Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

Spark

Changes to the development pipeline
Q2 2021 update

New to phase I

2 NMEs:
RG6189 FAP-CD40 – solid tumors
RG6338 NME – metabolic diseases

New to phase II

3 NMEs:
RG6139 PD1xLAG3 – solid tumors
RG7769 PD1xTIM3 – solid tumors
RG7835 IgG-IL2 – autoimmune diseases

1 AI:
RG6058 tiragolumab+Tecentriq – neoadj+adj NSCLC

New to phase III

1 NME:
RG6422 AT-527 – SARS-CoV-2

4 AIs:
RG3502 Kadcyla+Tecentriq – HER2+ eBC high-risk
RG6321 PDS with ranibizumab – wAMD 36-week refill interval
RG7446 Tecentriq – ctDNA+ high-risk MIBC
RG7159 Gazyva – membranous nephropathy

New to registration

1 NME:
RG7716 faricimab – DME

2 AIs:
RG7446 Tecentriq – adj NSCLC
RG7716 faricimab – wAMD

Removed from phase I

5 NMEs:
RG6247 4D-110 - choroideremia
RG6296 BCMA x CD16a – r/r MM
RG7876 selicrelumab combos – solid tumors
4DMT 4D-125 – X-linked retinitis pigmentosa
Chugai NME- hyperphosphatemia

Removed from phase II

1 AI:
RG7601 Venclexta+fulvestrant – 2L HR+ BC

Removed from phase III

1 AI:
RG7440 ipatasertib+fulvestrant+palbociclib – 1L HR+ mBC

Approvals

1 NME approved in EU:
RG6168 Enspryng - NMOSD

2 AIs approved in EU:
RG7446 Tecentriq Dx+ - 1L sq/non-sq NSCLC
RG7601 Venclexta+azacitidine – 1L AML

Status as of July 22, 2021

Roche Group development pipeline

Phase I (39 NMEs + 12 AIs)

RG6007	HLA-A2-WT1 x CD3	AML
RG6026	glofitamab monotherapy and combos	heme tumors
RG6058	tiragolumab combos	heme & solid tumors
RG6076	CD19-4-1BBL	heme tumors
RG6115	TLR7 agonist (4)	HCC
RG6160	cevostamab (FcRH5 x CD3)	r/r MM
RG6171	giredestrant (SERD)	ER+/HER2- BC
RG6180	autogene cevumeran±T	solid tumors
RG6185	belvarafenib (pan-RAF inh)+Cotellic	solid tumors
RG6189	FAP-CD40	solid tumors
RG6194	HER2 x CD3	BC
RG6232	TYRP1 x CD3	metastatic melanoma
RG6234	-	multiple myeloma
RG6279	PD1-IL2v	solid tumors
RG6286	-	colorectal cancer
RG6290	MAGE-A4 ImmTAC	solid tumors
RG6292	CD25 MAb ± T	solid tumors
RG6323	IL15/IL15Ra-Fc	solid tumors
RG6330	KRAS G12C	solid tumors
RG6433	SHP2i	solid tumors
RG7440	ipatasertib + rucaparib	mCRPC, solid tumors
	ipatasertib	prostate cancer, pretreated
RG7446	Morpheus platform	solid tumors
	T + Venclexta	maintenance 1L ES-SCLC
RG7601	Venclexta + AMG176	AML
	Venclexta ± azacitidine	r/r MDS
	Venclexta + gilteritinib	r/r AML
RG7802	cibisatamab ± T	solid tumors
RG7827	FAP-4-1BBL + combos	solid tumors
RG7828	mosunetuzumab monotherapy + combos	heme tumors
CHU	FIXa x FX	haemophilia
CHU	glypican-3 x CD3	solid tumors
CHU	codrituzumab	HCC
CHU	CD137 switch antibody	solid tumors
CHU	-	solid tumors & endometriosis
SQZ	PBMC vaccine	solid tumors
RG6287	-	IBD
RG6418	NLRP3 inh	inflammation
RG6315	-	immunologic disorders
RG6006	Abx MCP	bacterial infections
RG6084	PD-L1 LNA	HBV
RG6338	-	metabolic diseases
RG6091	UBE3A LNA	Angelman syndrome
RG6182	-	neurodegenerative diseases
RG6237	-	neuromuscular disorders
RG7637	-	neurodevelopmental disorders
RG6120	VEGF-Ang2 DutaFab	nAMD
RG6179	-	DME
RG6312	-	geographic atrophy
RG7921	-	nAMD
CHU	PTH1 recep. ago	hypoparathyroidism

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

Metabolism
Neuroscience
Ophthalmology
Other

RG-No - Roche/Genentech
CHU - Chugai managed
IONIS – IONIS managed

SQZ - SQZ Biotechnology managed
NOV - Novimmune managed

T=Tecentriq

Phase II (25 NMEs + 13 AIs)

RG6058	tiragolumab + T	NSCLC
	tiragolumab + T + chemo	1L non-squamous NSCLC
	tiragolumab + T + chemo	neoadj-adj NSCLC
	tiragolumab + T	cervical cancer
	tiragolumab + T	1L PD-L1+ mSCCHN
RG6139	PD1 x LAG3	solid tumors
RG6171	giredestrant (SERD)	neoadjuvant ER+ BC
	giredestrant (SERD)	2/3L ER+/HER2- mBC
RG6180	autogene cevumeran + pembrolizumab	1L melanoma
RG6354	rhPTX-2 (PRM-151)	myelofibrosis
RG6357	SPK-8011	hemophilia A
RG6358	SPK-8016	hemophilia A with inhibitors to factor VIII
RG7601	Venclexta + carfilzomib	r/r MM t(11;14)
RG7769	PD1 x TIM3	solid tumors
CHU	Oncolytic Type 5 adenovirus	esophageal cancer
RG6173	anti-tryptase	asthma
RG7835	IgG-IL2	autoimmune diseases
RG7880	efmarodocokin alfa	inflammatory diseases
NOV	TLR4 MAb	autoimmune diseases
IONIS	ASO factor B	IgA nephropathy
RG6413+RG6412[1]	casirivimab+imdevimab	SARS-CoV-2 hospitalised
RG7854/RG7907/ RG6346[2]	TLR7 ago(3)/CpAM (2)/siRNA	HBV
RG6359	SPK-3006	Pompe disease
RG7992	FGFR1 x KLB MAb	NASH
RG6100	semorinemab	Alzheimer's
RG6102	brain shuttle gantenerumab	Alzheimer's
RG6356	micro-dystrophin (SRP-9001)	DMD
RG7412	crenezumab	familial Alzheimer's healthy pts
RG7816	GABA Aa5 PAM	ASD
RG7906	ralmitaront	schizophrenia
RG7935	prasinezumab	Parkinson's
RG6147	HtrA1	geographic atrophy
RG6367	SPK-7001	choroideremia
RG7774	-	retinal disease
IONIS	ASO factor B	geographic atrophy

[1]combination contributing as two entities
[2]combination platform

Status as of July 22, 2021

Roche Group development pipeline

Phase III (15 NMEs + 39 AIs)

RG3502	Kadcyla + T	2L+ HER-2+ PD-L1+ mBC
	Kadcyla + T	HER-2+ eBC high-risk
RG6013	Hemlibra	mild to moderate hemophilia A
RG6026**	glofitamab + chemo	2L+ DLBCL
RG6058	tiragolumab + T + chemo	1L SCLC
	tiragolumab + T	1L PD-L1+ NSCLC
	tiragolumab + T	locally advanced esophageal cancer
	tiragolumab + T	stage III unresectable 1L NSCLC
RG6107	crovalimab	PNH
RG6114	inavolisib (mPI3K alpha inh)	1L HR+ mBC
RG6171	giredestrant (SERD)	ER+/HER2- mBC
RG6268	Rozlytrek ROS1+	1L NSCLC
RG7440	ipatasertib + abiraterone	1L CRPC
RG7596	Polivy	1L DLBCL
RG7446	Tecentriq + platinum chemo	NSCLC neoadj
	Tecentriq	NMIBC, high risk
	Tecentriq	RCC adj
	Tecentriq + cabozantinib	advanced RCC
	Tecentriq + cabozantinib	2L NSCLC
	T ± chemo	SCCHN adj
	T + capecitabine or carbo/gem	1L TNBC
	T + paclitaxel	TNBC adj
	T + Avastin	HCC adj
	T ± chemo	1L mUC
	Tecentriq	SC NSCLC
	Tecentriq	ctDNA+ high-risk MIBC
RG7601	Venclexta	r/r MM t(11:14)
	Venclexta + azacitidine	1L MDS
RG7828**	mosunetuzumab + lenalidomide	2L+ FL
RG7853	Alecensa	ALK+ NSCLC adj
RG1569	Actemra	COVID-19 pneumonia
RG3648	Xolair	food allergy
RG6354	rhPTX-2 (PRM-151)	idiopathic pulmonary fibrosis
RG7159	Gazyva	lupus nephritis
	Gazyva	membranous nephropathy
RG7413	etrolizumab	Crohn's
RG6152	Xofluza	influenza, pediatric (0-1 year)
	Xofluza	influenza, pediatric (1-12 years)
	Xofluza	influenza direct transmission
RG6413+ RG6412*	casirivimab+imdevimab	SARS-CoV-2 prophylaxis
	casirivimab+imdevimab	SARS-CoV-2 ambulatory
RG6422	AT-527	SARS-CoV-2
RG1450	gantenerumab	Alzheimer's
RG1594	Ocrevus high dose	RMS & PPMS
RG6042	tominersen	Huntington's
RG7845	fenebrutinib	PPMS
RG7845	fenebrutinib	RMS
RG6321	port delivery system with ranibizumab	DME
	port delivery system with ranibizumab	DR
	port delivery system with ranibizumab	wAMD, 36-week
RG7716	faricimab	BRVO
	faricimab	CRVO

T=Tecentriq
*combination contributing as two entities
** phI safety run-in ongoing

Registration (3 NMEs + 4 AIs)

RG6396	Gavreto (pralsetinib) [1]	RET+ NSCLC
	Gavreto (pralsetinib) [2]	RET+ MTC
RG7446	T + nab-paclitaxel [3]	TNBC neoadj
	Tecentriq	NSCLC adj
RG6321	port delivery system with ranibizumab	wAMD
RG7716	faricimab [4]	DME
	faricimab [4]	wAMD

[1] Approved in US, filed in EU
[2] Approved in US
[3] Filed in EU
[4] FDA acceptance pending

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

Status as of July 22, 2021

NME submissions and their additional indications

Projects in phase II and III

2021		2022		2023		2024 and beyond					
RG7828	**mosunetuzumab** 3L+ FL	RG6026	**glofitamab** 3L+ DLBCL	RG6058	**tiragolumab + T** 1L PD-L1+ NSCLC	RG6026	**glofitamab + chemo** 2L DLBCL	RG6180	**autogene cevumeran** 1L melanoma	RG6100	**semorinemab** Alzheimer's
RG6413+ RG6412	**casirivimab+imdevimab** SARS-CoV-2 prophylaxis	RG6058	**tiragolumab + Tecentriq (T)** 1L SCLC	RG6114	**inavolisib** (mPI3K alpha inh) 1L HR+ BC	RG6058	**tiragolumab + T** 1L PD-L1+ cervical ca	RG6354	**rhPTX-2 (PRM-151)** myelofibrosis	RG6102	**brain shuttle gantenerumab** Alzheimer's
RG6413+ RG6412	**casirivimab+imdevimab** SARS-CoV-2 ambulatory	RG6107	**crovalimab** PNH[1]	RG6321	**port delivery system with ranibizumab** DME	RG6058	**tiragolumab + T** locally adv esophageal cancer	RG7769	**PD1xTIM3** solid tumors	RG6356	**micro-dystrophin SRP-9001** DMD
RG6413+ RG6412	**casirivimab+imdevimab** SARS-CoV-2 hospitalised	RG6171	**giredestrant (SERD)** 2L/3L ER+/HER2- mBC	RG6321	**port delivery system with ranibizumab** DR	RG6058	**tiragolumab + T** Stage III unresectable 1L NSCLC	RG7828	**mosunetuzumab + lenalidomide** 2L FL	RG7816	**GABA Aa5 PAM** ASD
RG6321	**port delivery system with ranibizumab** wAMD ✓	RG7440	**ipatasertib + abiraterone** 1L CRPC	RG7716	**faricimab** BRVO/CRVO	RG6058	**tiragolumab + T** 1L non-sq NSCLC	RG6173	**Anti-tryptase** asthma	RG7845	**fenebrutinib** PPMS
RG7716	**faricimab** DME✓	RG7413	**etrolizumab** Crohn's			RG6058	**tiragolumab + T** 1L PD-L1+ mSCCHN	RG6354	**rhPTX-2 (PRM-151)** IPF	RG7845	**fenebrutinib** RMS
RG7716	**faricimab** wAMD✓	RG6422	**AT-527** SARS-CoV-2			RG6058	**tiragolumab+T+/- chemo** neoadj/adj NSCLC	RG7880	**efmarodocokin alfa** (IL22-Fc) inflammatory diseases	RG7906	**ralmitaront** schizophrenia
		RG1450	**gantenerumab** Alzheimer's			RG6139	**PD1xLAG3** solid tumors	RG7907/ RG7854/ RG6346	**TLR7 ago (3)/ CpAM (2) /siRNA** HBV	RG7935	**prasinezumab** Parkinson's
						RG6171	**giredestrant (SERD)** 1L ER+/HER2- mBC	RG7992	**FGFR1 x KLB MAb** NASH	RG6321	**port delivery system with ranibizumab** wAMD, 36-week refill

✓ Indicates submission to health authorities has occurred
Unless stated otherwise submissions are planned to occur in US and EU
[1] First filing in China

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

Status as of July 22, 2021

AI submissions for existing products

Projects in phase II and III

New Molecular Entity (NME)
Additional Indication (AI)
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Ophthalmology
Other

