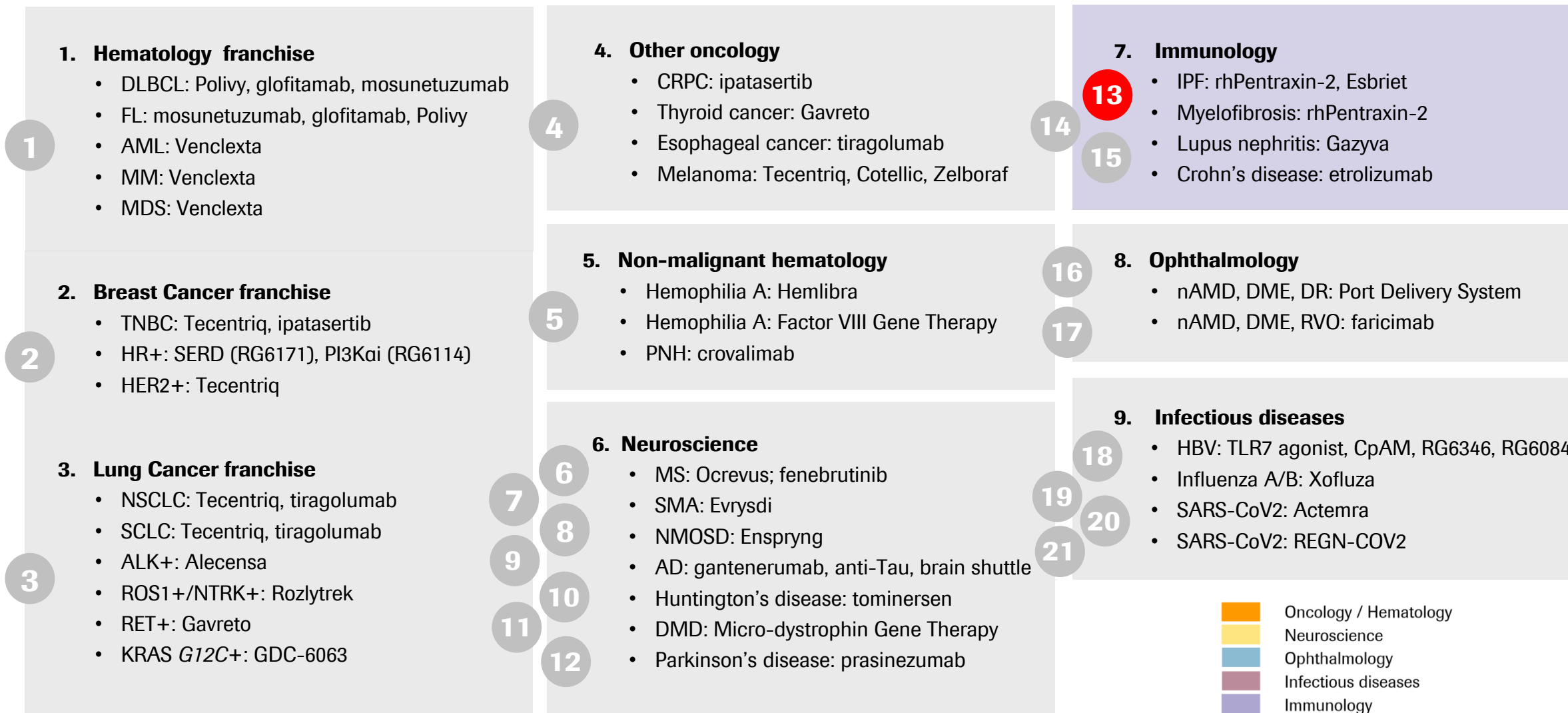

Roche Pharma Day 2020

Late Stage Immunology, Ophthalmology & Infectious Disease

Cristin Hubbard | Senior Vice President, Immunology, Infectious Disease & Ophthalmology, Global Product Strategy

Late stage pipeline update



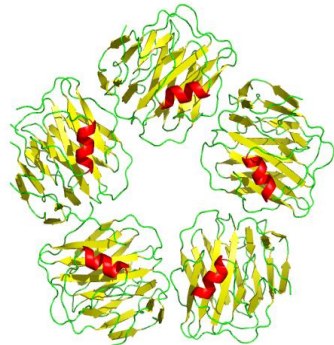
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Recombinant human Pentraxin-2 in fibrotic diseases

