Roche

Roche Late Stage Pipeline Event 2021

Late Stage Pipeline Neuroscience

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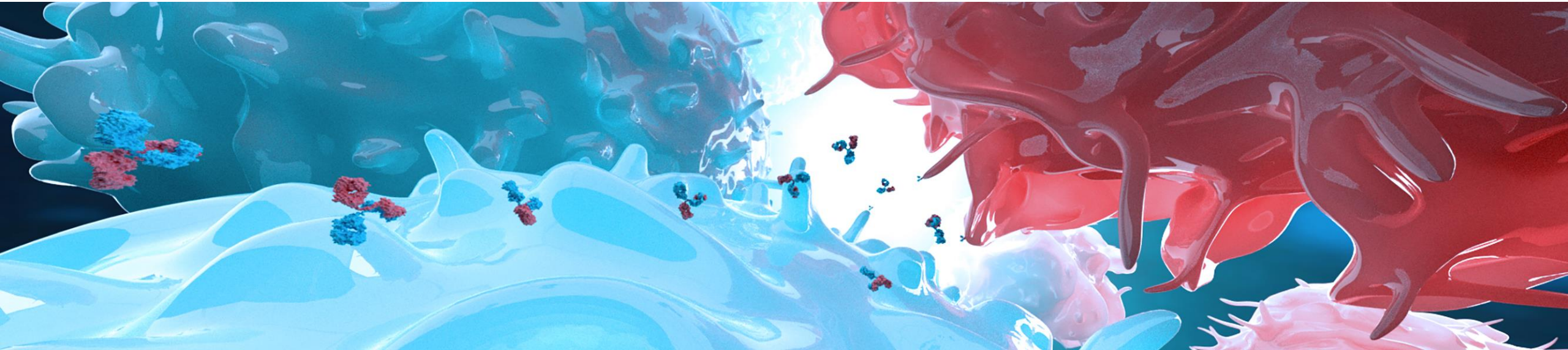
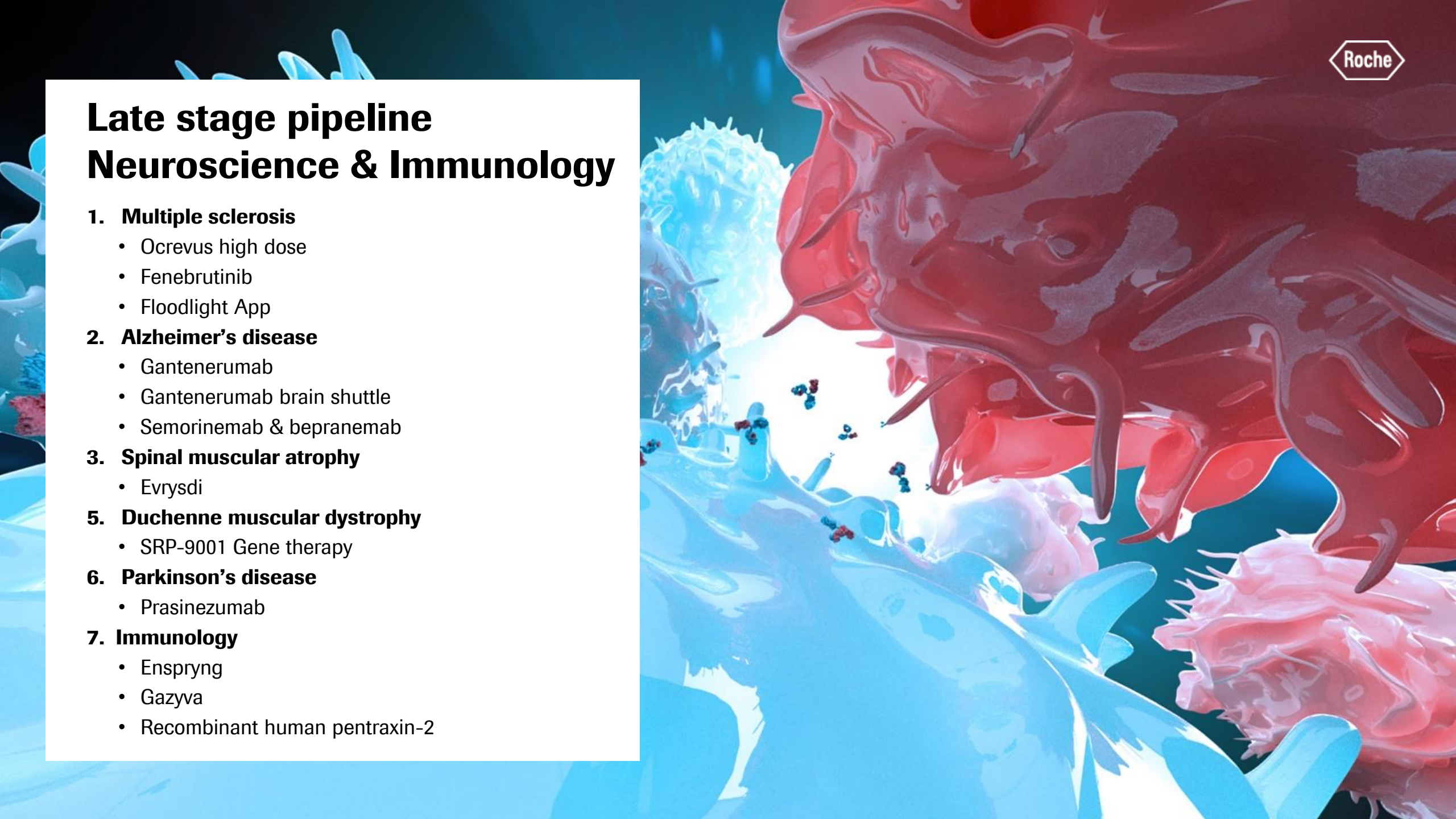


Late stage pipeline
Neuroscience & Immunology

1. **Multiple sclerosis**
   - Ocrevus high dose
   - Fenebrutinib
   - Floodlight App
2. **Alzheimer's disease**
   - Gantenerumab
   - Gantenerumab brain shuttle
   - Semorinemab & bepranemab
3. **Spinal muscular atrophy**
   - Evrysdi
5. **Duchenne muscular dystrophy**
   - SRP-9001 Gene therapy
6. **Parkinson's disease**
   - Prasinezumab
7. **Immunology**
   - Enspryng
   - Gazyva
   - Recombinant human pentraxin-2



Neuroscience and rare diseases portfolio

Strongly differentiated pipeline

Ph I (4 NMEs)	
RG6091	**UBE3A LNA** Angelman syndrome
RG7637	undisclosed
RG6237	undisclosed
RG6182	undisclosed

Ph II (7 NMEs)	
RG7935	**prasinezumab** Parkinson's
RG6100	**semorinemab** Alzheimer's
UCB 0107	**bepranemab** Alzheimer's
RG6102	**brain shuttle gantenerumab** Alzheimer's
RG7412	**crenezumab** Alzheimer's
RG7906	**ralmitaront** Schizophrenia
RG7816	**$GABA_A$ α5 PAM** Autism spectrum disorder

Ph III (3 NMEs, 1LE)	
RG1450	**gantenerumab** Alzheimer's
SRP 9001	**microdystrophin gene therapy** DMD RD
RG7916	**Enspryng** gMG RD
RG7845	**fenebrutinib** MS

Launched (3)		
RG1594	**Ocrevus** MS	✓
RG7916	**Enspryng** NMOSD RD	✓
RG7916	**Evrysdi** SMA type 1/2/3 RD	✓

✓ FDA approval

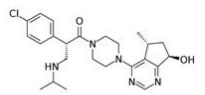
RD RD = Rare disease

Neuro-immunologic disorders | Neuro-degenerative disorders | Neuro-developmental disorders | Neuro-muscular disorders | Psychiatric disorders

NME=new molecular entity; LE=line extension; NMOSD=neuromyelitis optica spectrum disorders; DMD=Duchenne muscular dystrophy; gMG=generalised myasthenia gravis; MS=Multiple sclerosis; SMA=spinal muscular atrophy; Risdiplam is developed in collaboration with PTC therapeutics and the SMA Foundation

New technology platforms applied in Neuroscience and I2O*

Small molecules

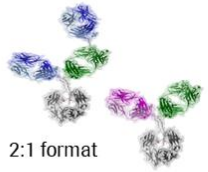


- ipatasertib
- inavolisib
- giredestrant
- KRAS G12C
- TLR7 agonist
- belvarafenib
- SHP2i

Target oncogenes, induce apoptosis, supress tumor growth

- fenebrutinib
- ralmitaront
- GABA Aa5 PAM
- PTH1R agonist
- NLRP3 inhibitor
- Abx MCP
- CpAM
- AT-527