2021

RG6152	**Xofluza** influenza, pediatric (1-12 yrs)
RG1569	**Actemra**[1] COVID-19 pneumonia
RG6013	**Hemlibra** Mild to moderate hemophilia A (EU)
RG6268	**Rozlytrek (BFAST)** 1L NSCLC ROS1+
RG7446	**Tecentriq** NSCLC adj ✓
RG7596	**Polivy** 1L DLBCL

2022

RG7446	**Tecentriq** RCC adj
RG7446	**Tecentriq ± chemo** 1L mUC
RG7853	**Alecensa** ALK+ NSCLC adj

2023

RG6152	**Xofluza** direct transmission
RG6152	**Xofluza** influenza, pediatric (0-1 year)
RG3648	**Xolair** Food allergy
RG7446	**Tecentriq** SC NSCLC
RG7446	**Tecentriq + cabozantinib** 2L NSCLC
RG7446	**Tecentriq + cabozantinib** adv RCC
RG7446	**Tecentriq + Avastin** HCC adj
RG7446	**Tecentriq**[2] NSCLC neo adj
RG7601	**Venclexta** r/r MM t(11:14)
RG7601	**Venclexta + azacitidine** 1L MDS

2024 and beyond

RG3502	**Kadcyla + Tecentriq** 2L+ HER-2+ PD-L1+ mBC
RG3502	**Kadcyla + Tecentriq** HER-2+ eBC high-risk
RG7446	**Tecentriq + paclitaxel** TNBC adj
RG7446	**Tecentriq** High risk NMIBC
RG7446	**Tecentriq + chemo** SCCHN adj
RG7446	**Tecentriq + capecitabine or carbo/gem** TNBC
RG7446	**Tecentriq** ctDNA+ high-risk MIBC
RG7159	**Gazyva** lupus nephritis
RG7159	**Gazyva** membranous nephropathy
RG1594	**Ocrevus** high dose RMS & PPMS

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

Status as of July 22, 2021

Major pending approvals 2021

US		EU		China		Japan-Chugai	
RG6321	**PDS with ranibizumab** wAMD Filed April 2021	**RG6396**	**Gavreto (pralsetinib)** **RET+ NSCLC** Filed May 2020	**RG7446**	**Tecentriq** NSCLC adj Filed June 2021	**RG7716**	**faricimab** DME Filed June 2021
RG7716	**faricimab** DME Filed May 2021	**RG7446**	**Tecentriq + nab-paclitaxel** TNBC neoadj Filed Nov 2020 (non-US)			**RG7716**	**faricimab** wAMD Filed June 2021
RG7716	**faricimab** wAMD Filed May 2021	**RG7446**	**Tecentriq** NSCLC adj Filed June 2021			**RG7446**	**Tecentriq** NSCLC adj Filed July 2021
RG7446	**Tecentriq** NSCLC adj Filed June 2021	**RG6321**	**PDS with ranibizumab** wAMD Filed April 2021				
		RG7716	**faricimab** DME Filed May 2021				
		RG7716	**faricimab** wAMD Filed May 2021				

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PDS=port delivery system

Status as of July 22, 2021

Major granted approvals 2021

US

RG7853	**Alecensa (BFAST)** 1L NSCLC ALK+ Jan 2021
RG1569	**Actemra** SSc-ILD March 2021
RG3648	**Xolair** Self-injection April 2021

EU

RG6152	**Xofluza** influenza, otherwise healthy Jan 2021
RG6152	**Xofluza** influenza, high risk Jan 2021
RG6152	**Xofluza** post exposure prophylaxis Jan 2021
RG7916	**Evrysdi** SMA March 2021
RG6168	**Enspryng** NMOSD June 2021
RG7446	**Tecentriq** 1L non-sq + sq NSCLC Dx+ May 2021
RG7601	**Venclexta+ azacitidine** 1L AML May 2021

China

RG6152	**Xofluza** influenza, otherwise healthy April 2021
RG6152	**Xofluza** influenza, high risk April 2021
RG6013	**Hemlibra** Hemophilia A April 2021
RG7446	**Tecentriq** 1L non-sq + sq NSCLC Dx+ April 2021
RG6168	**Enspryng** NMOSD April 2021
RG7916	**Evrysdi** SMA May 2021
RG3502	**Kadcyla** 2L HER2+ BC June 2021
RG7159	**Gazyva** 1L FL and r/r FL June 2021
RG7446	**Tecentriq + pemetrexed** 1L non-sq NSCLC June 2021

Japan-Chugai

RG7596	**Polivy** r/r DLBCL March 2021
RG7916	**Evrysdi** SMA June 2021
RG6413+ RG6412	**casirivimab+imdevimab** SARS-CoV-2 July 2021

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Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

Spark

Hemlibra

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 HAVEN 3**	**Phase III HAVEN 4**
# of patients	N=135	N=46
Design	Patients on FVIII episodic treatment prior to study entry: ▪ **ARM A:** Hemlibra prophylaxis qw ▪ **ARM B:** Hemlibra prophylaxis q2w ▪ **ARM C:** Episodic FVIII treatment; switch to Hemlibra prophylaxis possible after 24 weeks Patients on FVIII prophylaxis prior to study entry: ▪ **ARM D:** Hemlibra prophylaxis qw	Multicenter, open-label, non-randomized study to assess the efficacy, safety, pharmacokinetics, and pharmacodynamics of Hemlibra administered every 4 weeks. ▪ **Part 1:** Pharmacokinetic (PK) run-in part (N=6) ▪ **Part 2:** Expansion part (N=40)
Primary endpoint	▪ Number of bleeds over 24 weeks	▪ Number of bleeds over 24 weeks
Status	▪ FPI Q3 2016, recruitment completed Q2 2017 ▪ Study met primary and key secondary endpoints Q4 2017 ▪ FDA granted Breakthrough Therapy Designation April 2018 ▪ Data presented at WFH 2018 ▪ Filed in US (priority review) and EU in Q2 2018 ▪ Data published in *NEJM* 2018; 379: 811-822	▪ FPI Q1 2017, recruitment completed Q2 2017 ▪ PK run-in data at ASH 2017 ▪ Positive interim analysis outcome reported Q4 2017 ▪ Data presented at WFH 2018 ▪ Interim data filed in US and EU in Q2 2018 ▪ Data published in Lancet Haematology 2019 Jun;6(6):e295-e305
	▪Approved in US Q4 2018 and EU Q1 2019	
CT Identifier	NCT02847637	NCT03020160

In collaboration with Chugai

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

Hemlibra

Factor VIII mimetic for treatment of hemophilia A

Indication	Hemophilia A patients with and without inhibitors to Factor VIII	Hemophilia A mild to moderate patients without inhibitors to Factor VIII
Phase/study	**Phase III** **HAVEN 5**	**Phase III** **HAVEN 6**
# of patients	N=85	N=70
Design	Patients with Hemophilia regardless of FVIII inhibitor status on prophylactic or episodic treatment prior to study entry: ▪ **Arm A**: emicizumab prophylaxis qw ▪ **Arm B**: emicizumab prophylaxis q4w ▪ **Arm C**: No prophylaxis (control arm)	Multicenter, open-label study to evaluate the safety, efficacy, pharmacokinetics, and pharmacodynamics of Hemlibra in patients with mild or moderate Hemophilia A without FVIII inhibitors
Primary endpoint	▪ Number of bleeds over 24 weeks	▪ Safety and efficacy
Status	▪ FPI Q2 2018 ▪ Recruitment completed Q1 2019 ▪ Filed in China Q2 2020 ▪ Approved in China Q2 2021	▪ FPI Q1 2020 ▪ Recruitment completed Q1 2021
CT Identifier	NCT03315455	NCT04158648

In collaboration with Chugai

Alecensa

New CNS-active inhibitor of anaplastic lymphoma kinase

Indication	Treatment-naïve ALK+ advanced NSCLC	Adjuvant ALK+ NSCLC
Phase/study	**Phase III ALEX**	**Phase III ALINA**
# of patients	N=286	N=255
Design	▪ **ARM A:** Alecensa 600mg BID ▪ **ARM B:** Crizotinib 250mg BID	▪ **ARM A:** Alecensa 600 mg BID ▪ **ARM B:** Platinum-based chemotherapy
Primary endpoint	▪ Progression-free survival	▪ Disease-free survival
Status	▪ Recruitment completed Q3 2015 ▪ Primary endpoint met Q1 2017 ▪ Data presented at ASCO 2017, 2018, ESMO 2017, 2018 ▪ Data published in *NEJM* 2017; 377:829-838 ▪ CNS data presented at ESMO 2017 ▪ Final PFS and updated OS presented at ESMO 2019 ▪ Approved in US Q4 2017 (priority review) and in EU Q4 2017	▪ FPI Q3 2018
CT Identifier	NCT02075840	NCT03456076

In collaboration with Chugai

NSCLC=non-small cell lung cancer; ASCO=American Society of Clinical Oncology; *NEJM*=New England Journal of Medicine; ESMO=European Society for Medical Oncology

Kadcyla

First ADC for HER2-positive breast cancer

Indication	HER2-positive early breast cancer high-risk patients	2L+ HER-2 positive PD-L1 positive mBC	HER2-positive early breast cancer high-risk patients
Phase/study	**Phase III KATHERINE**	**Phase III KATE 3**	**Phase III ASTEFANIA**
# of patients	N=1,484	N=350	N=1,590
Design	▪ **ARM A:** Kadcyla 3.6mg/kg q3w ▪ **ARM B:** Herceptin	▪ **ARM A:** Kadcyla plus Tecentriq ▪ **ARM B:** Herceptin plus placebo	▪ **ARM A:** Kadcyla plus Tecentriq ▪ **ARM B:** Kadcyla plus placebo
Primary endpoint	▪ Invasive disease-free survival	▪ Progression-free survival and overall survival	▪ Invasive disease-free survival
Status	▪ Recruitment completed Q4 2015 ▪ Stopped at pre-planned interim data analysis for efficacy Q4 2018 ▪ Data presented at SABCS 2018 ▪ BTD granted by FDA in Q1 2019 ▪ US filling completed under RTOR Q1 2019 and filed in EU Q1 2019 ▪ Approved in US Q2 2019 and in EU Q4 2019 ▪ Data published in *NEJM* 2019; 380:617-628	▪ FPI Q1 2021	▪ FPI Q2 2021
CT Identifier	NCT01772472	NCT04740918	NCT04873362

In collaboration with ImmunoGen, Inc.

ADC=antibody drug conjugate; SABCS=San Antonio Breast Cancer Symposium; RTOR=Real time oncology review; ORR=Objective Response Rate; *NEJM*=New England Journal of Medicine

Perjeta

First-in-class HER2 dimerization inhibitor

Indication	Adjuvant HER2-positive breast cancer	HER2-positive early breast cancer subcutaneous co-formulation	
Phase/study	**Phase III APHINITY**	**Phase III FeDeriCa**	**Phase II PHranceSCa**
# of patients	N=4,803	N=500	N=160
Design	▪ **ARM A:** Perjeta (840mg loading, 420 q3w) plus Herceptin for 52 weeks plus chemotherapy (6-8 cycles) ▪ **ARM B:** Placebo plus Herceptin (52 weeks) plus chemotherapy (6-8 cycles)	Fixed-dose combination (FDC) of Perjeta (P) and Herceptin (H) for subcutaneous administration in combination with chemotherapy in neoadjuvant/adjuvant setting ▪ **ARM A:** P IV+H IV+chemotherapy ▪ **ARM B:** FDC of PH SC+chemotherapy	▪ **ARM A:** PH IV followed by FDC SC ▪ **ARM B:** PH FDC SC followed by IV
Primary endpoint	▪ Invasive disease-free survival (IDFS)	▪ Trough Serum Concentration (Ctrough) of Pertuzumab during cycle 7	▪ Percentage who preferred PH FDC SC
Status	▪ Primary endpoint met Q1 2017 ▪ Data presented at ASCO 2017 and published in *NEJM* 2017; 377:122-131 ▪ Filed in US and EU Q3 2017 ▪ Approved in US Q4 2017 (priority review) and EU Q2 2018 ▪ Six year IDFS data presented at SABCS 2019	▪ Primary endpoint met Q3 2019 ▪ Data presented at SABCS 2019 ▪ Data published in Lancet Oncology 2021 Jan;22(1):85-97	▪ FPI Q4 2018 ▪ Final analysis completed, 85% patients preferred FDC SC ▪ Data presented at ESMO 2020
CT Identifier	NCT01358877	NCT03493854	NCT03674112

ddAC=dose-dense doxorubicin plus cyclophosphamide; FEC=fluorouracil, epirubicin and cyclophosphamide; ASCO=American Society of Clinical Oncology; *NEJM*=New England Journal of Medcine; SABCS=San Antonio Breast Cancer Symposium; IDMC=Independent Data Monitoring Committee; SC with Halozyme's rHuPH20/ Halozyme's human hyaluronidase

Tecentriq

Anti-PD-L1 cancer immunotherapy – lung cancer

Indication	1L non-squamous NSCLC	1L non-squamous and squamous NSCLC PD-L1-selected patients	1L extensive-stage SCLC
Phase/study	**Phase III IMpower132**	**Phase III IMpower110**	**Phase Ib**
# of patients	N=568	N=570	N=62
Design	▪ **ARM A:** Tecentriq plus carboplatin or cisplatin plus pemetrexed ▪ **ARM B:** Carboplatin or cisplatin plus pemetrexed	▪ **ARM A:** Tecentriq monotherapy ▪ **ARM B:** *NSq*: carboplatin or cisplatin plus pemetrexed *Sq:* carboplatin or cisplatin plus gemcitabine	▪ Carboplatin and etoposide +/- Tecentriq followed by maintenance Tecentriq plus Venclexta
Primary endpoint	▪ Progression-free survival and overall survival	▪ Overall survival	▪ Safety and efficacy
Status	▪ FPI Q2 2016 ▪ Recruitment completed Q2 2017 ▪ Study met co-primary endpoint of PFS in Q2 2018 ▪ Data presented at WCLC 2018 ▪ Final OS presented at ESMO Asia 2020 ▪ Data published in J Thorac Oncol 2021 Apr;16(4):653-664	▪ FPI Q3 2015 ▪ Recruitment completed Q1 2018 ▪ Study met primary endpoint in PD-L1 high (IC3/TC3) Q3 2019 ▪ Data presented at ESMO, ESMO-IO 2019 and final OS at WCLC 2021 ▪ Filed in EU and US (priority review) Q4 2019 ▪ Approved in US Q2 2020 and EU Q2 2021 ▪ Data published in NEJM 2020 Oct 1;383(14):1328-1339	▪ FPI Q3 2020
CT Identifier	NCT02657434	NCT02409342	NCT04422210