Evaluating new options to treat fibrosis in multiple diseases

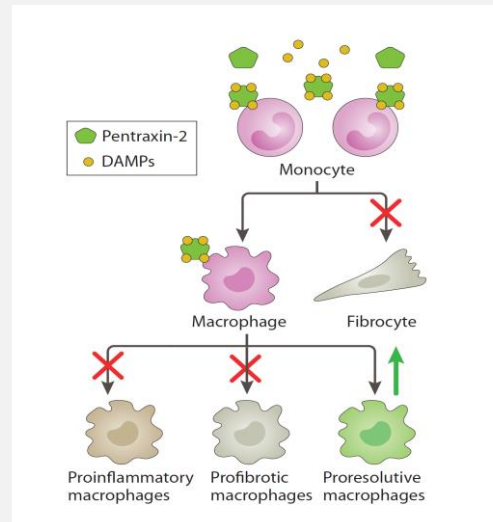
Recombinant human pentraxin-2 (rhPTX-2)

FDA BTD



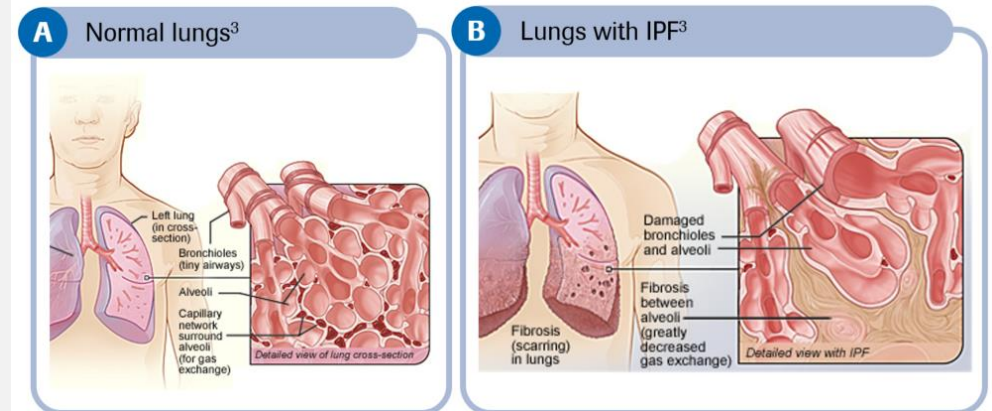
- First-in-class rhPTX-2
- PTX-2 is an immune regulatory protein that binds DAMPs with specificity for fibrotic tissue
- Received BTD for IPF

MOA: PTX-2 inhibits fibrosis formation



- PTX-2 binds monocytes and macrophages via the FcγR and shifts the balance of monocyte differentiation from pro-fibrotic macrophages, fibrocytes to pro-resolutive macrophages
- Serum PTX-2 levels are reduced in patients with IPF, myelofibrosis and other fibrotic diseases; low PTX-2 levels correlate with increased disease severity
- High unmet medical need remains for further slowing lung function decline on top of SOC