Bi-specifics

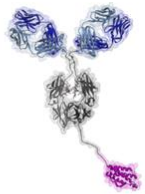


- mosunetuzumab
- glofitamab
- cibisatamab
- Her2 x CD3
- glypican-3 x CD3
- cevostamab
- PD1 x TIM3
- PD1 x LAG3
- TYRP1-CD3

Engage and activate T cells to kill tumour cells

- faricimab
- FIXa x FX
- FGFR1 x KLB
- VEGF x Ang2 Duta

Fusion protein



- PD1-IL2v
- CD19-4-1BBL
- FAP-4-1BBL
- MAGE-A4 ImmTAC
- IL15/IL15Ra-Fc
- FAP-CD40

Amplify immune response

- brain shuttle gantenerumab
- efmarodocokin alfa
- IgG-IL2

mAb

- tiragolumab
- CD25 mAb
- codrituzumab
- CD137

Amplify immune response

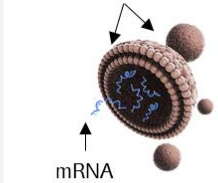
- crovalimab
- gantenerumab
- prasinezumab
- semorinemab
- etrolizumab
- TLR4 mAb
- HtrA1 mAb
- anti-tryptase

Antibody drug conjugate

- preclinic

Targeted toxic payload

Neoantigen vaccines

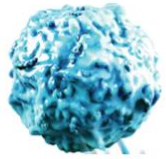


- autogene cevumeran

Patient's neo-antigens for anti-tumour immune response

Neuroscience and I2O pipeline

Personalized T cells

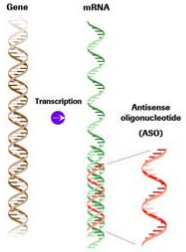


- programmed T cells

Patient's neo-antigens for anti-tumour immune response

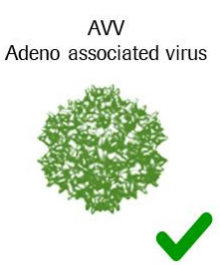
= Products approved

Antisense RNA



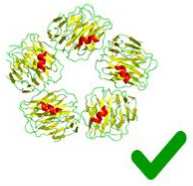
- Factor B ASO
- HBV siRNA
- PDL1 LNA
- UBE3A LNA

Gene therapy



- SPK-8011
- SPK-8016
- SPK-3006
- SPK-7001
- SRP-9001

Recombinant proteins



- rh pentraxin-2

Oncolytic adenovirus

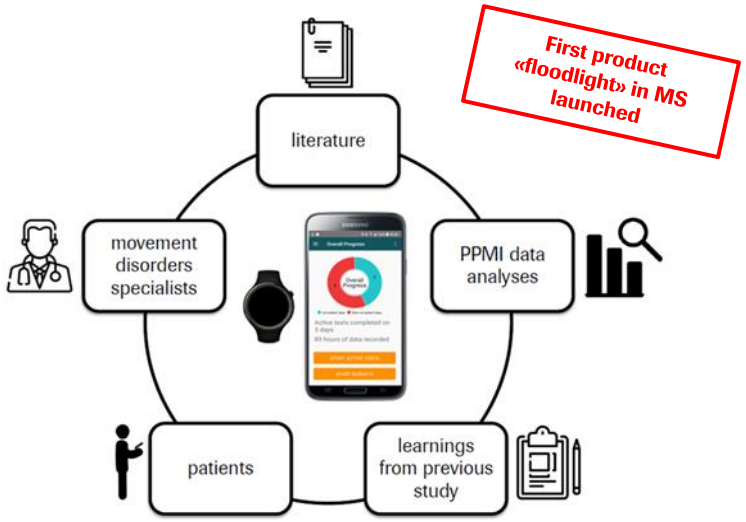
- Type 5 adenovirus

* List of pipeline molecules shown below is not complete; Molecules in the blue box are developed in Neuroscience and I2O (Immunology, Infectious diseases, Ophthalmology)

Digital endpoints to drive scientific progress

Delivering new patient insights and building holistic solutions for patients

Continuous product improvement



Broad development program in neuroscience

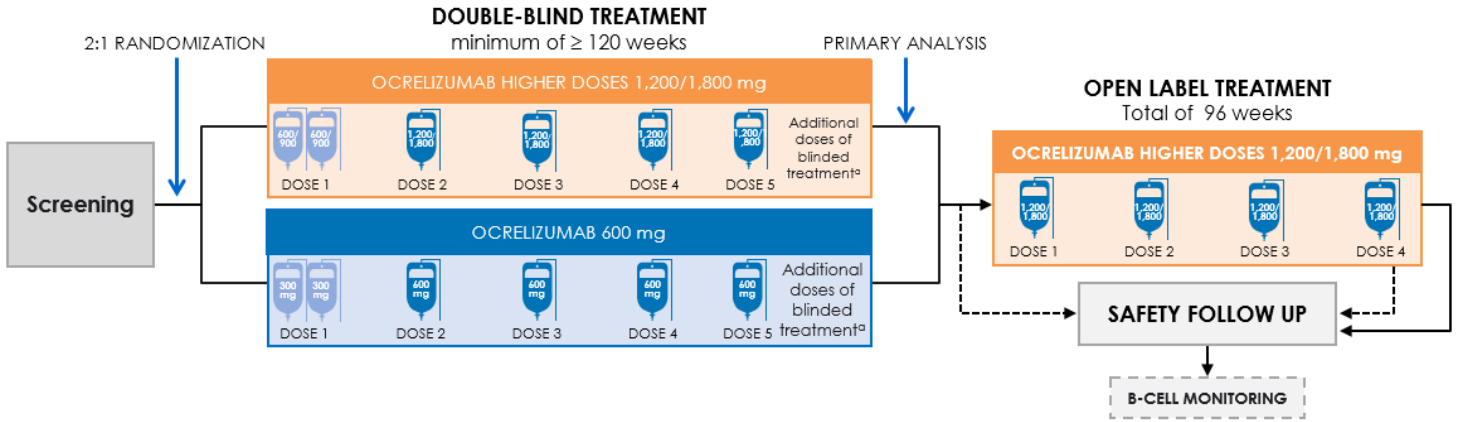
Disease Area	Cognition	Hand Motor Function	Gait & balance	Vocalization	Activity & sociability
Parkinson	●	●	●	●	●
Huntington	●	●	●	●	●
SMA		●	●	●	
Multiple Sclerosis	●	●	●		●
Alzheimer	●			●	●
Autism	●			●	●
Schizophrenia					●

- Clinical trials utilizing mobiles, wearables and gaming devices
- More sensitive, precise and objective data collection and monitoring of disease progression
- Continuous and longitudinal measurement captures episodic and rare events
- Reduced assessment burden and greater real-world relevance benefiting physicians and patients

Multiple sclerosis: Higher dose Ocrevus

New Ph III program in RMS and PPMS started in 2020

Ph III study design for Ocrevus Higher Dose versus 600 mg in RMS and PPMS



Study in patients with RMS (MUSETTE)

- Patient sample size, N=786
- Age: 18–55 years; EDSS score: 0–5.5
- Stratification for region, age, EDSS, weight

Study in patients with PPMS (GAVOTTE)

- Patient sample size, N=699
- Age: 18-55 years; EDSS score: 3–6.5
- Stratification for region, age, sex, weight

- Ocrevus showed a significant benefit on 12/24W-CDP, ARR, MRI measures in Ph III studies in RMS and PPMS and 7 year OLE
- Exposure/response analysis of Ph III data suggests a higher dose could lower the risk of disability progression without compromising safety
- Two double-blind, randomized Ph III studies were designed to test higher dose Ocrevus; the selected higher dose, given every 24 weeks, is 1,200 mg for patients <75 kg or 1,800 mg for patients ≥75 kg
- Ph III (MUSETTE) in RMS and Ph III (GAVOTTE) in PPMS started in 2020

Hauser S.L. et al, ACTRIMS-ECTRIMS 2020; 24W-CDP=24 week confirmed disability progression; AAR=annual relapse rate; MRI=magnetic resonance imaging; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; OLE=open label extension

Multiple sclerosis: Floodlight launched in US and EU

Building ecosystems to serve patients, society and scientific progress

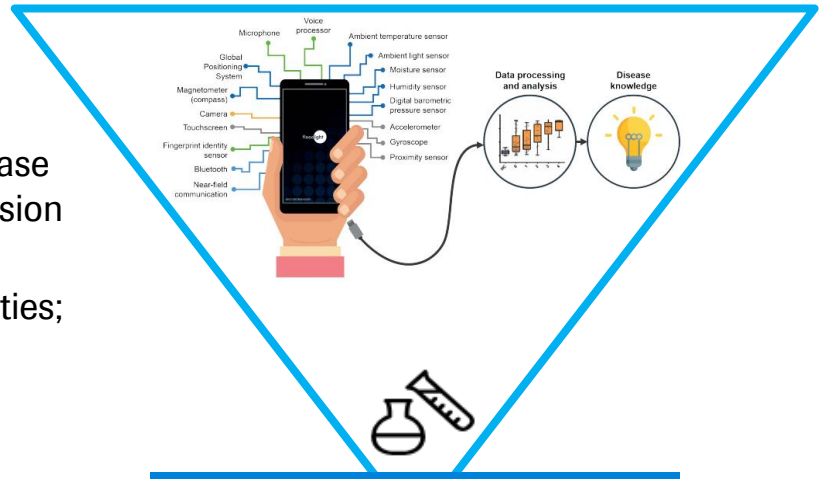
Roche's 1rst approved sensor-based SaMD

Value creation for patients

- MS progression, often undetected by current clinical scales
- Provides an objective assessment of disease status; empowers patients in shared decision making, enhancing earlier access to care
- Closely co-created with patient communities; studies show high retention rates