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

Tecentriq

Anti-PD-L1 cancer immunotherapy – lung cancer

Indication	Adjuvant NSCLC	Neoadjuvant NSCLC	2L NSCLC previously treated with an immune checkpoint inhibitor
Phase/study	**Phase III IMpower010**	**Phase III IMpower030**	**Phase III CONTACT-01**
# of patients	N=1,280	N=450	N=350
Design	Following adjuvant cisplatin-based chemotherapy ▪ **ARM A:** Tecentriq ▪ **ARM B:** Best supportive care	▪ **ARM A:** Tecentriq plus platinum-based chemotherapy ▪ **ARM B:** Platinum-based chemotherapy	▪ **ARM A:** Tecentriq plus cabozantinib ▪ **ARM B:** Docetaxel
Primary endpoint	▪ Disease-free survival	▪ Event free survival	▪ Overall survival
Status	▪ FPI Q3 2015 ▪ Trial amended from PD-L1+ selected patients to all-comers ▪ FPI for all-comer population Q4 2016 ▪ Recruitment completed Q3 2018 ▪ Study met primary endpoint Q1 2021 ▪ Data presented at ASCO 2021 ▪ Filed in US and EU Q2 2021	▪ FPI Q2 2018	▪ FPI Q3 2020
CT Identifier	NCT02486718	NCT03456063	NCT04471428

NSCLC=non-small cell lung cancer

Tecentriq

Anti-PD-L1 cancer immunotherapy – lung cancer

Indication	1L NSCLC	Stage IV NSCLC
Phase/study	**Phase II/III** **B-FAST**	**Phase Ib/III** **IMscin001**[1]
# of patients	N=660	N=375
Design	▪ **Cohort A:** ALK+ (Alecensa) ▪ **Cohort B:** RET+ (Alecensa) ▪ **Cohort C:** bTMB-high (Tecentriq) ▪ **Cohort D:** ROS1+ (Rozlytrek) ▪ **Cohort E:** BRAF+ (Zelboraf plus Cotellic plus Tecentriq) ▪ **Cohort F:** EGFR Exon 20+ (Tecentriq, Avastin, carboplatin, pemetrexed)	**Phase Ib** ▪ Dose finding, Tecentriq SC followed by Tecentriq IV **Phase III** ▪ 2L NSCLC non inferiority of Tecentriq SC vs Tecentriq IV
Primary endpoint	▪ Cohort A/B: Objective response rate ▪ Cohort C: Progression-free survival	▪ Observed concentration of Tecentriq in serum at cycle 1
Status	▪ FPI Q3 2017 ▪ Recruitment completed for cohort A Q3 2018 and cohort C Q3 2019 ▪ Cohort A: primary endpoint met Q3 2019; approved in US Q1 2021 ▪ Cohort C: did not show statistical significance for primary endpoint ▪ Cohort F: FPI Q2 2021	▪ FPI Q4 2018 ▪ FPI in phase III part Q4 2020
CT Identifier	NCT03178552	NCT03735121

[1]SC with Halozyme's rHuPH20/ Halozyme's human hyaluronidase
NSCLC=non-small cell lung cancer; ESMO=European Society for Medical Oncology

Tecentriq

Anti-PD-L1 cancer immunotherapy – SCCHN and melanoma

Indication	Adjuvant squamous cell carcinoma of the head and neck	First-line BRAFv600 mutation-positive metastatic or unresectable locally advanced melanoma
Phase/study	**Phase III** **IMvoke010**	**Phase III** **IMspire150 TRILOGY**[1]
# of patients	N=400	N=500
Design	▪ **ARM A:** Tecentriq 1200mg q3w ▪ **ARM B:** Placebo	Double-blind, randomized, placebo-controlled study ▪ **ARM A:** Tecentriq plus Cotellic plus Zelboraf[2] ▪ **ARM B:** Placebo plus Cotellic plus Zelboraf[2]
Primary endpoint	▪ Event-free survival and overall survival	▪ Progression-free survival
Status	▪ FPI Q1 2018 ▪ Recruitment completed Q1 2020	▪ FPI Q1 2017 ▪ Recruitment completed Q2 2018 ▪ Primary endpoint met Q4 2019 ▪ Data presented at AACR 2020 ▪ Data published in Lancet;395(10240):1835-1844 ▪ Filed in US Q2 2020 under Project Orbis[3] ▪ Approved in US Q3 2020
CT Identifier	NCT03452137	NCT02908672

SCCHN=squamous cell carcinoma of the head and neck; AML=acute myeloid leukemia; [1]In collaboration with Exelixis; [2]Zelboraf in collaboration with Plexxikon, a member of Daiichi Sankyo Group; [3] Project Orbis=FDA framework for concurrent submission and review of oncology products among international partners; AACR=American Association for Cancer Research

Tecentriq

Anti-PD-L1 cancer immunotherapy – UC

Indication	1L metastatic urothelial carcinoma	High-risk non-muscle-invasive bladder cancer	ctDNA+, high-risk muscle-invasive bladder cancer
Phase/study	**Phase III IMvigor130**	**Phase III ALBAN**	**Phase III IMvigor011**
# of patients	N=1,200	N=516	N=495
Design	▪ **ARM A:** Tecentriq plus gemcitabine and carboplatin or cisplatin ▪ **ARM B:** Tecentriq monotherapy ▪ **ARM C:** Placebo plus gemcitabine and carboplatin or cisplatin	▪ **ARM A**: BCG induction and maintenance ▪ **ARM B:** Tecentriq+plus BCG induction and maintenance	▪ **ARM A**: Tecentriq ▪ **ARM B:** Placebo
Primary endpoint	▪ Progression-free survival, overall survival and safety	▪ Recurrence-free survival	▪ Recurrence-free survival
Status	▪ FPI Q3 2016 ▪ FPI for arm B (amended study) Q1 2017 ▪ Recruitment completed Q3 2018 ▪ Study met co-primary endpoint of PFS Q3 2019 ▪ Data presented at ESMO 2019 and AACR 2021	▪ FPI Q4 2018	▪ FPI Q2 2021
CT Identifier	NCT02807636	NCT03799835	NCT04660344

UC=urothelial carcinoma; BCG=Bacille Calmette-Guérin

Tecentriq

Anti-PD-L1 cancer immunotherapy – renal cell cancer

Indication	Adjuvant renal cell carcinoma	Advanced renal cell carcinoma after immune checkpoint inhibitor treatment
Phase/study	**Phase III** **IMmotion010**	**Phase III** **Contact-03**[1]
# of patients	N=778	N=500
Design	▪ **ARM A:** Tecentriq monotherapy ▪ **ARM B:** Observation	▪ **ARM A:** Tecentriq plus cabozantinib ▪ **ARM B:** cabozantinib
Primary endpoint	▪ Disease-free survival	▪ Progression-free survival and overall survival
Status	▪ FPI Q1 2017 ▪ Recruitment completed Q1 2019	▪ FPI Q3 2020
CT Identifier	NCT03024996	NCT04338269

[1]In collaboration with Exelixis

Tecentriq

Anti-PD-L1 cancer immunotherapy – HCC

Indication	1L hepatocellular carcinoma	Adjuvant hepatocellular carcinoma
Phase/study	**Phase III** **IMbrave150**	**Phase III** **IMbrave050**
# of patients	N=501	N=662
Design	▪ **ARM A:** Tecentriq plus Avastin ▪ **ARM B:** Sorafenib	▪ **ARM A:** Tecentriq plus Avastin ▪ **ARM B:** Active surveillance
Primary endpoint	▪ Overall survival and progression free survival	▪ Recurrence-Free Survival (RFS)
Status	▪ FPI Q1 2018; recruitment completed Q1 2019 ▪ Data presented at ESMO Asia 2019 ▪ US filing completed under RTOR Q1 2020; filed in EU Q1 2020 ▪ Data published in *NEJM* 2020;382:1894-1905 ▪ Approved in US Q2 2020 and EU Q4 2020	▪ FPI Q4 2019
CT Identifier	NCT03434379	NCT04102098

ESMO=European Society for Medical Oncology; *NEJM*=New England Journal of Medicine; RTOR=Real time oncology review

Tecentriq

Anti-PD-L1 cancer immunotherapy – breast cancer

Indication	Previously untreated metastatic triple negative breast cancer	
Phase/study	**Phase III IMpassion130**	**Phase III IMpassion132**
# of patients	N=900	N=572
Design	▪ **ARM A:** Tecentriq plus nab-paclitaxel ▪ **ARM B:** Placebo plus nab-paclitaxel	▪ **ARM A:** Tecentriq plus capecitabine or carbo/gem ▪ **ARM B:** Placebo plus capecitabine or carbo/gem
Primary endpoint	▪ Progression-free survival and overall survival (co-primary endpoint)	▪ Overall survival
Status	▪ Recruitment completed Q2 2017 ▪ Study met co-primary endpoint of PFS in both PDL1+ and ITT populations Jul 2018 ▪ Primary PFS and interim OS data presented at ESMO 2018 and ASCO 2019 ▪ Data published in *NEJM* 2018; 379:2108-2121 ▪ US accelerated approval Q1 2019 ▪ Approved in EU Q3 2019 ▪ Final OS presented at ESMO Asia 2020	▪ FPI Q1 2018
CT Identifier	NCT02425891	NCT03371017

ESMO=European Society for Medical Oncology; ASCO=American Society of Clinical Oncology; *NEJM*=New England Journal of Medicine

Tecentriq

Anti-PD-L1 cancer immunotherapy – breast cancer

Indication	Neoadjuvant triple negative breast cancer	Adjuvant triple negative breast cancer
Phase/study	**Phase III** **IMpassion031**	**Phase III** **IMpassion030**
# of patients	N=324	N=2,300
Design	▪ **ARM A:** Tecentriq plus nab-paclitaxel ▪ **ARM B:** Placebo plus nab-paclitaxel	▪ **ARM A:** Tecentriq + paclitaxel followed by AC followed by Tecentriq + AC, followed by Tecentriq maintenance ▪ **ARM B:** Placebo + paclitaxel followed by AC followed by placebo
Primary endpoint	▪ Percentage of participants with pathologic complete response (pCR)	▪ Invasive Disease Free Survival
Status	▪ FPI Q3 2017 ▪ Recruitment completed Q2 2018 ▪ Study met primary endpoint Q2 2020 ▪ Data presented at ESMO 2020 ▪ Data published in Lancet 2020;396 (10257):1090-1100 ▪ Filed in EU Q4 2020	▪ FPI Q3 2018
CT Identifier	NCT03197935	NCT03498716

ESMO=European Society for Medical Oncology

Venclexta

Novel small molecule Bcl-2 selective inhibitor – CLL

Indication	Untreated CLL patients with coexisting medical conditions	Relapsed or refractory CLL	Untreated fit CLL patients
Phase/study	**Phase III CLL14**	**Phase III MURANO**	**Phase III CristaLLo**
# of patients	N=432	N=391	N=165
Design	▪ **ARM A:** Venclexta plus Gazyva ▪ **ARM B:** Chlorambucil plus Gazyva	▪ **ARM A:** Venclexta plus Rituxan ▪ **ARM B:** Rituxan plus bendamustine	▪ **ARM A:** Venclexta plus Gazyva ▪ **ARM B:** Fludarabine + cyclophosphamide + Rituxan or bendamustine + Rituxan
Primary endpoint	▪ Progression-free survival	▪ Progression-free survival	▪ MRD negativity rate in peripheral blood at 15 months
Status	▪ Study met primary endpoint at pre-specified interim analysis Q4 2018 ▪ BTD granted by FDA Q1 2019 ▪ US filing completed under RTOR Q1 2019 ▪ Filed in EU Q2 2019 ▪ Data presented at ASCO 2019, ASH 2019, ASH 2020 and EHA 2021 ▪ Data published in *NEJM* 2019; 380:2225-2236 ▪ Approved US Q2 2019 and EU Q1 2020	▪ Study met primary endpoint at interim analysis ▪ Data presented at ASH 2017 ▪ Filed in US Q4 2017 and EU Q1 2018 ▪ Data published in *NEJM* 2018; 378:1107–20 ▪ Updated data presented at ASCO 2018, ASH 2019 and ASH 2020 ▪ Approved in US Q2 2018 (priority review) ▪ EU approval Q4 2018	▪ FPI Q2 2020
CT Identifier	NCT02242942	NCT02005471	NCT04285567

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

CLL=chronic lymphocytic leukemia; ASH=American Society of Hematology; ASCO=American Society of Clinical Oncology; RTOR=Real time oncology review; *NEJM*=New England Journal of Medicine; MRD=Minimal Residual Disease

Venclexta

Novel small molecule Bcl-2 selective inhibitor – MM

Indication	Relapsed or refractory multiple myeloma		
Phase/study	**Phase I**	**Phase Ib/II**	**Phase III CANOVA**
# of patients	N=166	N=120	N=244
Design	▪ **Dose escalation cohort:** Venclexta dose escalation ▪ **Safety expansion cohort (t11;14):** Venclexta expansion ▪ **Combination:** Venclexta plus dexamethasone	▪ Venclexta plus carfilzomib plus dexamethasone in t(11;14) positive r/r MM	▪ Venclexta plus dexamethazone vs pomalidomide plus dexamethasone in t(11;14) positive r/r MM
Primary endpoint	▪ Safety and maximum tolerated dose	▪ Safety, objective response rate, PK, PD	▪ Progression-free survival
Status	▪ FPI Q4 2012 ▪ Data presented at ASCO 2015 ▪ Updated data presented at ASCO 2016 and ASH 2016 ▪ Data published in Blood 2017;130(22):2401-2409	▪ FPI Q1 2017	▪ FPI Q4 2018
CT Identifier	NCT01794520	NCT02899052	NCT03539744

