molecule** | **Anti-*S. aureus* TAC** (RG7861) |
| **Indication** | **Serious infections caused by *Staphylococcus aureus*** |
| **Phase/study** | **Phase Ib** |
| **# of patients** | N=24 |
| **Design** | ▪ Establish safety and PK in patients (*S. aureus* bacteremia) |
| **Primary endpoint** | ▪ Safety and PK |
| **Status** | ▪ FPI Q3 2017 |
| **CT Identifier** | NCT03162250 |
| **Collaborator** | Seattle Genetics, Symphogen |



TAC=THIOMAB™ antibiotic conjugate

# Ophthalmology development programs

gRED Genentech Research & Early Development

| | |
|---|---|
| **Molecule** | **NME** (RG6417) |
| **Indication** | **Geographic atrophy** |
| **Phase/study** | **Phase I** |
| **# of patients** | N≈44 |
| **Design** | Open-label study of RG6417 following single and multiple intravitreal administrations in patients with GA secondary to AMD<br>▪ **Stage 1:** Single dose-escalation (SAD)<br>▪ **Stage 2:** Multiple-dose (MD) stages |
| **Primary endpoint** | ▪ Safety/tolerability |
| **Status** | ▪ FPI Q3 2017 |
| **CT Identifier** | NCT03295877 |



GA=geographic atrophy; AMD=age-related macular degeneration

# Metabolic diseases development programs

gRED Genentech Research & Early Development

| Molecule | FGFR1/KLB MAb (RG7992) | |
|---|---|---|
| **Indication** | **Metabolic diseases** | |
| **Phase/study** | **Phase Ia** | **Phase Ib** |
| **# of patients** | N=79 | N=120 |
| **Design** | Healthy volunteer study<br>▪ Randomized, blinded, placebo-controlled, single ascending dose of RG7992 | Obese type 2 diabetes<br>▪ Randomized, blinded, placebo-controlled, multiple ascending dose of RG7992 |
| **Primary endpoint** | ▪ Safety and tolerability | ▪ Safety, tolerability and PK |
| **Status** | ▪ FPI Q4 2015<br>▪ Recruitment completed Q1 2017 | ▪ FPI Q1 2017 |
| **CT Identifier** | NCT02593331 | NCT03060538 |

FGFR1=fibroblast growth factor receptor 1; KLB=β-Klotho

*Doing now what patients need next*