"The tasks were all straightforward, and some almost fun."
Our 1st patient

Concept is spot on.
US Neurologist



Value creation for science

- Rigor of measurements & robust development define new standards
- Generate disease insights and support future drug development
- Collaborations create consensus on new digital measurements

Value creation for society

- Earlier intervention has the potential to improve health outcomes and reduce long term health care costs
- Floodlight MS is launched in close collaboration with healthcare providers, enabling RWD opportunities that improve health care utilization

"I'm 100% behind the initiative and am very enthusiastic about it. It's cool that this was clearly under development before the pandemic and it fits well with my challenges: 90% of patients are virtual and there are lots of time constraints between clinical visits."
Dr. Shin

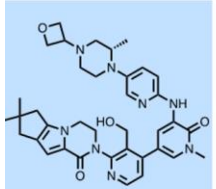
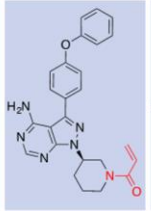
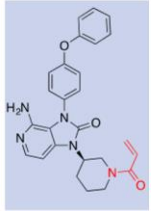
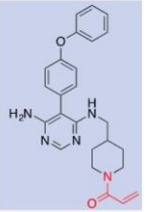
Pharma vision 2030: Providing more patient benefit at less cost to society

SaMD=software as medical device

Multiple sclerosis: Fenebrutinib in MS

Highly differentiated and potentially best-in-class BTKi

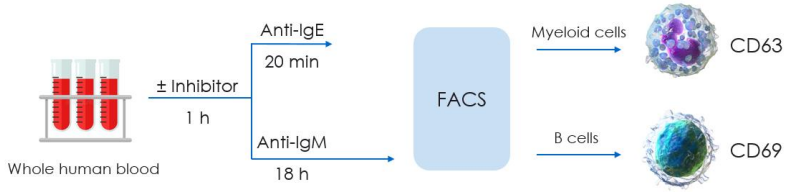
BTK inhibitor

Fenebrutinib (GDC-0853)	Ibrutinib	Tolebrutinib	Evobrutinib
Phase 3	Launched	Phase 3	Phase 3
MS	Oncology	MS	MS
			
Noncovalent, reversible	Covalent, irreversible	Covalent, irreversible	Covalent, irreversible
BTK IC_{50} 2 nM	1 nM	1 nM	32 nM
High selectivity	Low selectivity	Low selectivity	Low selectivity

- Oral, highly selective and only reversible noncovalent BTK inhibitor in Ph III
- Long residence time bound to BTK mimics durable inhibition of a covalent inhibitor, but without the potential safety risks of covalent BTK inhibition

Dual MOA

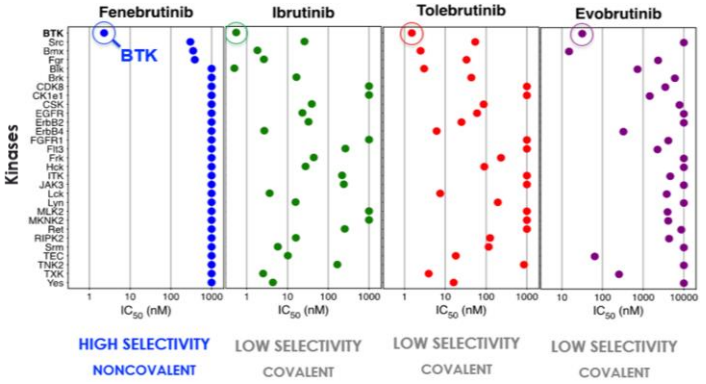
Inhibition of myeloid and B cell activation in whole human blood



Whole human blood assay	Fenebrutinib[1]	Ibrutinib[1]	Tolebrutinib[2]	Evobrutinib[3]
Myeloid cell CD63 IC_{50}, nM	31	171	166	1660
B cell CD69 IC_{50}, nM	8	12	10	84

Outstanding selectivity profile

Kinase selectivity assay



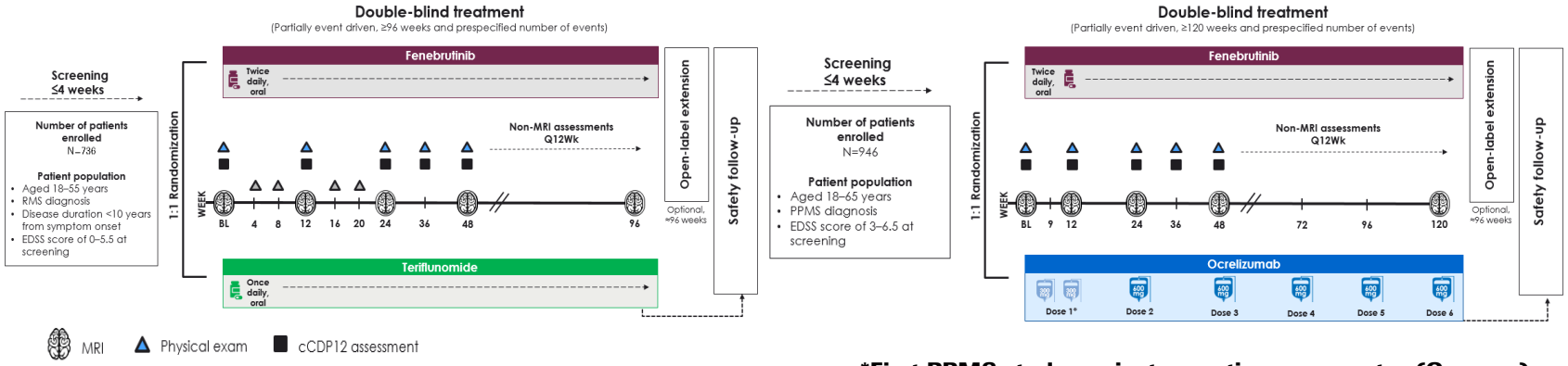
- Dual MOA: Fenebrutinib potently inhibits myeloid (basophil) and B cell activation in human blood; this may reduce both acute and chronic inflammation in MS
- In a kinase selectivity assay fenebrutinib was found to be 130x more selective for BTK which may reduce off target effects and thus improve safety

Johnson A. et al, ACTRIMS-ECTRIMS 2020; MOA=mechanism of action; MS=multiple sclerosis; BTK=Bruton's tyrosine kinase; nM=nano molar; FACS=fluorescent activated cell sorting

Multiple sclerosis: Fenebrutinib trials in RMS and PPMS started

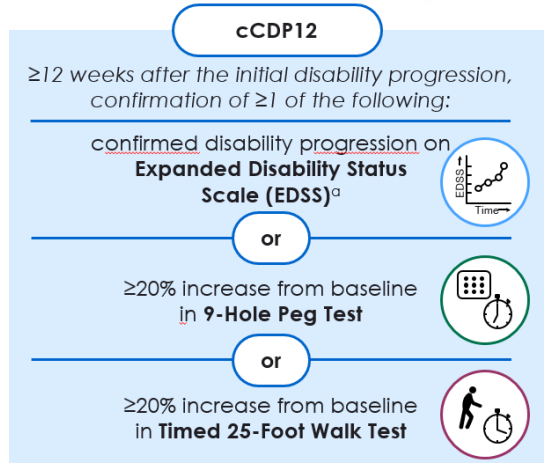
Well established clinical safety profile in autoimmune diseases