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

Novel small molecule Bcl-2 selective inhibitor – AML

Indication	Relapsed or refractory AML	Relapsed or refractory hematological malignancies
Phase/study	**Phase I**	**Phase I**
# of patients	N=52	N=86
Design	▪ Venclexta in combination with gilteritinib	▪ Venclexta plus AMG176 dose escalation ▪ Dose expansion phase to confirm safety and preliminary RPTD
Primary endpoint	▪ Dose and composite complete remission (CRc) Rate	▪ Maximum tolerated dose and safety
Status	▪ FPI Q4 2018 ▪ Initial data presented at ASH 2019 ▪ Updated data presented at ASH 2020	▪ FPI Q2 2019 ▪ Study on clinical hold
CT Identifier	NCT03625505	NCT03797261

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute;
AML=acute myeloid leukemia; ASH=American Society of Hematology; RPTD =recommended phase II dose

Venclexta

Novel small molecule Bcl-2 selective inhibitor – MDS

Indication	Relapsed or refractory myelodysplastic syndromes	Treatment-naive myelodysplastic syndromes	Newly diagnosed higher-risk myelodysplatic syndrome
Phase/study	**Phase Ib**	**Phase Ib**	**Phase III VERONA**
# of patients	N=70	N=137	N=500
Design	Cohort 1: ▪ **ARM A:** Venclexta 400 mg ▪ **ARM B:** Venclexta 800 mg Cohort 2: ▪ **ARM A:** Venclexta plus azacitidine Study expansion: ▪ Venclexta or Venclexta plus azacitidine	▪ **Dose escalation cohort:** Venclexta plus azacitidine dose escalation ▪ **Safety expansion cohort**	▪ **ARM A:** Venclexta plus azacitidine ▪ **ARM B:** Placebo plus azacitidine
Primary endpoint	▪ Safety, efficacy, PK and PD	▪ Safety, PK, recommended phase II dose (RP2D)	▪ Complete remission rate and overall survival
Status	▪ FPI Q1 2017	▪ FPI Q1 2017 ▪ Data presented at ASH 2019 ▪ Updated data presented at ASH 2020 ▪ BTD granted by FDA July 2021	▪ FPI Q4 2020
CT Identifier	NCT02966782	NCT02942290	NCT04401748

Joint project with AbbVie, in collaboration with The Walter and Eliza Hall Institute
MDS=myelodysplastic syndromes; ASH=American Society of Hematology

Polivy (polatuzumab vedotin)

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=329	N=875
Design	▪ **PIb:** Dose escalation ▪ **PhII:** Polatuzumab vedotin plus BR vs. BR ▪ **PhII expansion:** Polatuzumab vedotin plus Gazyva (non-randomized)	▪ **ARM A:** Polatuzumab vedotin plus R-CHP ▪ **ARM B:** R-CHOP
Primary endpoint	▪ Safety and response by PET/CT	▪ Progression-free survival
Status	▪ FPI Q4 2014 ▪ PRIME Designation (Q2 2017) and Breakthrough Therapy Designation (Q3 2017) granted for r/r DLBCL ▪ Pivotal randomized Ph2 in r/r DLBCL presented at ASH 2017 and ASH 2020 ▪ Filed in US and EU Q4 2018; US priority review granted Q1 2019 ▪ Approved in US Q2 2019 and in EU Jan 2020 ▪ Published in J Clin Oncol. 2020 Jan 10;38(2):155-165	▪ FPI Q4 2017 ▪ Recruitment completed Q2 2019
CT Identifier	NCT02257567	NCT03274492

In collaboration with Seagen Inc.

ADC=antibody–drug conjugate; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; r/r=relapsed or refractory; ASH=American Society of Hematology; BR=bendamustine and Rituxan; R-CHP=Rituxan, cyclophosphamide, hydroxydoxorubicin, prednisone; R-CHOP=Rituxan, cyclophosphamide, doxorubicin, vincristine, and prednisone

Rozlytrek (entrectinib)

CNS-active and selective inhibitor of NTRK/ROS1

Indication	Locally Advanced or Metastatic tumors with ROS1 gene rearrangement	Locally Advanced or Metastatic tumors with NTRK1/2/3 gene rearrangement	Pediatric tumors with NTRK 1/2/3, ROS-1 or ALK rearrangement
Phase/study	**Phase II STARTRK2**	**Phase II STARTRK2**	**Phase I/Ib STARTRK - NG**
# of patients	N~300 total	N~300 total	N~80
Design	Single arm with Baskets based on tumor type and genomic alteration status	Single arm with Baskets based on tumor type and genomic alteration status	Single arm with Baskets based on tumor type and genomic alteration status
Primary endpoint	▪ Objective response rate	▪ Objective response rate	▪ Maximum tolerated dose (MTD) and recommended phase II dose (RP2D)
Status	▪ FPI Q1 2016 ▪ Data presented at WCLC 2018	▪ FPI Q1 2016 ▪ Data presented at ESMO 2018	▪ FPI Q2 2016 ▪ Initial data presented at ASCO 2019
	▪ Breakthrough Therapy Designation granted by FDA (Q2 2017), PRIME designation granted by EMA (Q1 2018) and Sakigake Designation granted by MHLW (Q4 2017) for NTRK fusion-positive, locally advanced or metastatic solid tumors ▪ Filed in US Q4 2018 and EU Q1 2019 ▪ Approved in US Q3 2019 and EU Q3 2020 ▪ Published in Lancet Oncol. 2020 Feb;21(2):261-271 and 271-282		
CT Identifier	NCT02568267	NCT02568267	NCT02650401

WCLC=World Conference on Lung Cancer; ESMO=European Society for Medical Oncology; ASCO=American Society of Clinical Oncology; NTRK=neurotrophic receptor tyrosine kinase; PRIME= priority medicines

Gavreto (pralsetinib, RG6396)

Highly selective RET inhibitor

Indication	RET+ NSCLC, thyroid cancer and other advanced solid tumors	1L RET fusion-positive, metastatic NSCLC
Phase/study	**Phase I/II ARROW**	**Phase III AcceleRET Lung**
# of patients	N=647	N=250
Design	▪ **Part 1:** Gavreto 30-600mg dose-escalation ▪ **Part 2:** Gavreto 400mg dose expansion	▪ **Arm A:** Gavreto 400mg ▪ **Arm B:** Platinum-based chemotherapy +/- pembrolizumab
Primary endpoint	▪ Safety and efficacy	▪ Progression-free survival
Status	▪ Data presented at ASCO (NSCLC) and ESMO (medullary thyroid cancer) 2020 ▪ Filed in US and EU for RET fusion-positive NSCLC and US for RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer ▪ Approved in US Q3 2020 in RET fusion-positive NSCLC, in Q4 2020 in RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer ▪ Updated data presented at ASCO 2021 ▪ Data published in Lancet Oncol 2021 Jul;22(7):959-969	▪ Study initiated in Q1 2020
CT Identifier	NCT03037385	NCT04222972

In collaboration with Blueprint Medicines

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

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: ▪ **ARM A:** Ocrelizumab 2x300 mg iv followed by 600 mg iv every 24 weeks ▪ **ARM B:** Interferon β-1a	96-week treatment period: ▪ **ARM A:** Ocrelizumab 2x300 mg iv followed by 600 mg iv every 24 weeks ▪ **ARM B:** Interferon β-1a	120-week treatment period: ▪ **ARM A:** Ocrelizumab 2x300 mg iv every 24 weeks ▪ **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, OLE ongoing ▪ Primary data presented at ECTRIMS 2015 ▪ Updated data presented at AAN and ECTRIMS 2017, AAN and EAN 2018 ▪ Data published in *NEJM* 2017; 376:221-234 ▪ Data published on COVID-19 in Mult Scler Relat Disord on Ocrevus treated people with MS, doi.org/10.1016/j.msard.2020.102725		▪ Primary endpoint met Q3 2015 ▪ Primary data presented at ECTRIMS 2015, updated data presented at AAN and ECTRIMS 2017, AAN and EAN 2018 ▪ Data published in *NEJM* 2017; 376:209-220
	▪ Approved in US Q1 2017 and EU Q1 2018		
CT Identifier	NCT01247324	NCT01412333	NCT01194570

OLE=Open label extension; ECTRIMS=European Committee for Treatment and Research in Multiple Sclerosis; AAN=Annual Meeting of the American Academy of Neurology; EAN=European Academy of Neurology; *NEJM*=New England Journal of Medicine

Ocrevus (ocrelizumab, RG1594)

Humanized mAb selectively targeting CD20+ B cells

Indication	Relapsing and primary progressive multiple sclerosis (RMS & PPMS)	Primary progressive multiple sclerosis (PPMS)
Phase/study	**Phase IIIb ENSEMBLE PLUS**	**Phase IIIb ORATORIO-HAND**
# of patients	N=1225	N ~ 1000
Design	▪ Substudy of ongoing phase IIIb, open-label, single-arm ENSEMBLE study ▪ Shorter two-hour infusion time	120-week treatment period: ▪ **ARM A:** Ocrelizumab 600mg IV every 24 weeks ▪ **ARM B:** Placebo
Primary endpoint	▪ Safety, measured by the proportion of patients with IRRs following the first randomised 600 mg infusion (frequency/severity assessed during and 24-hours post infusion)	▪ Time to upper limb disability progression confirmed for at least 12 weeks
Status	▪ Filed in US and EU Q1 2020 ▪ Approved in EU Q2 2020 and US Q4 2020 ▪ Data published Neurol, Neuroimmunol and Neuroinflamm Sept 2020; 7(5), e807	▪ FPI Q3 2019
CT Identifier	NCT03085810	NCT04035005

Ocrevus (ocrelizumab, RG1594)

Humanized mAb selectively targeting CD20+ B cells

Indication	Primary progressive multiple sclerosis (PPMS)	Relapsing multiple sclerosis (RMS)
Phase/study	**Phase IIIb GAVOTTE**	**Phase IIIb MUSETTE**
# of patients	N ~ 699	N ~ 786
Design	120-week treatment period: ▪ **ARM A:** Ocrelizumab 600mg IV every 24 weeks ▪ **ARM B:** Ocrelizumab 1200mg if body weight <75kg or 1800mg if body weight > or equal to 75kg every 24 weeks	120-week treatment period: ▪ **ARM A:** Ocrelizumab 600mg IV every 24 weeks ▪ **ARM B:** Ocrelizumab 1200mg if body weight <75kg or 1800mg if body weight > or equal to 75kg every 24 weeks
Primary endpoint	▪ Superiority of Ocrelizumab higher dose versus approved dose on composite confirmed disability progression (cCDP)	▪ Superiority of Ocrelizumab higher dose versus approved dose on composite confirmed disability progression (cCDP)
Status	▪ FPI Q4 2020	▪ FPI Q4 2020
CT Identifier	NCT04548999	NCT04544436

Evrysdi (risdiplam, RG7916)

Oral SMN2 splicing modifier

Indication	Spinal muscular atrophy		
Phase/study	**Phase II/III FIREFISH**	**Phase II/III SUNFISH**	**Phase II JEWELFISH**
# of patients	N=21 (Part 1), 41 (Part 2)	N=51 (Part 1), 180 (Part 2)	N=174
Design	Open-label study in infants with type 1 spinal muscular atrophy: ▪ **Part 1 (dose-finding):** At least 4 weeks ▪ **Part 2 (confirmatory):** 24 months	Randomized, double-blind, placebo-controlled study in adult and pediatric patients with type 2 or type 3 spinal muscular atrophy: ▪ **Part 1 (dose-finding):** At least 12 weeks ▪ **Part 2 (confirmatory):** 24 months	▪ Open-label single arm study in adult and pediatric patients with previously treated SMA type 1, 2 and 3
Primary endpoint	▪ Safety, tolerability, PK, PD and efficacy	▪ Safety, tolerability, PK, PD and efficacy	▪ Safety, tolerability and PK/PD
Status	▪ Recruitment completed for part 2 Q4 2018 ▪ 12 month data from Part 1 presented at AAN, CureSMA and EAN 2019; 16 month data presented at WMS 2019 ▪ Study met primary endpoint in part 2 Jan 2020 ▪ Part 2 1-year data presented at AAN 2020, part 1 2-year data at WMS 2020 ▪ Data published in *NEJM* 2021;384:915-923 ▪ Part 2 2-year data presented at AAN 2021	▪ Recruitment completed for part 2 Q3 2018 ▪ 12 month data from Part 1 presented at AAN, CureSMA and EAN 2019; 16 month data presented at WMS 2019 ▪ Study met primary endpoint in part 2 Q4 2019 ▪ Part 2 1-year data presented at SMA Europe 2020 and 2-year data at MDA 2021	▪ FPI Q1 2017 ▪ Data presented at WMS 2017, AAN 2018, WMS 2018, CureSMA 2019, WMS 2019, CureSMA 2020 and 2021 ▪ Recruitment completed Q1 2020
	▪ Orphan drug designation granted by FDA Q1 2017 and EU Q1 2019, PRIME designation in Q4 2018 ▪ Approved in US Q3 2020 and EU Q1 2021		
CT Identifier	NCT02913482	NCT02908685	NCT03032172

In collaboration with PTC Therapeutics and SMA Foundation

SMN=survival motor neuron; AAN=American Academy of Neurology; WMS=World Muscle Society; EAN=European Academy of Neurology; *NEJM*=New England Journal of Medicine; PRIME=priority medicines