Fibrotic tissue in IPF



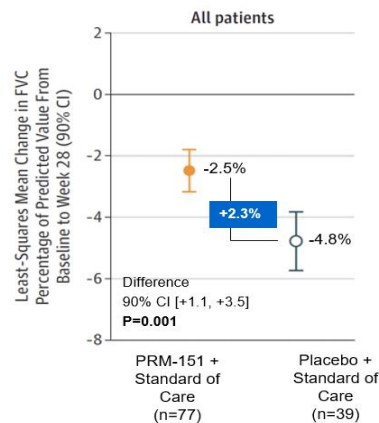
Recombinant human Pentraxin-2 in IPF

Efficacy as monotherapy or in combination with standard of care

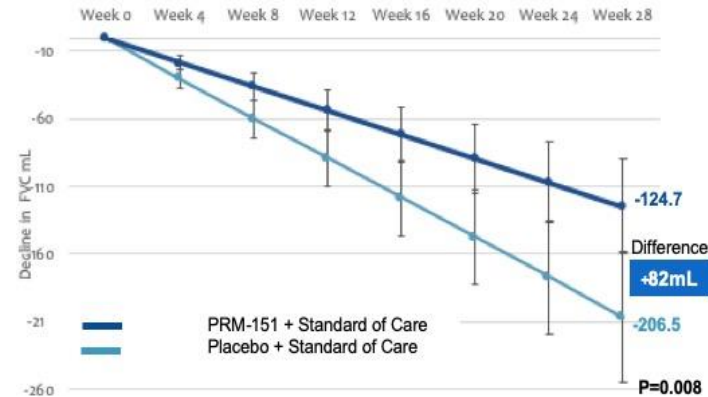


Ph II results in IPF

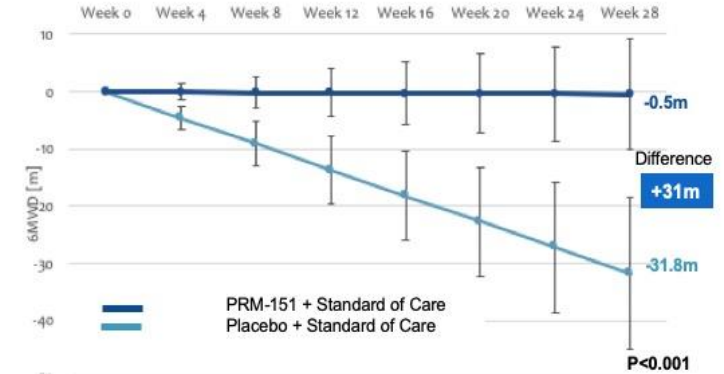
Mean change in FVC (%) from baseline to week 28