Ph III trials in RMS and PPMS run against active comparators



***First PPMS study against an active comparator (Ocrevus)**

Key endpoint on progression



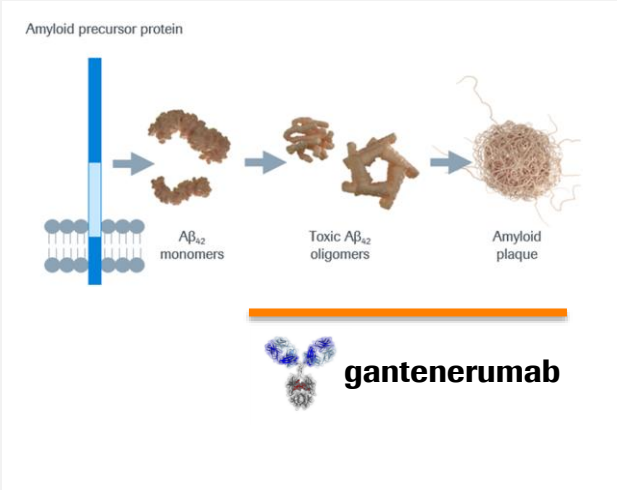
- Innovative Ph III trial design with cCDP12 providing a more thorough approach to “disease progression” by assessing upper limb function, which might lead to earlier detection of disease progression
- Well established safety profile due to 14 clinical studies (across 3 autoimmune diseases) with overall 1360 study participants:
  - Generally well tolerated, mostly non-serious, mild and self-limiting adverse events
  - Other potential BTKi class effects (infection, severe bleeding, tachyarrhythmias) appear less relevant due to the high BTK selectivity seen
- Ph III program in RMS and PPMS started in 2020

Oh. J. et al., AAN 2021; Hauser S. L. et al, ACTRIMS-ECTRIMS 2020; MS=multiple sclerosis; RMS=relapsing MS; PPMS=primary progressive MS; BL=base line; Q12W=every 12 weeks; [a] Defined as an increase of ≥1 point from a baseline score of ≤5.5, or an increase of ≥0.5 points from a baseline score of >5.5; EDSS=Expanded Disability Status Scale; 9HPT=9-Hole Peg Test; T25FWT=Timed 25-Foot Walk Test

Alzheimer's disease: Gantenerumab SC targeting Amyloid β (Aβ)

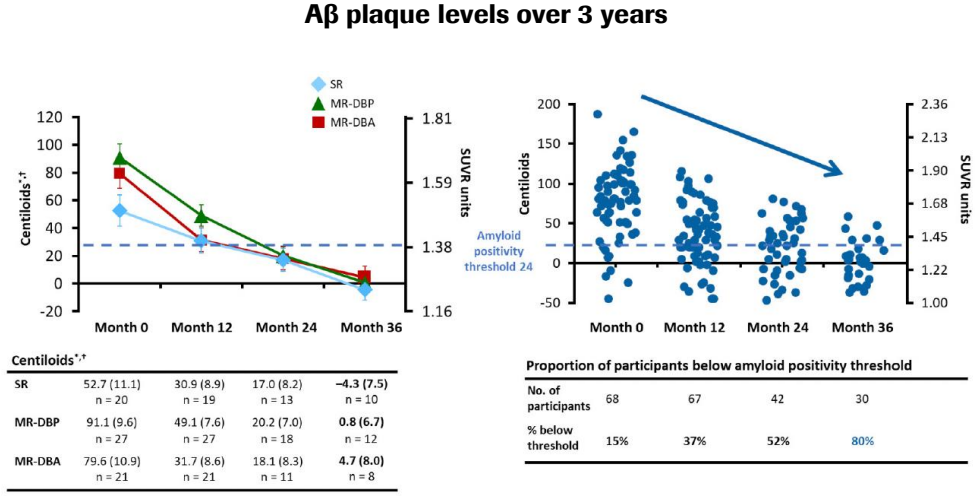
Strong target engagement and downstream biological impact

Anti-Aβ mAb



- Fully human, anti-Aβ mAb (IgG1) with high affinity to aggregated forms of Aβ
- Highest affinity for neurotoxic oligomers and plaques [1,2]
- SC administration enables flexibility of home administration

OLE studies shows robust Aβ plaque removal*



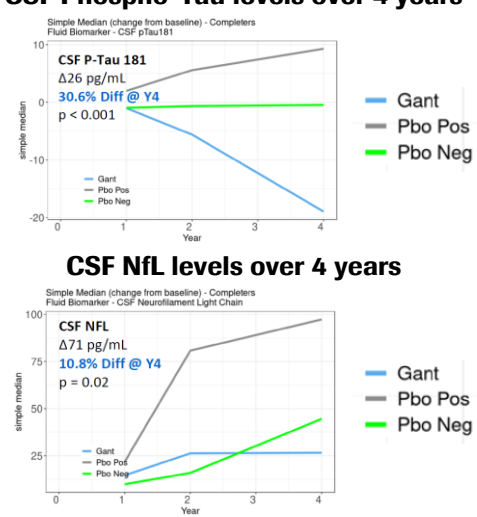
Centiloids*,†

	Month 0	Month 12	Month 24	Month 36
SR	52.7 (11.1) n = 20	30.9 (8.9) n = 19	17.0 (8.2) n = 13	−4.3 (7.5) n = 10
MR-DBP	91.1 (9.6) n = 27	49.1 (7.6) n = 27	20.2 (7.0) n = 18	0.8 (6.7) n = 12
MR-DBA	79.6 (10.9) n = 21	31.7 (8.6) n = 21	18.1 (8.3) n = 11	4.7 (8.0) n = 8

Proportion of participants below amyloid positivity threshold

	Month 0	Month 12	Month 24	Month 36
No. of participants	68	67	42	30
% below threshold	15%	37%	52%	80%

DIAN-TU study shows downstream impact



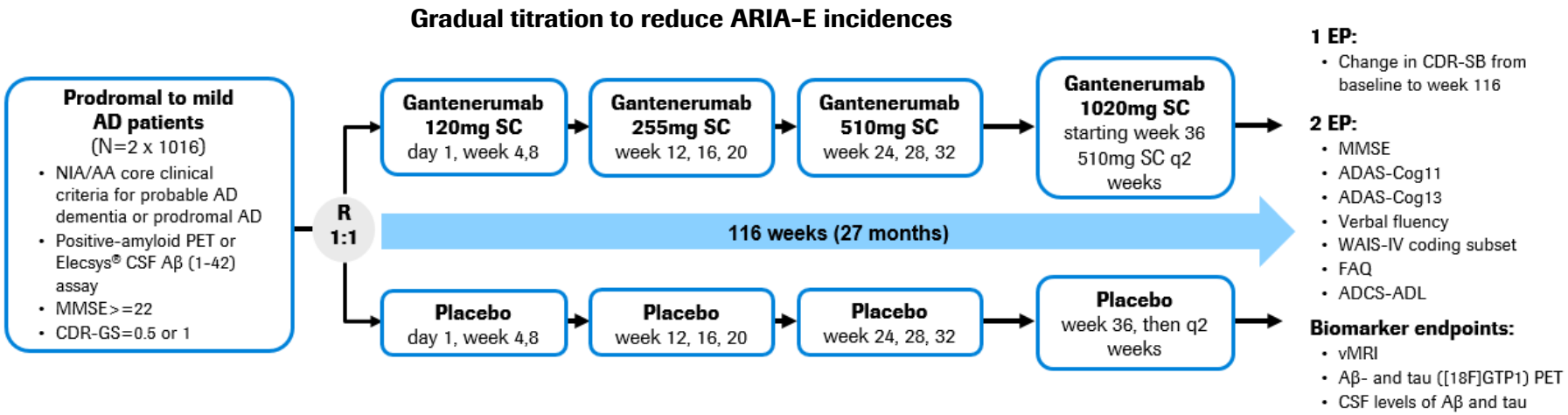
- OLE studies: Gantenerumab lowers Aβ plaques below positivity threshold towards floor levels without plateau
- 80% of patients Aβ-negative after 3 years
- Gantenerumab reduces levels of downstream biomarkers (p-Tau, t-TAU) and blocks increases of markers of neurodegeneration (NfL) in patients with familial AD (DIAN-TU study)

[1] Bohrmann B, et al. J Alzheimer's Dis 2012; 2. Ostrowitzki S, et al. Arch Neurol 2012; Bateman R. J. et al, AAT-AD/PD 2020; Klein G et al, CTAD 2020; Klein G. et al., J Prev Alzheimers Dis 2021;8(1); OLE=open label extension; NfL=neurofilament light chain; * OLE studies for the former Ph III studies SCarlet RoAD and Marguerite RoAD; SC=subcutaneous; CSF=cerebrospinal fluid

Alzheimer's disease: Gantenerumab SC in early AD patients

Ph III program with optimized design to maximize exposure

Global, randomized, double-blind, placebo-controlled Ph III trial design (GRADUATE I/II)