Evrysdi (risdiplam, RG7916)

Oral SMN2 splicing modifier

Indication	Spinal muscular atrophy
Phase/study	**Phase II** **RAINBOWFISH**
# of patients	N=25
Design	Open-label, single-arm, multicenter study in infants aged from birth to 6 weeks who have been genetically diagnosed with SMA but are not yet presenting with symptoms
Primary endpoint	▪ Proportion of participants with two copies of the SMN2 gene (excluding the known SMN2 gene modifier mutation c.859G>C) and baseline CMAP>=1.5 millivolt who are sitting without support
Status	▪ FPI Q3 2019 ▪ Initial data presented at CureSMA 2021
CT Identifier	NCT03779334

In collaboration with PTC Therapeutics and SMA Foundation
SMN=survival motor neuron; CMAP=compound muscle action potential

Enspryng (satralizumab, RG6168, SA237)

Anti-IL-6 receptor humanized monoclonal antibody

Indication	Neuromyelitis optica spectrum disorder (NMOSD)	
Phase/study	**Phase III Sakura Star**	**Phase III Sakura Sky**
# of patients	N=95	N=70 (adults); N=6 (adolescents)
Design	Satralizumab as monotherapy: ▪ **Group A:** Satralizumab 120mg SC monthly ▪ **Group B:** Placebo SC monthly	Add-on therapy of satralizumab: ▪ **Group A:** Satralizumab 120mg SC monthly ▪ **Group B:** Placebo SC Both arms on top of baseline therapies: azathioprine, mycophenolate mofetil or oral corticosteroids
Primary endpoint	▪Efficacy (time to first relapse) and safety, PD, PK	▪ Efficacy (time to first relapse) and safety, PD, PK
Status	▪ Primary endpoint met Q4 2018 ▪ Data presented at ECTRIMS 2019 ▪ Published in Lancet Neurology 2020; 19(5): 402-412	▪ FPI Q3 2017 ▪ Primary endpoint met Q3 2018 ▪ Data presented at ECTRIMS 2018 and AAN 2019 ▪ Published in *NEJM* 2019; 381:2114-2124
	▪ BTD granted by FDA Q4 2018 ▪ Filed in EU Q3 2019; US acceptance of filing Q4 2019, ▪ Approved in US Q3 2020 and EU Q2 2021	
CT Identifier	NCT02073279	NCT02028884

*Trials managed by Chugai (Roche opted-in)

ECTRIMS=European Committee for Treatment and Research in Multiple Sclerosis; AAN=American Academy of Neurology; *NEJM*=New England Journal of Medicine

Enspryng (satralizumab, RG6168, SA237)

Anti-IL-6 receptor humanized monoclonal antibody

Indication	Generalised Myasthenia Gravis
Phase/study	**Phase III** **Luminesce**
# of patients	N=240
Design	▪ **Group A:** Satralizumab plus SoC ▪ **Group B:** Placebo plus SoC
Primary endpoint	▪ Mean change from baseline in total MG-ADL score at week 24 in AChR+ population
Status	▪ FPI expected Q3 2021
CT Identifier	NCT04963270

MG-ADL= Myasthenia Gravis Activities of Daily Living; SoC=Standard of Care; AChR=Acetylcholine receptor

Gazyva (obinutuzumab)

Immunology development program

Indication	Lupus nephritis		Membranous nephropathy
Phase/study	**Phase II NOBILITY**	**Phase III REGENCY**	**Phase III MAJESTY**
# of patients	N=126	N=252	N=140
Design	▪ **ARM A:** Obinutuzumab 1000mg IV plus mycophenolate mofetil / mycophenolic acid ▪ **ARM B:** Placebo IV plus mycophenolate mofetil / mycophenolic acid	▪ **ARM A:** Obinutuzumab 1000 mg IV (six doses through Week 52) plus mycophenolate mofetil ▪ **ARM B:** Obinutuzumab 1000 mg IV (five doses through Week 52) plus mycophenolate mofetil ▪ **ARM C:** Placebo IV plus mycophenolate mofetil	▪ **ARM A:** Obinutuzumab 1000 mg IV dosed at baseline and weeks 0, 2, 24, and 26 on top of renin-angiotensin inhibitors ▪ **ARM B:** Tacrolimus treatment for 12 months
Primary endpoint	▪ Percentage of participants who achieve complete renal response (CRR)	▪ Percentage of participants who achieve complete renal response (CRR)	▪ Percentage of patients who achieve complete remission at week 104
Status	▪ Recruitment completed Q4 2017 ▪ Primary endpoint met Q2 2019 ▪ Breakthrough therapy designation granted by the FDA Q3 2019 ▪ Data presented at ASN and ACR 2019	▪ FPI Q3 2020	▪ FPI Q2 2021
CT Identifier	NCT02550652	NCT04221477	NCT04629248

In collaboration with Biogen
ASN=American Society of Nephrology; ACR=American College of Rheumatology

Actemra/RoActemra (RG-1569)

Interleukin 6 receptor inhibitor

Indication	Adult hospitalised with severe COVID-19 pneumonia	
Phase/study	**Phase III COVACTA[1]**	**Phase III REMDACTA[2]**
# of patients	N=450	N=650
Design	▪ **Arm A:** tocilizumab plus standard of care ▪ **Arm B:** placebo plus standard of care	▪ **Arm A:** remdesivir plus tocilizumab ▪ **Arm B:** remdesivir plus placebo
Primary endpoint	▪ Clinical status assessed using 7-Category Ordinal Scale (Day 28) ▪ Primary endpoint not met Q3 2020	▪ Time to hospital discharge or ready for discharge
Status	▪ FPI Q1 2020 ▪ Recruitment completed Q2 2020 ▪ Published in NEJM 2021 Feb 25;doi: 10.1056/NEJMoa2028700	▪ FPI Q2 2020 ▪ Recruitment completed Jan 2021 ▪ Study did not meet primary endpoint Q1 2021
CT Identifier	NCT04320615	NCT04409262

[1]In collaboration with US Biomedical Advanced Research and Development Authority (BARDA); [2]In collaboration with Gilead Sciences, Inc.

Actemra/RoActemra (RG-1569)

Interleukin 6 receptor inhibitor

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

NEJM=New England Journal of Medicine

Xolair

Humanized mAb that selectively binds to IgE

Indication	Food allergy
Phase/study	**Phase III** **OUtMATCH[1]**
# of patients	N=225
Design	▪ Xolair by subcutaneous injection either every 2 weeks or every 4 weeks for 16 to 20 weeks
Primary endpoint	▪ Number of participants who successfully consume ≥600 mg of peanut protein without dose-limiting symptoms
Status	▪ FPI July 2019
CT Identifier	NCT03881696

In collaboration with Novartis; [1] Sponsor of the study is the National Institute of Allergy and Infectious Diseases (NIAID)

Xofluza (baloxavir marboxil, RG6152, S-033188)

Small molecule, novel CAP-dependent endonuclease inhibitor

Indication	Influenza	
Phase/study	**Phase III** **miniSTONE 1 (0-1 year old)**	**Phase III** **miniSTONE 2 (1-12 years old)**
# of patients	N=30	N=176
Design	▪ Xofluza on Day 1 (based on body weight and age) in healthy pediatric patients from birth to <1 year with influenza-like symptoms	▪ Xofluza vs Tamiflu in healthy pediatric patients 1 to <12 years of age with influenza-like symptoms
Primary endpoint	▪ Safety	▪ Safety
Status	▪ FPI Q1 2019	▪ FPI Q4 2018 ▪ Recruitment completed Q1 2019 ▪ Primary endpoint met Q2 2019 ▪ Data presented at OPTIONS X 2019 ▪ Filed in US Q1 2020 ▪ Data published in Pediatric Infectious Disease 2020 Aug;39(8):700-705 ▪ Not approved in the US, determining path forward with the FDA
CT Identifier	NCT03653364	NCT03629184

In collaboration with Shionogi & Co., Ltd.

Xofluza (baloxavir marboxil, RG6152, S-033188)

Small molecule, novel CAP-dependent endonuclease inhibitor

Indication	Influenza	
Phase/study	**Phase III** **BLOCKSTONE**	**Phase IIIb** **CENTERSTONE**
# of patients	N=752	N=3,160
Design	▪ Post exposure prophylaxis to prevent disease onset in household contacts. Used after known exposure to infected person. ▪ Household contacts treated with Xofluza vs placebo	▪ Reduction of direct transmission of influenza from otherwise healthy patients to household contacts ▪ Patients treated with Xofluza vs placebo
Primary endpoint	▪ Percentage of household contacts who developed clinical influenza	▪ Percentage of household contacts who are PCR-positive for influenza by day 5 post randomization of index patients
Status	▪ Study met primary endpoint Q2 2019 ▪ Data presented at OPTIONS X 2019 ▪ Filed in US Q1 2020 ▪ Data published in *NEJM* 2020; 383:309-320 ▪ Approved in US Q4 2020 and EU Jan 2021	▪ FPI Q4 2019
CT Identifier	JapicCTI-184180	NCT03969212

In collaboration with Shionogi & Co., Ltd.
PCR=Polymerase chain reaction; *NEJM*=New England Journal of Medicine

Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

Spark

Ipatasertib (RG7440, GDC-0068)

Highly selective small molecule inhibitor of Akt

Indication	1L castration-resistant prostate cancer	Advanced prostate cancer and solid tumors	Prostate cancer previously treated with androgen receptor-targeted therapy
Phase/study	**Phase III IPATential150**	**Phase Ib**	**Phase Ib**
# of patients	N=1,100	N=54	N=50
Design	▪ **ARM A:** Ipatasertib plus abiraterone ▪ **ARM B:** Placebo plus abiraterone	▪ Ipatasertib plus rucaparib **Stage 1**: Dose escalation in advanced breast, ovarian and prostate cancer ▪ **Stage 2:** Dose expansion in prostate cancer	▪ Ipatasertib plus Tecentriq plus docetaxel
Primary endpoint	▪ Radiographic progression-free survival (rPFS) in patients with PTEN loss tumors and overall population	▪ Safety and efficacy	▪ Safety and efficacy
Status	▪ FPI Q2 2017 ▪ Recruitment completed Jan 2019 ▪ Study met co-primary endpoint in rPFS in patients with PTEN loss tumors Q2 2020 ▪ Data presented at ESMO 2020 ▪ Published in Lancet 2021; 398:131-142	▪ FPI Q2 2019	▪ FPI Q3 2020
CT Identifier	NCT03072238	NCT03840200	NCT04404140

In collaboration with Array BioPharma
ESMO=European Society for Medical Oncology

Ipatasertib (RG7440, GDC-0068)

Highly selective small molecule inhibitor of Akt

Indication	1L HR+ mBC
Phase/study	**Phase Ib/III** **IPATunity150**
# of patients	N=370
Design	▪ **ARM A:** Ipatasertib plus fulvestrant and palbociclib ▪ **ARM B:** Placebo plus fulvestrant and palbociclib
Primary endpoint	▪ Progression free survival in ITT and in patients with PIK3CA/AKT1/PTEN altered tumors
Status	▪ FPI Q4 2019 in Phase Ib part ▪ Data from Phase Ib part did not support move to Ph III
CT Identifier	NCT04060862

In collaboration with Array BioPharma

Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT

Indication	1L NSCLC PD-L1 TPS>50%	1L ES-SCLC	Stage III unresectable 1L NSCLC
Phase/study	**Phase III SKYSCRAPER-01**	**Phase III SKYSCRAPER-02**	**Phase III SKYSCRAPER-03**
# of patients	N=500-560	N=470	N=800
Design	▪ **Arm A:** Tiragolumab plus Tecentriq ▪ **Arm B:** Placebo plus Tecentriq	▪ **Arm A:** Tiragolumab plus Tecentriq, carboplatin and etoposide ▪ **Arm B:** Placebo plus Tecentriq, carboplatin and etoposide	▪ **Arm A:** Tiragolumab plus Tecentriq for up to 12 months ▪ **Arm B:** Durvalumab for up to 12 months
Primary endpoint	▪ Overall survival and progression free survival	▪ Overall survival and progression free survival	▪ Progression-free survival
Status	▪ FPI Q1 2020	▪ FPI Q1 2020 ▪ Recruitment completed Q1 2021	▪ FPI Q3 2020
CT Identifier	NCT04294810	NCT04256421	NCT04513925

NSCLC=Non-small cell lung cancer; ES-SCLC=Extensive stage small cell lung cancer

Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT

Indication	Metastatic and/or recurrent PD-L1+ cervical cancer	Neoadjuvant and adjuvant NSCLC	1L non-squamous NSCLC
Phase/study	**Phase II SKYSCRAPER-04**	**Phase II SKYSCRAPER-05**	**Phase II SKYSCRAPER-06**
# of patients	N=172	N=82	N=200
Design	▪ **Arm A:** Tiragolumab plus Tecentriq ▪ **Arm B:** Tecentriq	▪ **Arm A:** (PD-L1 high) neoadjuvant tiragolumab plus Tecentriq followed by adjuvant tiragolumab plus Tecentriq or adjuvant chemo ▪ **Arm B:** (PD-L1 all-comers) neoadjuvant tiragolumab plus Tecentriq plus chemo followed by adjuvant tiragolumab plus Tecentriq	▪ **Arm A:** Tiragolumab plus Tecentriq plus pemetrexed plus chemo followed by maintenance tiragolumab plus Tecentriq plus pemetrexed ▪ **Arm B:** Placebo plus pembrolizumab plus pemetrexed plus chemo followed by maintenance placebo plus pembrolizumab plus pemetrexed
Primary endpoint	▪ Objective Response Rate (ORR)	▪ Pathologic complete response, major pathological response and safety	▪ Objective response rate (ORR) and progression-free survival
Status	▪ FPI Q2 2020	▪ FPI Q2 2021	▪ FPI Q4 2020
CT Identifier	NCT04300647	NCT04832854	NCT04619797