Change in FVC (mL) from baseline to week 28

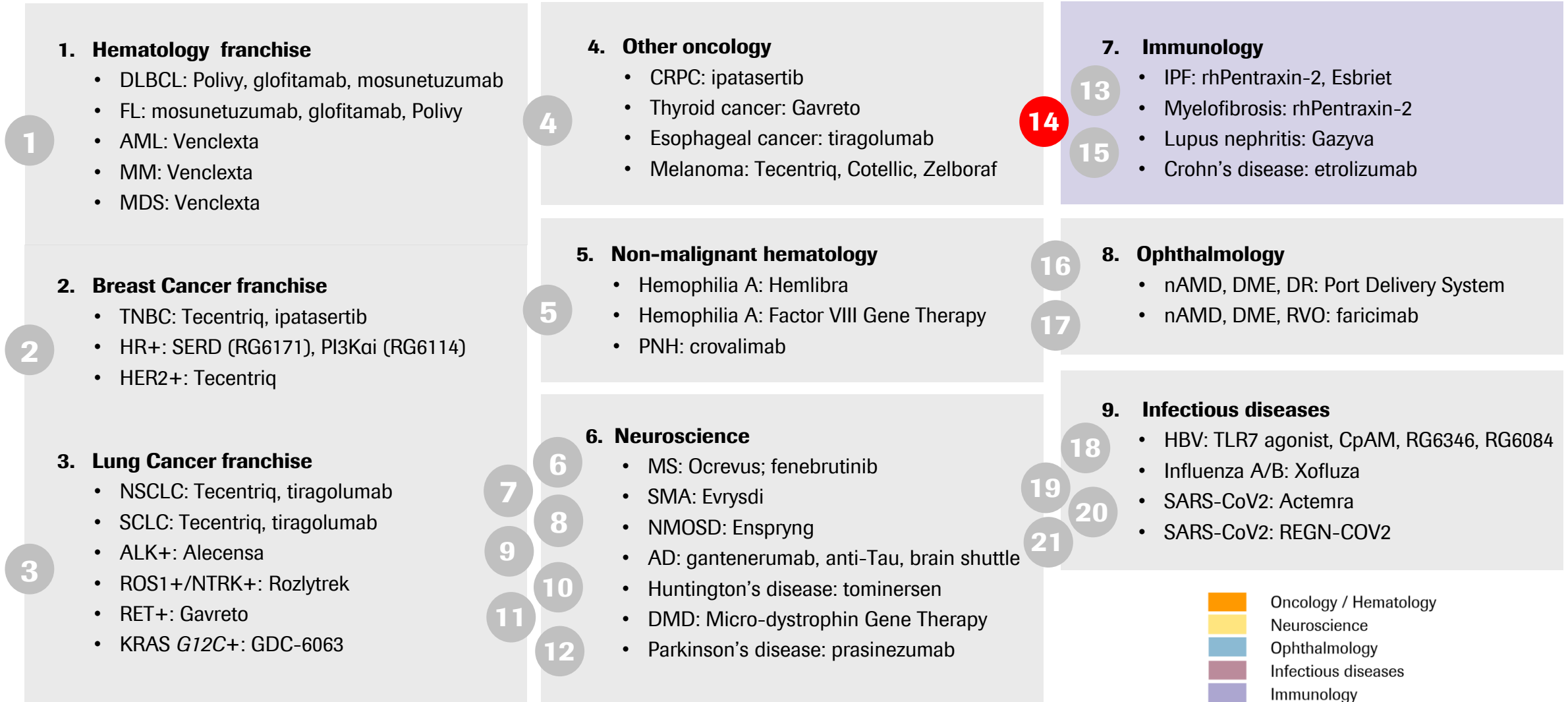


Change in 6MWD (m) from baseline to week 28



- rhPTX-2 resulted in a significantly slower decline in lung function over 28 weeks vs placebo (-2.5% vs -4.8%); most patients received parallel treatment with SoC and no unexpected adverse events with combination treatment were noted
- Ph III (STARSCAPE) of rhPTX-2 + SOC (Esbriet or Ofev) in IPF to start in Q4 2020
- Ph II trial in myelofibrosis on-going; first results expected in Q4 2020

Late stage pipeline update



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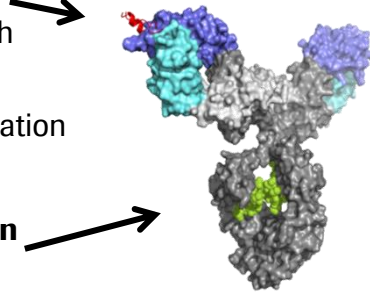
Gazyva in B-cell mediated diseases

Potential benefit in B-cell mediated diseases

Gazyva increases B-cell depletion

Type II anti-CD20 region

- Increased direct cell death
- Decreased CDC
- Reduced CD20 internalization



Glycoengineered Fc region

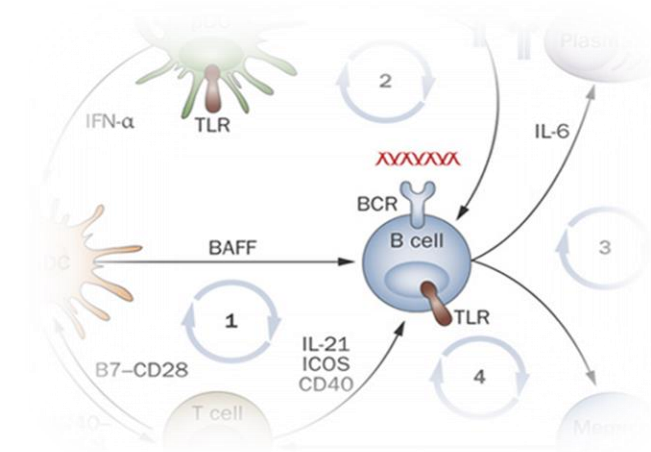
- Higher FcγR affinity
- Increased ADCC/ADCP

- Greater potency than Rituxan in depleting peripheral and tissue B-cells
- Recent studies suggest that tissue based B-cells play a major role in lupus nephritis and a more complete depletion is needed

Evaluating Gazyva in B-cell mediated diseases with high unmet need

• Autoreactive B cells in LN:

- Secrete pathogenic autoantibodies & pro-inflammatory cytokines
- Present self-antigens
- Activate T cells