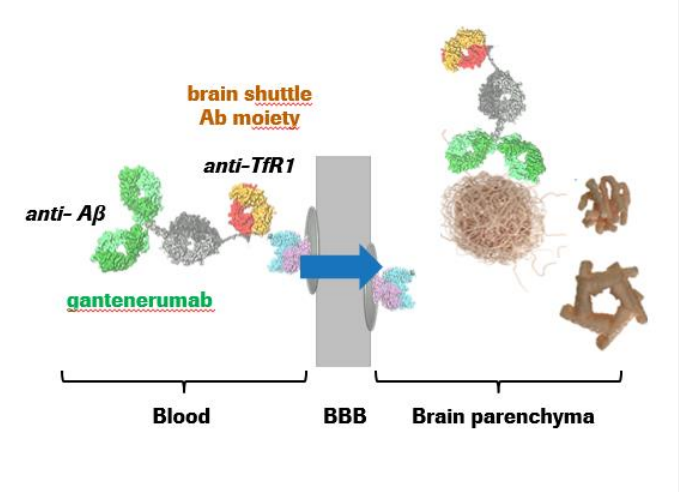
- Two parallel studies with large sample size of ~1,000 participants patients each expected to deliver a clear and robust data set in 2022
- Optimized titration scheme to reduce incidence of ARIA-E and maximize exposure for all patients regardless of ApoE4 genotype
- Well powered PET substudies to detect biomarker changes including Aβ and tau
- Treatment duration of 27 months to optimize detection of clinical benefit
- First and only late-stage AD program to offer SC formulation enabling flexibility and convenience of home administration

AD=Alzheimer's Disease; SC=subcutaneous; Aβ=amyloid-beta; NIA/AA=National Institute on Aging/Alzheimer's Association; PET=positron emission tomography; CSF=cerebrospinal flu; CDR-SOB=Clinical DementiaRating ScaleSumofBoxes; ADAS-Cog13=Alzheimer's Disease Assessment Scale-Cognitive subscale; MMSE=Mini-Mental State Examination; FAQ=Functional Activities Question; ADCS-ADL=Alzheimer's Disease Cooperative Study-Activities of daily living; vMRI=volumetric magnetic resonance imaging; ARIA-E= amyloid-related imaging abnormalities edema; In collaboration with MorphoSys AG

Alzheimer's disease: Gantenerumab brain shuttle

Vision: Superior target access leading to slowing of AD progression

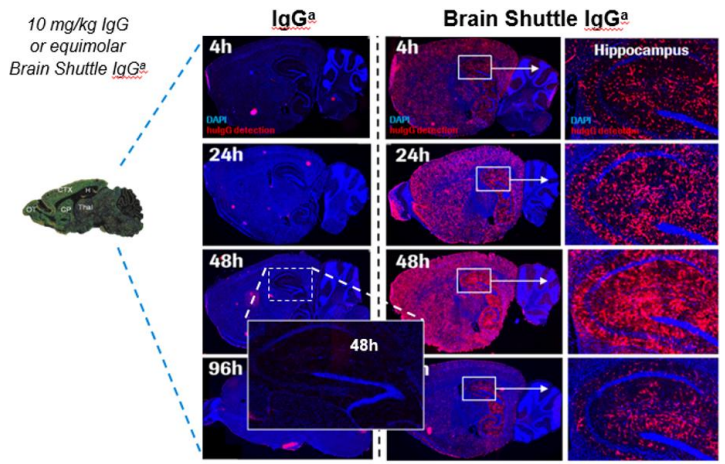
Gantenerumab brain shuttle



- Gantenerumab brain shuttle is a fusion protein combining gantenerumab with a transferrin receptor (TfR1) binding Ab moiety to achieve efficient transport over the BBB and target Aβ plaque engagement in the brain
- Technology could also be applied to other CNS disorders

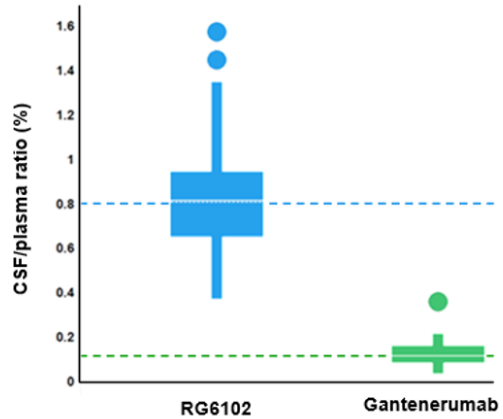
Preclinical data

Immunofluorescence staining[1]



Ph I PK/PD data in healthy volunteers

CSF/plasma ratio[2]



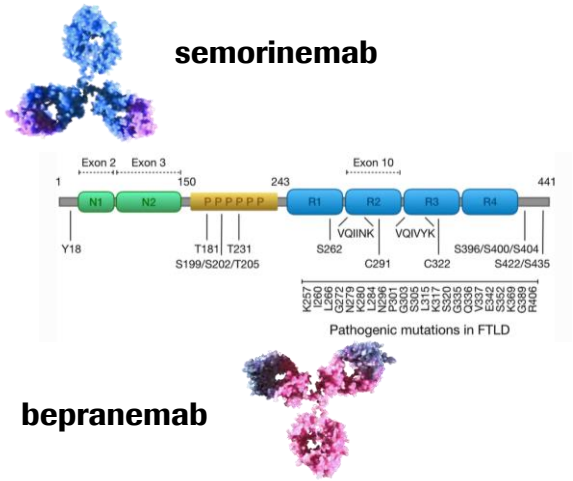
- Preclinical work in mouse and monkey models provides in vitro and in vivo evidence that TfR1 receptor binding facilitates transcellular transport across the Blood Brain Barrier (BBB)
- Initial Ph I PK data show encouraging 6 to 8-fold increase in the CSF/plasma concentration ratio when comparing the gantenerumab brain shuttle to historical gantenerumab data
- Phase I/II study is underway to test safety, tolerability, PK, and PD (amyloid PET) in people with prodromal or mild-to-moderate AD

Kulic L. et al., ADPD 2021; AD=Alzheimer's disease; BBB=blood brain barrier; IgG=immunoglobulin G; mAb=monoclonal antibody; TfR1=transferrin receptor 1; Aβ=Amyloid β; CNS=central nervous system; CSF=cerebrospinal fluid; PD=pharmacodynamics; PK=pharmacokinetics; [1] Unpublished data from Dr E. Urich and Dr T. Poeschinger: Immunofluorescence staining highlights the distribution of classical IgG vs Brain Shuttle IgG targeting a neuronal target in mouse brain at 4, 24, 48, and 96 hours after a single IV dose (10 mg/kg each); [2] Gantenerumab brain shuttle results were compared with historical data obtained from a previous gantenerumab SAD trial (BN18726).

Alzheimer's disease: Two anti-TAU mAbs in development

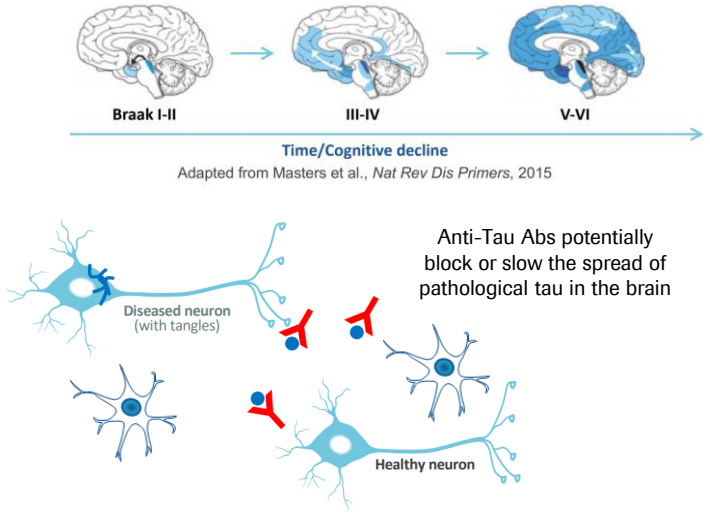
Ph II (LAURIET) semorinemab results show first hint of clinical activity

Anti-Tau mAbs



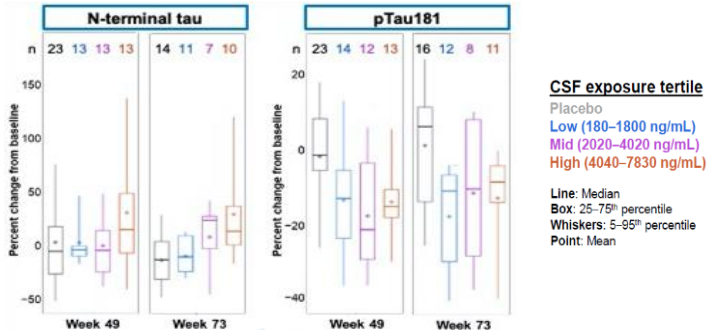
- Semorinemab: N-terminal anti-tau mAb binding to all isoforms independent of their phosphorylation status; optimized for high dosing
- Bepranemab: Mid-domain anti-tau mAb binding to a different epitope

Proposed MOA



Ph II (TAURIEL) PD results

Semorinemab had pharmacodynamic activity suggestive of target engagement



- Ph II (LAURIET) study with semorinemab in mild-to moderate AD showed statistically significant and potentially clinically meaningful effect on cognition as measured by ADAS-Cog11; no treatment effect observed on ADCS-ADL, MMSE or CDR-SB
- LAURIET OLE is continuing, with additional analyses in progress; data to be presented at CTAD
- Ph II study in early AD (TAURIEL) did not meet its primary (CDR-SB) or secondary endpoints