NSCLC=Non-small cell lung cancer

Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT

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

NSCLC=Non-small cell lung cancer

Tiragolumab (anti-TIGIT, RG6058, MTIG7192A)

Monoclonal antibody targeting the immune checkpoint inhibitor TIGIT

Indication	Solid tumors	NSCLC	R/R Multiple Myeloma (MM) or R/R B-cell NHL
Phase/study	**Phase I**	**Phase II CITYSCAPE**	**Phase I**
# of patients	N=540	N=135	N=52
Design	▪ **Phase Ia:** Dose escalation and expansion of tiragolumab ▪ **Phase Ib:** Dose escalation and expansion of tiragolumab in combination with Tecentriq and/or other anti-cancer therapies	▪ **Arm A:** Tecentriq plus tiragolumab ▪ **Arm B:** Tecentriq monotherapy	▪ Phase Ia: Tiragolumab monotherapy ▪ Phase Ib: Tiragolumab plus daratumumab (r/r MM) or rituximab (r/r NHL)
Primary endpoint	▪ Safety, tolerability, PK variability and preliminary efficacy	▪ Overall response rate and progression-free survival	▪ Safety, tolerability, PK/PD and preliminary efficacy
Status	▪ FPI Q2 2016 ▪ Data presented at AACR 2020	▪ FPI Q3 2018 ▪ Recruitment completed Q2 2019 ▪ Data presented at ASCO 2020 and WCLC 2021 ▪ Breakthrough therapy designation granted by FDA Dec 2020	▪ FPI Q2 2019
CT Identifier	NCT02794571	NCT03563716	NCT04045028

NSCLC=Non-small cell lung cancer; r/r=Relapsed refractory; NHL=Non-Hodgkin's lymphoma; ASCO=American Society of Clinical Oncology; AACR=American Association for Cancer Research

Glofitamab (CD20-TCB, RG6026)

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

Indication	Relapsed or refractory Non-Hodgkin's lymphoma		Non-Hodgkin's lymphoma
Phase/study	**Phase I**	**Phase Ib**	**Phase Ib**
# of patients	N=700	N=140	Part I: 15-60 Part II: ~66-104
Design	**Cohort 1:** Single-agent dose escalation study ▪ Initial dose escalation ▪ Expansion cohort in r/r DLBCL ▪ Expansion cohort in r/r FL All patients will receive pretreatment with a single dose of Gazyva (1000mg) **Cohort 2:** glofitamab plus Gazyva (i.e. continuous treatment with Gazyva)	Dose escalation and expansion ▪ **Arm A:** glofitamab plus Tecentriq ▪ **Arm B:** glofitamab plus Polivy	▪ **Part I:** Dose-finding for the combination of glofitamab plus G/R CHOP in r/r indolent NHL ▪ **Part II:** Dose expansion glofitamab plus G/R-CHOP or R-CHOP in 1L DLBCL ▪ **Part III:** glofitamab plus R-CHP plus Pola
Primary endpoint	▪ Safety	▪ Safety	▪ Safety
Status	▪ FPI Q1 2017 ▪ Data presented at ASH 2018, ICML and ASH 2019; EHA and ASH 2020; ASCO, EHA and ICML 2021 ▪ Data published online 19 March 2021 J Clin Oncology DOI: 10.1200/JCO.20.03175	▪ FPI Q2 2018 ▪ Data presented at ASH 2019	▪ FPI Q1 2018
CT Identifier	NCT03075696	NCT03533283	NCT03467373

DLBCL=diffuse large B cell lymphoma; FL=Follicular lymphoma; ASH=American Society of Hematology; EHA=European Hematology Association; ICML=International Conference on Malignant Lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine and prednisone; R=Rituxan/MabThera; G=Gazyva

Glofitamab (CD20-TCB, RG6026)

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

Indication	Relapsed/refractory DLBCL and High-Grade Large B-Cell Lymphoma	2L+ SCT-ineligible DLBCL
Phase/study	**Phase Ib**	**Phase III STARGLO**
# of patients	N=20	N=270
Design	▪ Glofitamab plus gemcitabine and oxaliplatin, followed by up to 4 cycles of glofitamab monotherapy ▪ A single dose of obinutuzumab will be administered 7 days prior to the first dose of glofitamab	▪ **Arm A:** glofitamab plus gemcitabine and oxaliplatin, followed by up to 4 cycles of glofitamab monotherapy ▪ **Arm B:** Rituxan in combination with gemcitabine and oxaliplatin A single dose of obinutuzumab will be administered 7 days prior to the first dose of glofitamab
Primary endpoint	▪ Safety	▪ Overall survival
Status	▪ FPI Q2 2020	▪ FPI Q1 2021
CT Identifier	NCT04313608	NCT04408638

DLBCL=diffuse large B cell lymphoma; SCT=stem cell transplant

Mosunetuzumab (CD20/CD3, RG7828)

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

Indication	3L+ FL, 3L+ DLBCL & other R/R NHL	1L DLBCL	R/R DLBCL
Phase/study	**Phase I**	**Phase Ib/II**	**Phase Ib**
# of patients	N=746	N=160	N=262
Design	▪ Dose escalation study of mosunetuzumab as single agent and in combination with Tecentriq ▪ Expansion cohorts for r/r FL, r/r DLBCL and subcutaneous in r/r NHL	▪ Mosunetuzumab plus CHOP ▪ Mosunetuzumab plus CHP plus polatuzumab vedotin ▪ Mosunetuzumab plus CHP-polatuzumab vedotin ▪ Rituximab plus CHP-polatuzumab vedotin	▪ Mosunetuzumab plus polatuzumab vedotin
Primary endpoint	▪ Safety, tolerability, dose/schedule, PK, and response rates	▪ Safety/tolerability and response	▪ Safety/tolerability and response
Status	▪ FPI Q3 2015 ▪ Data in r/r NHL presented at ASH 2018 and 2019, and in r/r FL at ASH 2020 ▪ BTD granted by FDA Q2 2020	▪ FPI Q1 2019 ▪ Data for M+CHOP presented at ASH 2020	▪ FPI Q3 2018 ▪ Initial data presented at ASCO 2021
CT Identifier	NCT02500407	NCT03677141	NCT03671018

FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma; r/r=relapsed/refractory; NHL=non-Hodgkin's lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone; CHP=cyclophosphamide, doxorubicin, and prednisone); ASH=American Society of Hematology; R=Rituximab

Mosunetuzumab (CD20/CD3, RG7828)

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

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

FL=follicular lymphoma; DLBCL=diffuse large B cell lymphoma; r/r=relapsed/refractory

Inavolisib (RG6114, GDC-0077)

A potent, orally available, and selective PI3Kα inhibitor

Indication	PIK3CA-mutant HR+ mBC	PIK3CA mutant solid tumors and metastatic ER+ HER2-neg breast cancer
Phase/study	**Phase III INAVO120**	**Phase I**
# of patients	N=400	N=156
Design	▪ **Arm A:** GDC-0077 plus palbociclib plus fulvestrant ▪ **Arm B:** Placebo plus palbociclib plus fulvestrant	Monotherapy and in combination with SoC (letrozole; letrozole plus palbociclib; fulvestrant) ▪ **Stage 1:** Dose escalation ▪ **Stage 2:** Expansion
Primary endpoint	▪ Progression-free survival	▪ Safety, tolerability and PK
Status	▪ FPI Q1 2020	▪ FPI Q4 2016 ▪ Preclinical/molecule discovery data presented at AACR 2017 ▪ Data presented at SABCS 2019 and 2020
CT Identifier	NCT04191499	NCT03006172

AACR=American Association for Cancer Research; SABCS=San Antonio Breast Cancer Symposium

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

A selective estrogen receptor degrader or downregulator

Indication	ER+ HER2-neg metastatic breast cancer	ER+ HER2-neg Stage I-III operable breast cancer	Neoadjuvant ER+ breast cancer
Phase/study	**Phase I**	**Phase I**	**Phase II coopERA Breast Cancer**
# of patients	N=220	N=75	N=215
Design	▪ Dose escalation and expansion at recommended phase II dose (RP2D) ▪ Single agent and in combination with palbociclib and/or luteinizing hormone–releasing hormone (LHRH) agonist	▪ Open-label, pre-operative administration ▪ Dose escalation	▪ **ARM A:** Single agent followed by combo with palbociclib ▪ **ARM B:** anastrazole followed by anastrazole plus palbociclib
Primary endpoint	▪ Safety	▪ Safety, tolerability and PK/PD	▪ Safety, tolerability and PK/PD
Status	▪ FPI Q4 2017 ▪ Data presented at SABCS 2019, ASCO 2020 and ASCO 2021	▪ FPI Q3 2019 ▪ Data presented at ASCO 2021	▪ FPI Q3 2020
CT Identifier	NCT03332797	NCT03916744	NCT04436744

SABCS=San Antonio Breast Cancer Symposium; ASCO=American Society of Clinical Oncology

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

A selective estrogen receptor degrader or downregulator

Indication	2L/3L ER+/HER2-negative metastatic breast cancer	1L ER+ metastatic breast cancer	Adjuvant ER+ breast cancer
Phase/study	**Phase II acelERA Breast Cancer**	**Phase III persevERA Breast Cancer**	**Phase III lidERA Breast Cancer**
# of patients	N=300	N=978	N=4,100
Design	▪ **Arm A:** giredestrant monotherapy ▪ **Arm B:** endocrine monotherapy (fulvestrant or aromatase inhibitor)	▪ **Arm A:** giredestrant plus palbociclib ▪ **Arm B:** letrozole plus palbociclib	▪ **Arm A:** giredestrant monotherapy ▪ **Arm B:** tamoxifen or aromatase inhibitor
Primary endpoint	▪ Progression-free survival	▪ Progression-free survival	▪ Invasive disease-free survival (IDFS)
Status	▪ FPI Q4 2020	▪ FPI Oct 2020	▪ FPI expected Q3 2021
CT Identifier	NCT04576455	NCT04546009	NCT04576455

rhPTX-2 (RG6354)

Recombinant human innate immunity protein pentraxin-2

Indication	Myelofibrosis
Phase/study	**Phase II**
# of patients	N=125
Design	▪ Multiple dose study of rhPTX-2
Primary endpoint	▪ Bone marrow response rate
Status	▪ Study completed Q1 2021
CT Identifier	NCT01981850

rhPTX-2 (RG6354)

Recombinant human innate immunity protein pentraxin-2

Indication	Idiopathic pulmonary fibrosis (IPF)	
Phase/study	**Phase II**	**Phase III STARSCAPE**
# of patients	N=117	N=658
Design	▪ Randomized, double-blind, placebo-controlled trial: 4-week screening period, 24-week randomized treatment period, 4-week follow-up visit (week 28) ▪ rhPTX-2 at days 1, 3 and 5 then every 4 weeks vs placebo	▪ Randomized, double-blind, placebo-controlled trial: 4-week screening period, 52-week randomized treatment period ▪ rhPTX-2 at days 1, 3 and 5 then every 4 weeks vs placebo
Primary endpoint	▪ Least-squares mean change in forced vital capacity (FVC) percentage of predicted value from baseline to week 28	▪Absolute change from baseline to week 52 in FVC
Status	▪ Study met primary endpoint ▪ Data published in JAMA 2018;319(22):2299-2307 and Lancet Respir Med 2019 Aug;7(8):657-664	▪ FPI Q1 2021
CT Identifier	NCT02550873	NCT04552899

JAMA=Journal of the American Medical Association

Fenebrutinib (RG7845, GCD-0853)

Highly selective and reversible (noncovalent) bruton tyrosine kinase

Indication	Primary progressive multiple sclerosis (PPMS)	Relapsing multiple sclerosis (RMS)	
Phase/study	**Phase III FENtrepid**	**Phase III FENhance 1**	**Phase III FENhance 2**
# of patients	N=946	N=734	N=734
Design	▪ **ARM A:** Fenebrutinib twice daily oral ▪ **Arm B:** Ocrelizumab 2x300 mg IV every 24 weeks	▪ **Arm A:** Fenebrutinib twice daily oral ▪ **Arm B:** Teriflunomide once daily oral	▪ **Arm A:** Fenebrutinib twice daily oral ▪ **Arm B:** Teriflunomide once daily oral
Primary endpoint	▪ Time to onset of composite 12-week confirmed disability progression (cCDP12)	▪ Time to onset of composite 12-week confirmed disability progression (cCDP12) and annualized relapse rate	▪ Time to onset of composite 12-week confirmed disability progression (cCDP12) and annualized relapse rate
Status	▪ FPI Q4 2020	▪ FPI Q1 2021	▪ FPI Q1 2021
CT Identifier	NCT04544449	NCT04586023	NCT04586010

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** **BERGAMOT** Induction and maintenance study	**Phase III** **JUNIPER** Open label extension study for BERGAMOT
# of patients	N=1,150	N=900
Design	▪ **ARM A:** Etrolizumab SC 210 mg (induction only) ▪ **ARM B:** Etrolizumab SC 105 mg and maintenance ▪ **ARM C:** Placebo	▪ Etrolizumab SC 105mg q4w
Primary endpoint	▪ Induction and maintenance of clinical remission	▪ Safety
Status	▪ FPI Q1 2015 ▪ Cohort 1 data presented at UEGW 2017 ▪ Recruitment completed Q2 2021	▪ FPI Q2 2015
CT Identifier	NCT02394028	NCT02403323

UEGW=United European Gastroenterology Week

Crovalimab (RG6107; SKY59)

A humanized monoclonal antibody against complement C5

Indication	Paroxysmal nocturnal hemoglobinuria (PNH)
Phase/study	**Phase I/II** **COMPOSER**
# of patients	N=59
Design	Healthy volunteers and treatment naïve and pretreated patients with PNH: ▪ **Part 1:** single ascending dose study in healthy subjects ▪ **Part 2:** intra-patient single ascending dose study in PNH patients ▪ **Part 3:** Multiple-dose study in PNH patients ▪ **Part 4:** Dose confirmation in PNH patients
Primary endpoint	▪ Safety, PK, PD
Status	▪ Part 1: FPI Q4 2016 ▪ Part 2/3: FPI Q2 2017 ▪ Part 4: FPI Q2 2019 ▪ Nonclinical data published in Scientific Reports 2017 Apr; 7(1):1080 ▪ Data presented for Part 2 and 3 at ASH 2018 and 2019
CT Identifier	NCT03157635