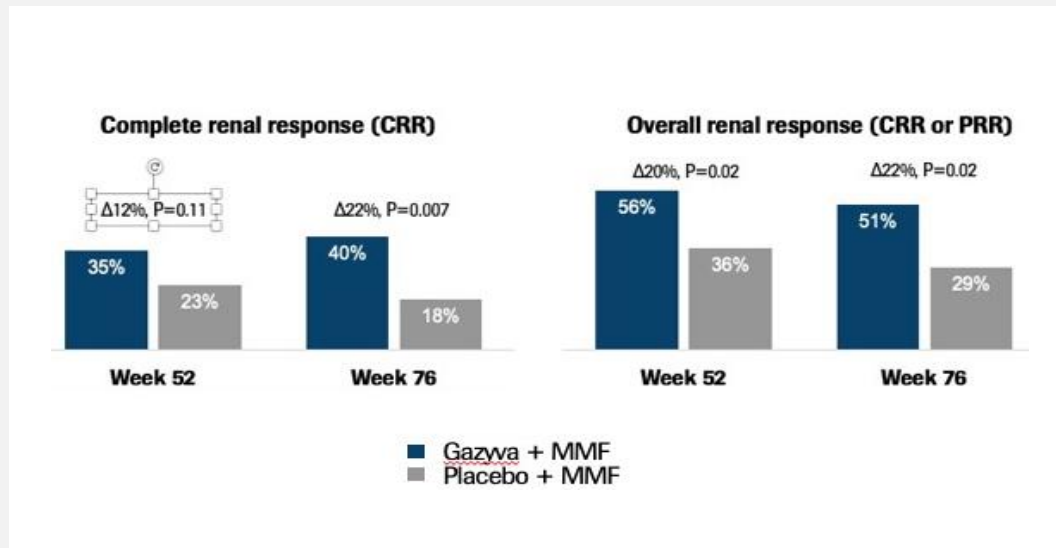
- ✓ • Lupus nephritis (Ph III (REGENCY) to start in Q3 2020)
- ✓ • Membranous nephropathy (Ph III expected to start H1 2021)
- Potential additional opportunities
 - Non-renal systemic lupus erythematosus
 - Several other diseases

Gazyva in lupus nephritis (LN)