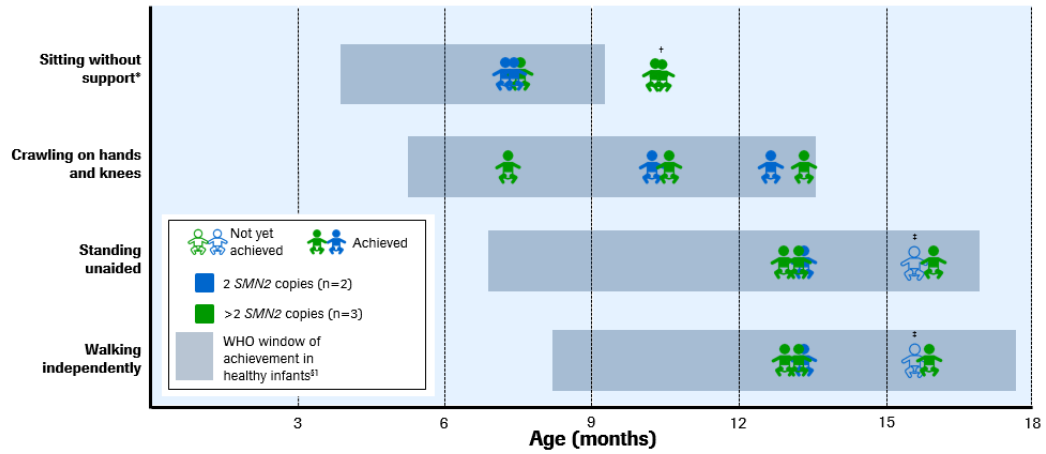
Wildsmith et al, AAT-AD/PD 2021; Teng E. et al. CTAD 2019; PD=pharmacodynamics; AD=Alzheimer's disease; ADAS-Cog=Alzheimer's Disease Assessment Scale–Cognitive subscale; ADCS-ADL=Alzheimer's Disease Cooperative Study–Activities of Daily Living Inventory; MMSE=Mini-Mental State Examination; CDR-SB=Clinical Dementia Rating–Sum of Boxes; Semorinemab partnered with AC Immune; Bepranemab (UCB0107) partnered with UCB.

Spinal muscular atrophy: Evrysdi in type 1/2/3 SMA

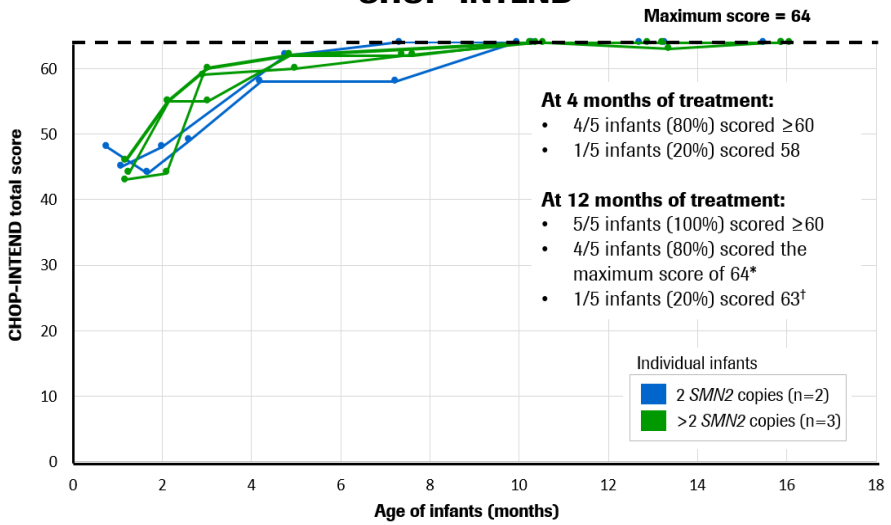
Excellent preliminary data in presymptomatic babies

Ph III (RAINBOWFISH) interim results in presymptomatic babies with SMA

Motor milestones within the WHO windows for healthy children



CHOP-INTEND



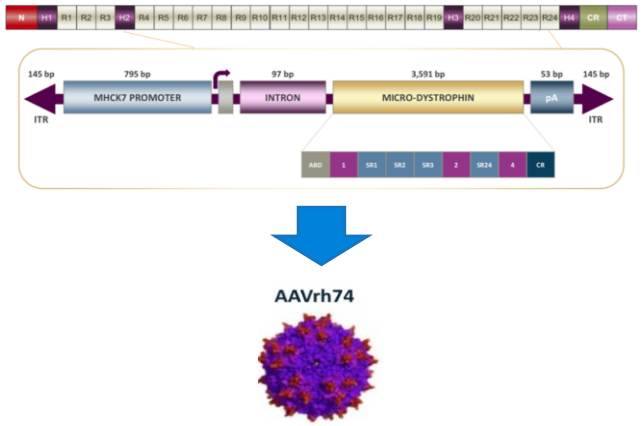
- Presymptomatic babies treated with Evrysdi for at least 12 months were able to sit, stand and walk and achieved motor milestones within the WHO windows for healthy children
- They reached near maximum CHOP-INTEND scores by 4–5 months of age
- Evrysdi expected to become the most prescribed SMA treatment in the US in 2021

Finkel R. S. et al. CureSMA 2021; Third edition; WHO=world health organization; CHOP-INTEND=Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; Risdiplam in collaboration with PTC Therapeutics and the SMA Foundation

Duchenne muscular dystrophy: Gene therapy SRP-9001

Positive expression and safety data for commercial drug material

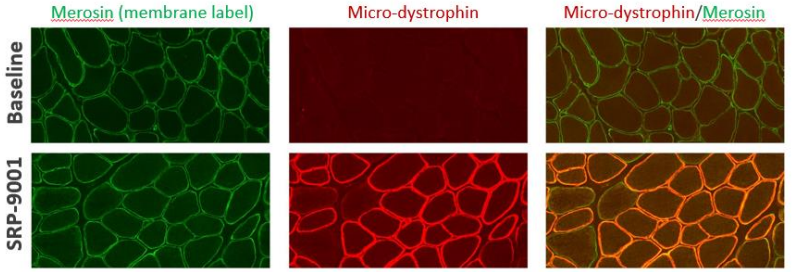
Micro-dystrophin gene therapy



- AAVrh74 vector: low likelihood of pre-existing immunity and high tropism for skeletal & cardiac muscles
- Expression potentiated by the MHCK7 promoter in cardiac & skeletal muscles
- Transgene retains critical elements of dystrophin for a functional protein

Ph Ib (SRP-9001-103, cohort 1) expression results at week 12 in 4-7 y.o. ambulatory patients (n=11)

Immunofluorescence (IF) staining



Expression summary

Vector genome copies per nucleus	3.87
% Normal expression by Western Blot	55.4 ± 43.4*
% Dystrophin positive fibers by IF	57.7 ± 22.2*
% Intensity by IF	75.9 ± 46.4*

* Change from baseline (CBO)

- Micro-dystrophin protein expression increased by +55.4% from baseline and muscle fibers positive for micro-dystrophin increased by +57.7% from baseline
- Safety profile consistent with prior studies, with no new safety signals identified
- Results provide preliminary confirmation of the manufacturing and analytics of commercially grade material, which enables building capacity to supply the DMD population
- Planning for global Ph III trials in ambulatory and non-ambulatory DMD patients are ongoing

Sarepta company presentation, May 18 2020; SRP-9001 partnered with Sarepta; License and collaboration agreement with Sarepta Therapeutics in Duchenne Muscular Dystrophy (DMD), securing exclusive ex-US commercial rights to SRP-9001, their gene therapy for DMD, and the right to opt-in to their broader DMD portfolio outside of the US; DMD=Duchenne's muscular dystrophy

Parkinson's disease: Prasinezumab with signals of efficacy

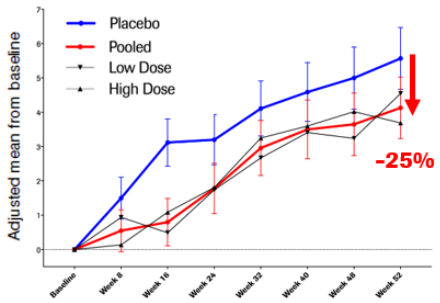
Ph IIb started to further define patient population and endpoints

Anti-α-synuclein mAb

- Humanized mAb designed to target aggregated forms of α-synuclein
- Inhibiting cell-to-cell spreading of pathogenic forms of α-synuclein, resulting in slowing of Parkinson's disease progression