In collaboration with Chugai
ASH=American Society of Hematology

Crovalimab (RG6107; SKY59)

A humanized monoclonal antibody against complement C5

Indication	Atypical Hemolytic Uremic Syndrome (aHUS)	Sickle Cell Disease (SCD) Acute treatment
Phase/study	**Phase III** **COMMUTE-a**	**Phase I** **CROSSWALK-a**
# of patients	N=90	N=30
Design	Single-arm study of aHUS patients ▪ Cohort 1: not previously treated with C5i ▪ Cohort 2: switching from C5i (Cohort 2) ▪ Cohort 3: known C5 polymorphism	▪ Cohort 1: Crovalimab ▪ Cohort 2: Placebo
Primary endpoint	▪ Proportion of patients with complete TMA response anytime between baseline and week 25 (cohort 2: maintenance of TMA control from baseline through week 25)	▪ Safety
Status	▪ FPI expected Q3 2021	▪ FPI expected Q3 2021
CT Identifier	NCT04861259	NCT04912869

In collaboration with Chugai
TMA=thrombotic microangiopathies

Crovalimab (RG6107; SKY59)

A humanized monoclonal antibody against complement C5

Indication	Paroxysmal Nocturnal Hemoglobinuria (PNH) patients switching from a C5 inhibitor	Paroxysmal Nocturnal Hemoglobinuria (PNH) C5 inhibitor naive patients	Paroxysmal Nocturnal Hemoglobinuria (PNH) C5 inhibitor naive patients (China only)
Phase/study	**Phase III COMMODORE 1**	**Phase III COMMODORE 2**	**Phase III COMMODORE 3**
# of patients	N=250	N=200	N=50
Design	▪ **Arm A:** Crovalimab ▪ **Arm B:** Eculizumab ▪ **Arm C:** Patients switching to crovalimab from ravulizumab, higher than labelled doses of eculizumab & C5 SNP patients (descriptive-arm)	▪ **Arm A:** Crovalimab ▪ **Arm B:** Eculizumab	▪ Crovalimab loading dose IV on Day 1, followed by weekly crovalimab subcutaneous doses for 4 weeks
Primary endpoint	▪ Non-inferiority of crovalimab compared to eculizumab - mean % change in LDH level (measure of haemolysis) from baseline to week 25	▪ Non-inferiority of crovalimab compared to eculizumab: - % pts with transfusion avoidance from baseline through week 25 - % pts with haemolysis control, as measured by LDH <=1.5ULN from week 5-25	▪ Percentage of patients with transfusion avoidance from baseline through week 25 ▪ Mean percentage of participants with hemolysis control (week 5 through week 25)
Status	▪ FPI Q3 2020	▪ FPI Q4 2020	▪ FPI Q1 2021
CT Identifier	NCT04432584	NCT04434092	NCT04654468

In collaboration with Chugai
LDH=Lactate Dehydrogenase

Crenezumab (RG7412)

Humanized mAb targeting all forms of Aβ

Indication	Alzheimer's Prevention Initiative (API) Colombia
Phase/study	**Phase II** Cognition study
# of patients	N=252
Design	▪ **ARM A:** PSEN1 E280A mutation carriers receive crenezumab SC ▪ **ARM B:** PSEN1 E280A mutation carriers receive placebo ▪ **ARM C:** non-mutation carriers receive placebo
Primary endpoint	▪ Change on Alzheimer's Prevention Initiative (API) Composite Cognitive Test total score at 260 weeks treatment
Status	▪ FPI Q4 2013 ▪ Recruitment completed Q1 2017
CT Identifier	NCT01998841

In collaboration with AC Immune
Aβ=amyloid-beta

Gantenerumab (RG1450)

Fully human mAb binding aggregated forms of Aβ

Indication	Prodromal to mild Alzheimer's disease	
Phase/study	**Phase III GRADUATE 1**	**Phase III GRADUATE 2**
# of patients	N=1,016	N=1,016
Design	104-week subcutaneous treatment period: ▪ **ARM A:** Gantenerumab ▪ **ARM B:** Placebo	104-week subcutaneous treatment period: ▪ **ARM A:** Gantenerumab ▪ **ARM B:** Placebo
Primary endpoint	▪ Change in CDR-SOB at 27 months	▪ Change in CDR-SOB at 27 months
Status	▪ FPI Q2 2018 ▪ Recruitment completed Q2 2020	▪ FPI Q3 2018 ▪ Recruitment completed Q2 2020
CT Identifier	NCT03443973	NCT03444870

In collaboration with MorphoSys AG

Aβ=amyloid-beta; CDR-SOB=Clinical Dementia Rating Scale Sum of Boxes

Gantenerumab (RG1450)

Fully human mAb binding aggregated forms of Aβ

Indication	Prodromal Alzheimer's disease	Mild Alzheimer's disease
Phase/study	**Phase II/III SCarlet RoAD**	**Phase III Marguerite RoAD**
# of patients	N=799	N=389
Design	104-week subcutaneous treatment period: ▪ **ARM A:** Gantenerumab (225 mg) ▪ **ARM B:** Gantenerumab (105 mg) ▪ **ARM C:** Placebo	104-week subcutaneous treatment period: ▪ **ARM A:** Gantenerumab ▪ **ARM B:** Placebo
Primary endpoint	▪ Change in CDR-SOB at 2 years ▪ Sub-study: change in brain amyloid by PET at 2 years	▪ Change in ADAS-Cog and CDR-SOB at 2 years (co-primary)
Status	▪ Phase I PET data: *Archives of Neurology*, 2012 Feb;69(2):198-207 ▪ Recruitment completed Q4 2013 ▪ Dosing stopped due to futility Q4 2014 ▪ FPI in open label extension study Q4 2015 ▪ Published in Alzheimers Res Ther 2017 Dec 8;9(1):95	▪ FPI Q1 2014 ▪ Recruitment stopped Q4 2015 ▪ FPI Q1 2016 for open label extension
	▪ 36 OLE data published in J Prev Alzheimers Dis 2021;8(1):3-6	
CT Identifier	NCT01224106	NCT02051608

In collaboration with MorphoSys AG

Aβ=amyloid-beta; CDR-SOB=Clinical Dementia Rating Scale Sum of Boxes; PET= positron emission tomography; ADAS-cog=Alzheimer's Disease Assessment Scale cognitive subscale; AAIC=Alzheimer's Association International Conference; CTAD=Clinical Trials on Alzheimer's Disease; AD/PD=Alzheimer's & Parkinson's Diseases Congress; AAN=American Academy of Neurology; MRI=Magnetic resonance imaging

Tominersen (RG6042, HTT ASO)

Antisense oligonucleotide (ASO) targeting human HTT mRNA

Indication	Huntington's disease	
Phase/study	**Phase I/IIa**	**Phase II OLE**
# of patients	N=46	N=46
Design	▪ Multiple ascending doses of RG6042 administered intrathecally to adult patients with early manifest Huntington's Disease	▪ Patients from phase I are enrolled into OLE
Primary endpoint	▪ Safety, tolerability, PK and PD	▪ Longer term safety, tolerability, PK, PD.
Status	▪ FPI Q3 2015 ▪ Data presented at CHDI 2018 and AAN 2018 ▪ PRIME designation granted 2018 ▪ Published in *NEJM* 2019; 380:2307-2316	▪ FPI Q1 2018 ▪ PK/PD data presented at AAN 2019 ▪ Update presented at CHDI 2020 ▪ Study completed, patients moved to GEN-EXTEND OLE
CT Identifier	NCT02519036	NCT03342053

In collaboration with Ionis Pharmaceuticals
AAN=American Academy of Neurology; *NEJM*=New England Journal of Medicine

Tominersen (RG6042, HTT ASO)

Antisense oligonucleotide (ASO) targeting human HTT mRNA

Indication	Huntington's disease	
Phase/study	**Phase III** **Generation HD1**	**Phase III** **GEN-EXTEND**
# of patients	N=791	N=1,050
Design	▪ **ARM A:** RG6042 120mg bimonthly ▪ **ARM B:** RG6042 120mg every four months ▪ **ARM C:** Placebo bimonthly	Open-Label Extension study in patients participating in prior Roche and Genentech sponsored studies ▪ **Arm A:** RG6042 120mg bimonthly ▪ **Arm B:** RG6042 120mg every four months
Primary endpoint	▪ cUHDRS globally ▪ TFC USA only	▪ Long term safety, tolerability
Status	▪ FPI Jan 2019 ▪ Q1 2019 protocol modified to allow for bi-monthly vs four-monthly dosing, FPI for new protocol July 2019 ▪ Recruitment completed Q2 2020 ▪ Dosing stopped in Q1 2021 based on IDMC recommendation regarding the potential benefit/risk profile for study participants. No new safety signals identified.	▪ FPI April 2019 ▪ Dosing stopped in Q1 2021
CT Identifier	NCT03761849	NCT03842969

In collaboration with Ionis Pharmaceuticals

cUHDRS=composite Unified Huntington's Disease Rating Scale; TFC=total function capacity; IDMC=Independent Data Monitoring Committee

Faricimab (RG7716)

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

Indication	Neovascular age related macular degeneration (nAMD)		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 ▪ **ARM B:** 1.5 mg faricimab, q4w ▪ **ARM C:** 6mg faricimab, q4w ▪ **ARM D:** 6mg faricimab, q4w / q8w ▪ **ARM E:** SoC q4w x 3 doses, switch group to 6 mg faricimab q4w	▪ **ARM A:** SoC (Lucentis), q4w ▪ **ARM B:** 6mg faricimab, q>8w (short interval duration) ▪ **ARM C:** 6mg faricimab, q>8w (long interval duration)	▪ **ARM A:** SoC (Lucentis), 0.3 mg q4w ▪ **ARM B:** 1.5mg faricimab, q4w ▪ **ARM C:** 6mg faricimab, 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 ▪ Recruitment completed Q1 2017 ▪ Data presented at Retina Society 2018 ▪ Data published *JAMA Ophthalmol* 2020; 138(9):955-963	▪ FPI Q1 2017 ▪ Recruitment completed Q1 2017 ▪ Data presented at Retina Society 2018 (24 week data) and AAO 2018 (full data) ▪ Data published *JAMA Ophthalmol* 2020; 138(9):964-972	▪ FPI Q2 2016 ▪ Recruitment completed Q1 2017 ▪ Data presented at Angiogenesis 2018 and Retina Society 2018 ▪ Data published in Ophthalmology 2019 Aug;126(8):1155-1170
CT Identifier	NCT02484690	NCT03038880	NCT02699450

BCVA=best corrected visual acuity; SoC=standard of care; AAO=American Academy of Ophthalmology

Faricimab (RG7716)

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

Indication	Center-involving diabetic macular edema (CI-DME)	
Phase/study	**Phase III YOSEMITE**	**Phase III RHINE**
# of patients	N=940	N=951
Design	▪ **ARM A:** Faricimab q8w ▪ **ARM B:** Faricimab PTI up to q16w ▪ **ARM C:** Aflibercept, q8w	▪ **ARM A:** Faricimab q8w ▪ **ARM B:** Faricimab PTI up to q16w ▪ **ARM C:** Aflibercept, q8w
Primary endpoint	▪ Change from baseline in BCVA at 1 year	▪ Change from baseline in BCVA at 1 year
Status	▪ FPI Q3 2018 ▪ Recruitment completed Q3 2019 ▪ Study met primary endpoint Q4 2020 ▪ Data presented at Angiogenesis 2021	▪ FPI Q4 2018 ▪ Recruitment completed Q3 2019 ▪ Study met primary endpoint Q4 2020 ▪ Data presented at Angiogenesis 2021
	▪ Filed in US and EU Q2 2021	
CT Identifier	NCT03622580	NCT03622593

PTI=Personalized Treatment Interval; BCVA=best corrected visual acuity

Faricimab (RG7716)

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

Indication	Neovascular age related macular degeneration (nAMD)	
Phase/study	**Phase III TENAYA**	**Phase III LUCERNE**
# of patients	N=671	N=658
Design	▪ **ARM A:** Faricimab 6.0mg Q16 flex after 4 initiating doses (IDs) ▪ **ARM B:** Aflibercept 2.0mg Q8 after 3 IDs	▪ **ARM A:** Faricimab 6.0mg Q16 flex after 4 initiating doses (IDs) ▪ **ARM B:** Aflibercept 2.0mg Q8 after 3 IDs
Primary endpoint	▪ Change from baseline in BCVA Week 40, 44 & 48	▪ Change from baseline in BCVA Week 40, 44 & 48
Status	▪ FPI Q1 2019 ▪ Recruitment completed Q4 2019 ▪ Study met primary endpoint Jan 2021 ▪ Data presented at Angiogenesis 2021	▪ FPI Q1 2019 ▪ Recruitment completed Q4 2019 ▪ Study met primary endpoint Jan 2021 ▪ Data presented at Angiogenesis 2021
	▪ Filed in US and EU Q2 2021	
CT Identifier	NCT03823287	NCT03823300

BCVA=best corrected visual acuity

Faricimab (RG7716)

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

Indication	Macular edema secondary to branch retinal vein occlusion	Macular edema secondary to central retinal vein occlusion
Phase/study	**Phase III BALATON**	**Phase III COMINO**
# of patients	N=570	N=750
Design	▪ **ARM A:** Faricimab, q4w/PTI ▪ **ARM B:** Aflibercept, q4w	▪ **ARM A:** Faricimab, q4w/PTI ▪ **ARM B:** Aflibercept, q4w
Primary endpoint	▪ Change from baseline in BCVA at week 24	▪ Change from baseline in BCVA at week 24
Status	▪ FPI Q1 2021	▪ FPI Q1 2021
CT Identifier	NCT04740905	NCT04740931