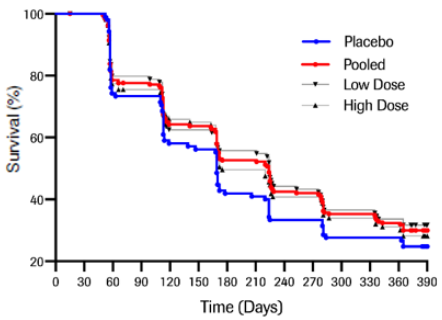
Ph II (PASADENA part 1) results at 52 weeks

Change in MDS UPDRS part III



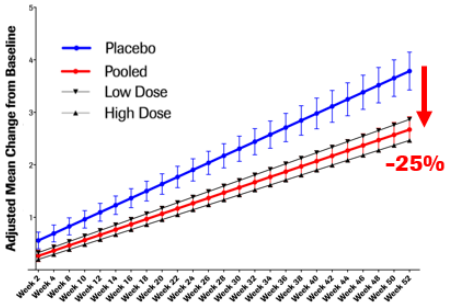
Pooled: −1.44, 80% CI=(-2.83, -0.06); **−25%**,
Low dose: −1.88, 80% CI=(-3.49, -0.27); **−34%**
High dose: −1.02, 80% CI= (-2.64, 0.61); **−18%**

Time to worsening of motor signs (+5pts MDS UPDRS part III)



Pooled: **HR 0.82**, 80% CI=0.64 to 0.99
Low dose: **HR 0.77**, 80% CI=0.63 to 0.96
High dose: **HR 0.87**, 80% CI=0.70 to 1.07

Digital Motor Score



Pooled: −0.030, 80% CI=(−0.050, −0.010); **−25%**
Low dose: −0.040, 80% CI=(-0.063, -0.017); **−30.3%**
High dose: −0.029, 80% CI= (-0.052, -0.006); **−21.5%**

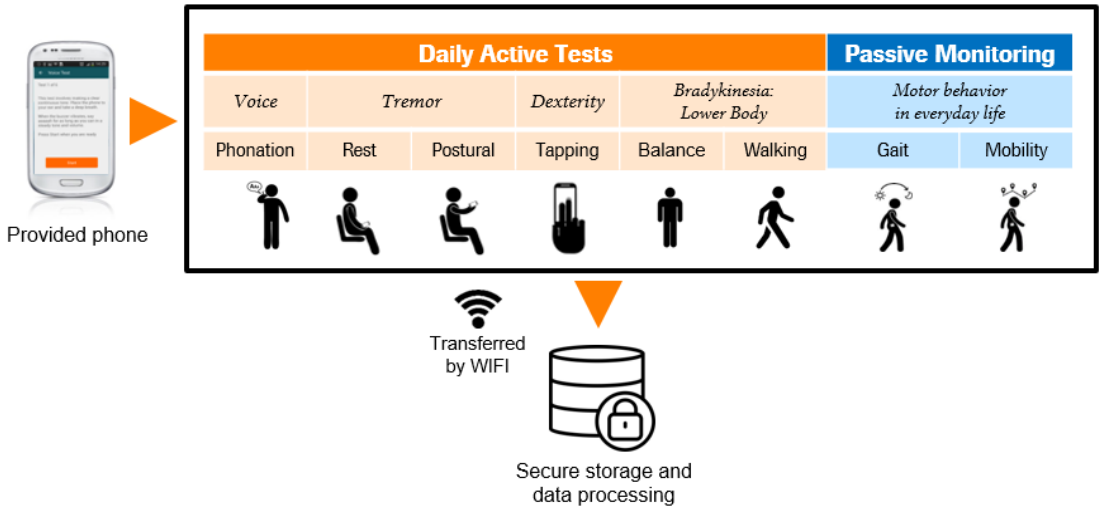
- Ph II (PASADENA) study did not meet its primary endpoint (MDS UPDRS total score)
- Prasinezumab was well tolerated showing efficacy signals in slowing of clinical decline of motor symptoms (MDS UPDRS part IIII, digital motor outcome measures) warranting further follow up; longer term data to be presented at upcoming conferences
- Ph IIb (PADOVA) started in 2021 in patients with early PD that are on symtomatics incl L-DOPA

Pagano, G et al, MDS poster 2020; MDS-UPDRS=Movement Disorder Society-Unified Parkinson's Disease Rating Scale (Sum of Parts I, II and III which assess non-motor [I and II] and motor [III] experiences in daily living); Prasinezumab partnered with Prothena Biosciences; HR=hazard ratio; CI=confidence interval; PD=Parkinson's disease

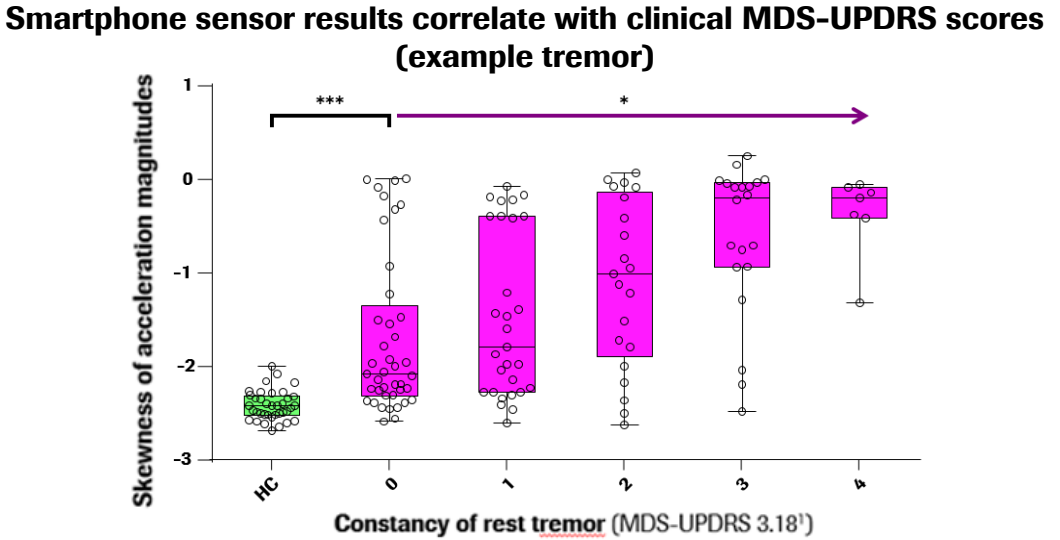
Parkinson's disease: First Ph II digital biomarker results

Digital biomarkers support clinical drug development

Daily assessment for 6 months



Ph II (PASADENA) digital biomarker results



- The PASADENA digital biomarker test suite on the smart phone enables daily quantification of fluctuating symptoms in Parkinson's disease
- Preliminary data show clinical validity, strong patient adherence and high test-retest reliability
- Digital endpoints provide already today decision-making support for drug development
- Potential future use in patient & treatment monitoring, identifying subclinical signs in prodromal patients, or as primary outcomes measures

http://www.roche.com/media/store/roche_stories/roche-stories-2015-08-10.htm

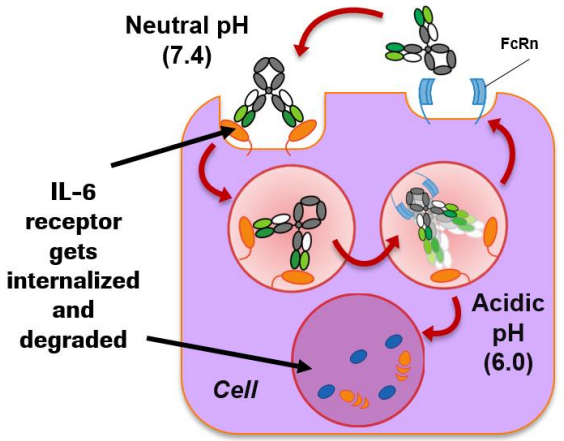
Enspryng in myasthenia gravis (MG)

Recycling Ab for maximal inhibition of IL-6 signaling

ENSPRYNG™ satralizumab-mwge subcutaneous injection 120 mg/mL

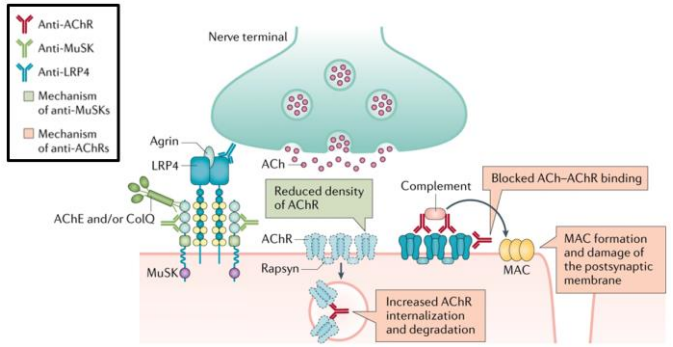
Roche

Anti-IL-6 receptor mAb

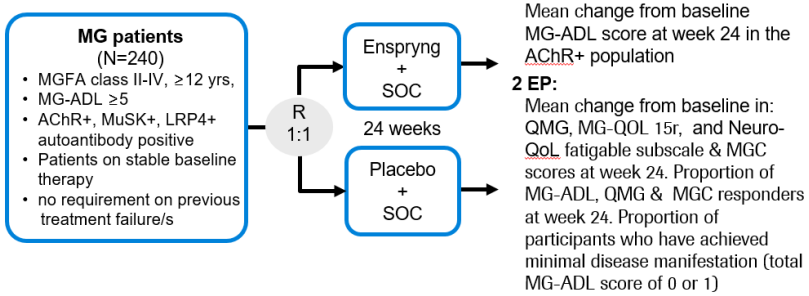


- Recycling mAb with high-affinity to soluble and membrane-bound IL-6R
- Engineered to enable maximal inhibition of IL-6 signalling
- Convenient SC Q4W home dosing

MG: Autoantibodies at the neuromuscular junction



Ph III (LUMINESCE) trial design



- MG is a chronic, autoimmune disease of the neuromuscular junction, causing fatigable muscle weakness; pathophysiology involves autoantibodies (~80% have anti-AChR Abs; 10% anti-MuSK Abs; <5% anti-LRP4 Abs) at the neuromuscular junction disrupting neuromuscular transmission
- IL6 blockade has the potential to lower pathogenic autoantibody production
- High unmet need: 10% of patients failing therapies; ~80% with no complete stable remission
- Ph III (LUMINESCE) in MG initiated; actively exploring other potential indications

Gilhus N.E. et al., Nat Rev Dis Primers. 2019 May 2;5(1):30.; MG=myasthenia gravis; SC=subcutaneous; Q4W=every 4 weeks; MOA=mechanism of action; AChR=acetylcholine receptor; MuSK= muscle-specific tyrosine kinase; LRP4=lipoprotein receptor-related protein 4; MG-ADL=Myasthenia Gravis Activities of Daily Living; QMG=Quantitative Myasthenia Gravis; MG-QOL 15r=Myasthenia Gravis Quality of Life 15 Scale; Neuro-QoL=Quality of Life in Neurological Disorders; MGC=Myasthenia Gravis Composite

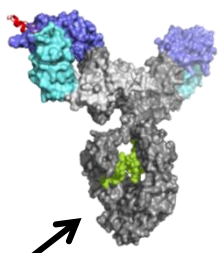
Immunology: Gazyva in LN, MN, SLE

Potential benefit in autoimmune diseases through sustained B cell depletion

Glycoengineered anti-CD20 mAb to increases B-cell depletion

Type II anti-CD20 region

- Increased direct cell death
- Decreased CDC
- Reduced internalization



Glycoengineered Fc region

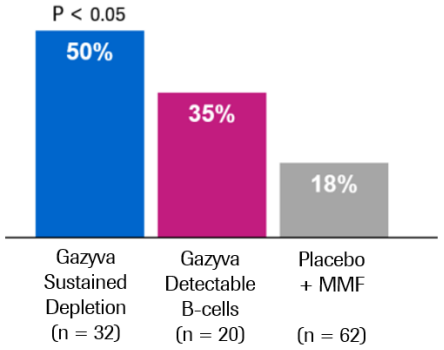
- Higher FcγR affinity
- Increased ADCC/ADCP

- Greater potency than Rituxan in depleting peripheral and tissue B-cells
- Studies suggest that tissue based B-cells play a major role in lupus nephritis

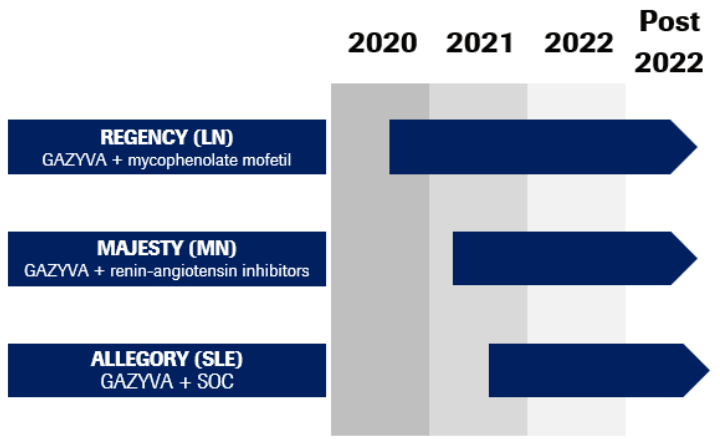
Ph II (NOBILITY) results in LN

FDA BTD

Sustained depletion leads to increased complete renal responses (CRR) at week 76



Ph III trial program



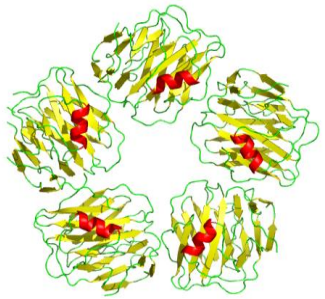
- Ph II (NOBILITY) met both primary and key secondary endpoints with no new safety signals; Ph III (REGENCY) in lupus nephritis (LN) started in Q3 2020
- Ph III (MAJESTY) in membranous nephropathy (MN) started in Q2 2021
- Ph III (ALLEGORY) in systemic lupus erythematosus (SLE) to start in Q4 2021
- Additional indications and combination studies with pipeline assets under evaluation

Furie R et al. Lupus Science & Medicine 2020;7 (Suppl 1):A27; Furie R. et al; ACR 2019; LN=lupus nephritis; MN=membranous nephropathy; SLE=systemic lupus erythematosus; CDC=complement-dependent cytotoxicity; ADCC=antibody-dependent cell-mediated cytotoxicity; ADCP=antibody-dependant cellular phagocytosis; MMF=mycophenolate mofetil

Immunology: Recombinant human pentraxin-2 in fibrotic diseases

Ph III in IPF started in 2021

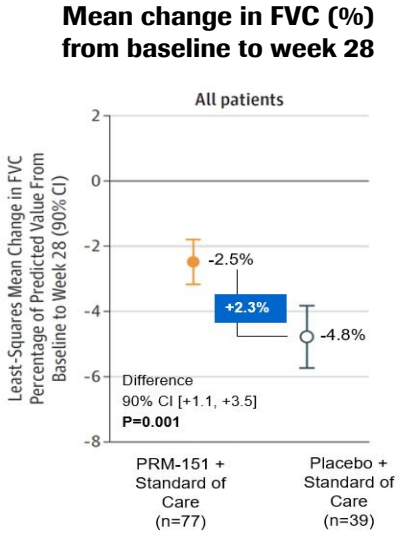
Recombinant human pentraxin-2 (rhPTX-2)



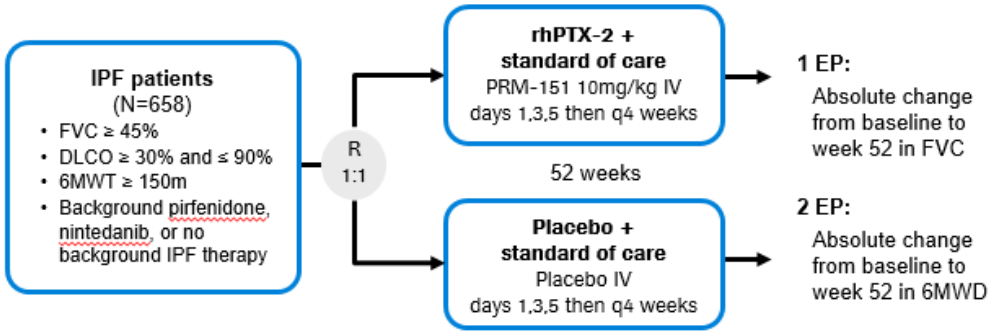
- PTX-2 is an immune regulatory protein that binds DAMPs (cell signals released from dying cells) with specificity for fibrotic tissue
- It plays a critical benefitial role during fibrosis shifting macrophages from a pro-inflammatory and pro-fibrotic to a pro-resolutive state

Ph II results

FDA BTD



Ph III (STARSCAPE) trial design in IPF



- Ph II results: rhPTX-2 slowed decline in lung function (FVC) and exercise capacity (6MWD) over 28 weeks compared with placebo, and a persistent treatment effect was observed in the open label extension study [1,2]
- Ph III (STARSCAPE) of rhPTX-2 + SOC (Esbriet or Ofev) in IPF started in Q1 2021

[1] Raghu et al; JAMA 2018;319(22):2299-2307; [2] Raghu G et al. Lancet Respir Med 2019;7:657-664; IPF=interstitial pulmonary fibrosis; FVC=forced vital capacity; 6MWD= Six minute walk distance; SOC=standard of care; PTX-2=pentraxin-2; DAMPs=damage-associated molecular patterns

Doing now what patients need next