PTI=Personalized Treatment Interval; BCVA=best corrected visual acuity

Port Delivery System with ranibizumab

First eye implant to achieve sustained delivery of a biologic medicine

Indication	wAMD		
Phase/study	**Phase III Archway**	**Phase II+III extension Portal**	**Phase IIIb Velodrome**
# of patients	N=418	N=500	N=442
Design	▪ **ARM A:** PDS with ranibizumab every 24 weeks ▪ **ARM B:** Intravitreal ranibizumab every 4 weeks	▪ Patients from LADDER or Archway will receive refills of 100 mg/mL ranibizumab q24w (patients without the PDS will receive the PDS and subsequent refills)	▪ **ARM A:** PDS with ranibizumab every 36 weeks ▪ **ARM B:** PDS with ranibizumab every 24 weeks
Primary endpoint	▪ Change in BCVA from baseline at the average of week 36 and week 40	▪ Safety and long term efficacy	▪ Change in BCVA from baseline averaged over weeks 68 and 72
Status	▪ FPI Q3 2018 ▪ Recruitment completed Q2 2019 ▪ Study met primary endpoint Q2 2020 ▪ Primary endpoint data presented at ASRS 2020 and 44/48 week data at Angiogenesis 2021 ▪ Filed in US (priority review) and EU Q2 2021	▪ FPI Q3 2018	▪ FPI achieved July 2021
CT Identifier	NCT03677934	NCT03683251	NCT04657289

BCVA=best corrected visual acuity; wAMD=wet age-related macular degeneration; ASRS=American Society of Retinal Specialists

Port Delivery System with ranibizumab

First eye implant to achieve sustained delivery of a biologic medicine

Indication	DME	Diabetic retinopathy without center-involved diabetic macular edema
Phase/study	**Phase III Pagoda**	**Phase III Pavilion**
# of patients	N=545	N=160
Design	▪ **ARM A:** PDS with ranibizumab every 24 weeks ▪ **ARM B:** Intravitreal ranibizumab every 4 weeks	▪ **Arm A:** Intravitreal ranibizumab (X2) followed by PDS implant (refill every 36 weeks) ▪ **Arm B:** Q4W comprehensive clinical monitoring until participants receive PDS (refill every 36 weeks)
Primary endpoint	▪ Change in BCVA from baseline at the average of week 48 and week 52	▪ Percentage of participants with a ≥2-step improvement from baseline on the ETDRS-DRSS at Week 52
Status	▪ FPI Q3 2019 ▪ Recruitment completed Q2 2021	▪ FPI Q3 2020
CT Identifier	NCT04108156	NCT04503551

DME=diabetic macular edema; BCVA=best corrected visual acuity; ETDRS=Early Treatment Diabetic Retinopathy Study; DRSS=Diabetic Retinopathy Severity Scale

AT-527 (RG6422)

Viral RNA polymerase inhibitor

Indication	Non-hospitalised adult patients with mild or moderate COVID-19	Adult patients SARS-COV-2 positive in an outpatient setting
Phase/study	**Phase II** **MOONSONG**	**Phase III** **MORNINGSKY**
# of patients	N=220	N=1,386
Design	▪ **ARM A:** AT-527 ▪ **ARM B:** Placebo	▪ **Arm A:** AT-527 550mg BID ▪ **Arm B:** Placebo
Primary endpoint	▪ Change from baseline in the amount of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus RNA	▪ Time to symptom alleviation
Status	▪ FPI Q1 2021	▪ FPI Q2 2021
CT Identifier	NCT04709835	NCT04889040

In collaboration with Atea Pharmaceuticals

Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

Spark

pRED oncology development programs –1

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Oncology					
TYRP1 x CD3 (RG6232)	Melanoma	I	210	FPI Q4 2020	NCT04551352
FAP-4-1BBL (RG7827)	Solid tumors	I	~150	FPI Q2 2018 Data presented at ESMO 2020 Recruitment completed Q2 2021	
	3L+ MSS mCRC	I	80	FPI July 2021 Combination study with cibisatamab	NCT04826003
CD19-4-1BBL (RG6076)	R/R B cell non-Hodgkin's lymphoma	I	207	Part I: FPI Q3 2019; Part II: FPI Q3 2020	NCT04077723
PD1-IL2v (RG6279)	Solid tumors	I	440	FPI Q2 2020	NCT04303858
cibisatamab (CEA x CD3, RG7802)	CEA-positive solid tumors	Ia	149	FPI Q4 2014 Data presented at ASCO 2017	NCT02324257
		Ib	228	FPI Q1 2016 Data presented at ASCO 2017	NCT02650713
	3L+ MSS mCRC	Ib	46	FPI Q1 2019	NCT03866239
PD1-TIM3 (RG7769)	Solid tumors	Ia/b	280	FPI Q4 2018	NCT03708328
PD1-LAG3 (RG6139)	Solid tumors	I	320	FPI Q4 2019	NCT04140500
PD1-LAG3, PD1-TIM3 (RG6139, RG7769)	Solid tumors	II	255	FPI Q2 2021 3-arm, randomized, compared with nivolumab	NCT04785820 TALIOS

pRED oncology development programs –2

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Oncology					
CD25 (RG6292)	Solid tumors	I	110	FPI Q4 2019	NCT04158583
	Advanced and metastatic solid tumors	I	160	FPI Jan 2021	NCT04642365
TLR7 agonist (4) (RG6115)	Hepatocellular carcinoma	I	100	FPI July 2020	NCT04338685
NME (RG6234)	Multiple myeloma	I	240	FPI Q4 2020	NCT04557150
HLA-A2-WT1 x CD3 (RG6007)	AML	I	160	FPI Q4 2020	NCT04580121
FAP-CD40 (RG6189)	Solid tumors	I	180	FPI Q2 2021	

pRED neuroscience development programs

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Neuroscience					
Brain Shuttle gantenerumab (RG6102)	Alzheimer's disease	II	~120	FPI Q1 2021	NCT04023994
ralmitaront (partial TAAR1 agonist, RG7906)	Schizophrenia	II	36	FPI Q4 2018; Recruitment completed Q3 2019	
		II	247	FPI Q4 2019	NCT03669640 (TWAIN I)
		II	308	FPI Q3 2020	NCT04512066 (TWAIN II)
prasinezumab[1] (anti-αSynuclein, RG7935, PRX002)	Parkinson's disease	II	316	Study did not meet its primary objective, but showed signals of efficacy on core motor signs in PD. Key study data presented at MDS Sep 2020 and ADPD 2021. Part 3 (OLE) started	NCT03100149 (PASADENA)
		IIb	575	FPI Q2 2021	NCT04777331 (PADOVA)
GABA-Aa5 PAM (RG7816)	Autism spectrum disorder	II	105	FPI Q1 2021	NCT04299464 (Aurora)
NME (RG7637)	Neurodevelopmental disorders	I	80	FPI July 2020	NCT04475848
UBE3A LNA (RG6091)	Angelman syndrome	I	66	FPI Q3 2020	NCT04428281
NME (RG6182)	Neurodegenerative disorder	I	30	FPI Q4 2020	

Partner: [1]Prothena

pRED immunology and ophthalmology development programs

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Immunology					
IgG-IL2 (RG7835)	Ulcerative Colitis	Ib	65	FPI Q2 2019	NCT03943550
	Autoimmune diseases	II	84	FPI Q2 2021	NCT04790916 GOLDSTONE
Ophthalmology					
NME (RG6179)[1]	DME	I	50	FPI July 2019	
VEGF-Ang2 DutaFab (RG6120)	nAMD	I	50	FPI Q4 2020	NCT04567303
NME (RG7774)	Retinal disease	II	180	FPI Q2 2020	NCT04265261 (CANBERRA)

Partner: [1]Sesen Bio

pRED infectious diseases development programs

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Infectious Diseases					
TLR7 agonist (3) (RG7854)	Chronic hepatitis B	I	150	FPI Q4 2016 Data presented at APASL 2019	NCT02956850
CpAM (RG7907)	Chronic hepatitis B	I/II	192	FPI Q4 2016 Data presented at EASL 2018, 2019 & 2020 Part 1 (healthy volunteers) published in Antimicrob Agents Chemother DOI: 10.1128/AAC.01323-20	NCT02952924
		I	22	FPI Q1 2021 Recruitment completed Q2 2021	NCT04729309
TLR7 agonist (3)/ CpAM/siRNA (RG7854/RG7907/RG6346)	Chronic hepatitis B	II	65	FPI July 2020	NCT04225715 (PIRANGA)
PDL1 LNA (RG6084)	Chronic hepatitis B	I	35	FPI Q1 2019 Part Ia complete, part Ib initiated	
Abx MCP (RG6006)	A. baumannii infections	I	168	FPI Q4 2020	NCT04605718

Abx MCP=antibiotic macrocyclic peptide

Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

Spark

gRED oncology development programs

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Oncology					
KRAS G12C (RG6330)	Metastatic solid tumors with KRAS G12C mutation	I	108	FPI Q3 2020	NCT04449874
cevostamab (anti-FcRH5 x CD3; RG6160)	R/R multiple myeloma	I	300	FPI Q3 2017	NCT03275103
HER2 x CD3 (RG6194)	Metastatic HER2-expressing cancers	I	440	FPI Q2 2018	NCT03448042
NME (RG6286)	Locally advanced or metastatic colorectal cancer	I	67	FPI Q3 2020	NCT04468607
IL15/IL15Ra-Fc (RG6323)[2]	Solid tumors	I/II	250	FPI Q1 2020	NCT04250155
autogene cevumeran (Individualized Neoantigen-Specific Therapy (iNeST); RG6180)[3]	Solid tumors	Ia/IIb	770	FPI Q4 2017 Data presented at AACR 2020	NCT03289962
	1L advanced melanoma	II	132	FPI Q1 2019	NCT03815058 (IMcode001)
SHP2i (RG6344)	solid tumors	Ia	~50	FPI Q1 2020	NCT04252339

Partner: [1]Affimed, [2]Xencor, [3]BioNTech

gRED immunology and ophthalmology development programs

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Immunology					
efmarodocokin alfa (IL-22Fc, RG7880)	Inflammatory diseases	Ib	90	FPI Q2 2016	NCT02749630
	Inflammatory bowel disease	II	270	FPI Q4 2018	NCT03558152
	aGVHD	Ib	24	FPI Q4 2020	NCT04539470
NME (RG6287, GDC-8264)	Inflammatory bowel disease	I	114	FPI Q1 2020	
Anti-tryptase (RG6173, MTPS9579A)	Asthma	I	70	FPI Q1 2018	
	Asthma	IIa	160	FPI Q4 2019	NCT04092582
NME (RG6315, MTBT1466A)	Immunologic disorders	I	~24	FPI Q3 2020	
Ophthalmology					
HtrA1 (RG6147)	Geographic atrophy	II	360	FPI Q2 2019	NCT03972709 (GALLEGO)
NME (RG6312)	Geographic atrophy	Ia	63	FPI Q4 2020	NCT04615325

Partner: [1]Amgen, [2]Amgen for ST2 MAb

gRED neuroscience and metabolic diseases development programs

Molecule	Indication	Phase	# of patients	Status	CT Identifier
Neuroscience					
Semorinemab (RG6100)[1]	Prodromal to mild Alzheimer's disease	II	457	FPI Q4 2017 Primary endpoint not met Q3 2020 Data at CTAD 2020	NCT03289143 (TAURIEL)
	Moderate Alzheimer's disease	II	267	FPI Q1 2019 Recruitment completed Q3 2020	NCT03828747 (LAURIET)
Metabolic Diseases					
FGFR1 x KLB (RG7992)	Metabolic diseases	Ia	79	FPI Q4 2015 Recruitment completed Q1 2017	NCT02593331
	Metabolic diseases	Ib	140	FPI Q1 2017 Recruitment completed Q2 2019	NCT03060538
	NASH	II	260	FPI Q3 2020	NCT04171765
NME (RG6338)	Metabolic diseases	Ia/Ib	116	FPI Q2 2021	

Partner: [1]AC Immune

Pipeline summary

Marketed products additional indications

Global Development late-stage trials

pRED (Roche Pharma Research & Early Development)

gRED (Genentech Research & Early Development)

Spark

Hemophilia A

Unique gene therapy platform

Molecule	SPK-8011 (RG6357)		SPK-8016 (RG6358)
Indication	**Hemophilia A**		**Hemophilia A with inhibitors to Factor VIII**
Phase/study	**Phase I**	**Phase I/II**	**Phase I/II**
# of patients	N=100	N=30	N=30
Design	▪ Long term follow up study of patients who have received SPK-8011 in any prior Spark-sponsored SPK-8011 study	▪ Gene transfer, dose-finding safety, tolerability, and efficacy study of SPK-8011	▪ Gene transfer, dose-finding safety, tolerability, and efficacy study of SPK-8016 in individuals with FVIII inhibitors
Primary endpoint	▪ Safety	▪ Safety and changes from baseline in FVIII activity levels at week 52	▪ Safety; peak and steady state FVIII activity levels at week 52
Status	▪ Ongoing	▪ FPI Q1 2017 ▪ Updated data presented at ISTH 2020 and 2021 ▪ Recruitment completed Q1 2021	▪ FPI Q1 2019
CT Identifier	NCT03432520	NCT03003533	NCT03734588

Choroideremia

Unique gene therapy platform

Molecule	**SPK-7001 (RG6367)**
Indication	**Choroideremia**
Phase/study	**Phase I/II**
# of patients	N=15
Design	▪ Safety study in subjects with CHM (choroideremia) gene mutations
Primary endpoint	▪ Safety and tolerability
Status	▪ FPI Q1 2015 ▪ Recruitment completed Q2 2017
CT Identifier	NCT02341807

Pompe disease

Unique gene therapy platform

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

Doing now what patients need next