Ph III (REGENCY) to start in Q3 2020

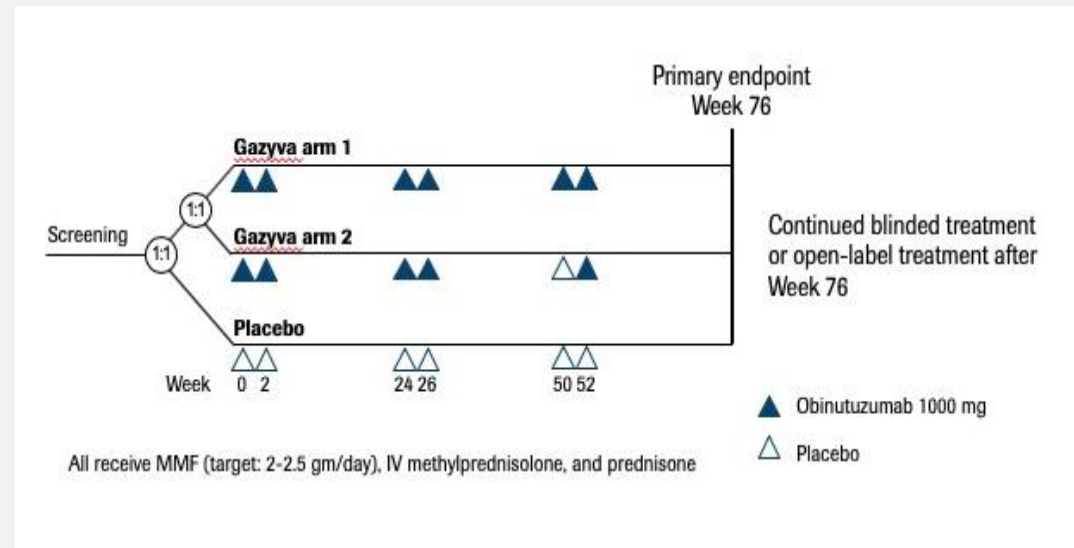


Ph II (NOBILITY) results



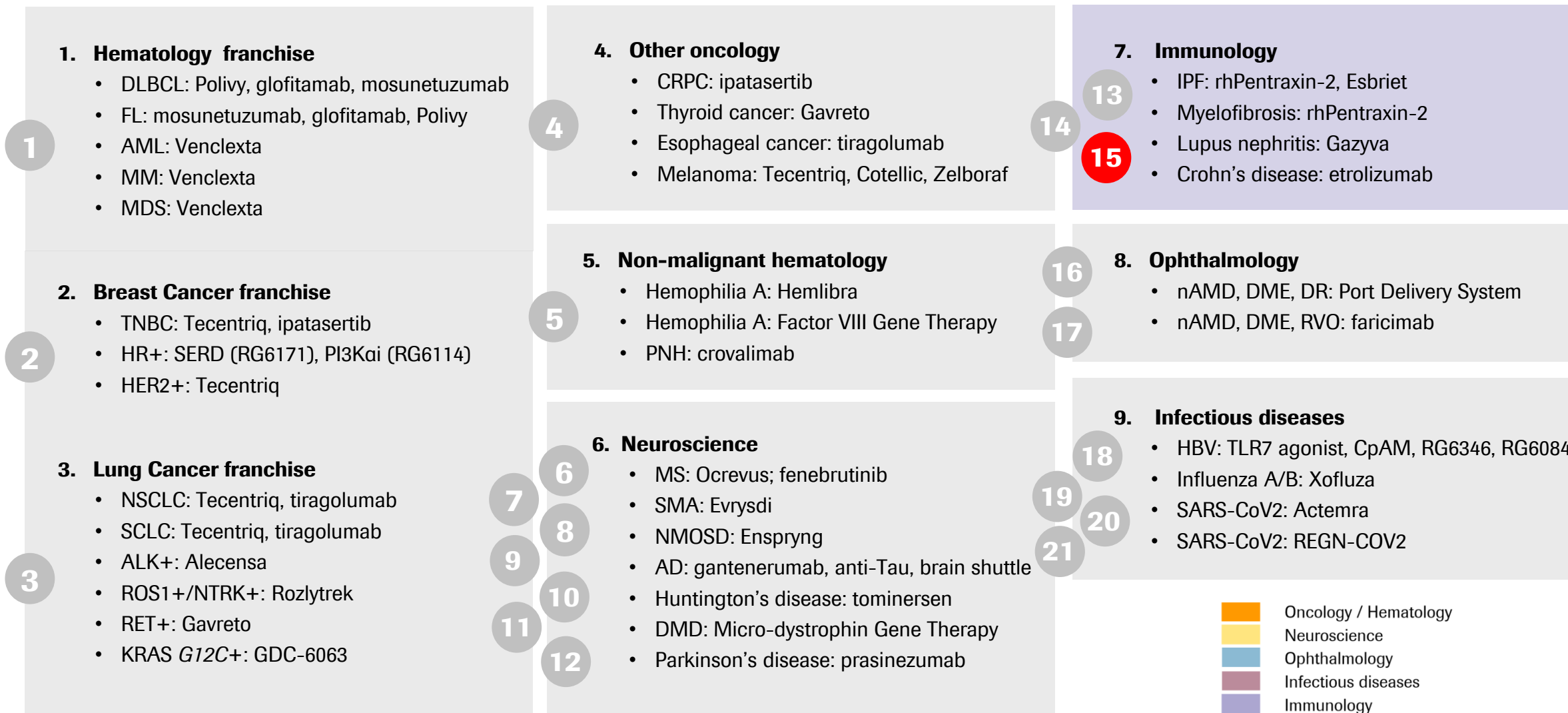
- Ph II (NOBILITY) met both primary and key secondary endpoints with no new safety signals
- BTB for Gazyva in LN awarded by the FDA
- Ph II update (104 weeks) to be presented

Ph III trial design (REGENCY)



- Single pivotal Ph III to replicate Ph II (NOBILITY)
- Primary endpoint is complete renal response (CRR); secondary endpoints include partial clinical response (PRR)
- Ph III (REGENCY) to start in Q3 2020

Late stage pipeline update



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Inflammatory bowel disease (IBD) program on-going

Ph III program of etrolizumab in Crohn's Disease reading out in 2021

Ph III

Etrolizumab

- Gut-selective, dual $\alpha 4\beta 7/\alpha E\beta 7$ anti-integrin antibody
- Development of novel patient-reported outcome measures for UC and Crohn's disease continues

Ph II

IL-22-Fc fusion protein

- Novel non-immunosuppressive MOA
- Restores and protects gut epithelium
- Ph IIb in UC ongoing; N~270

Ph I

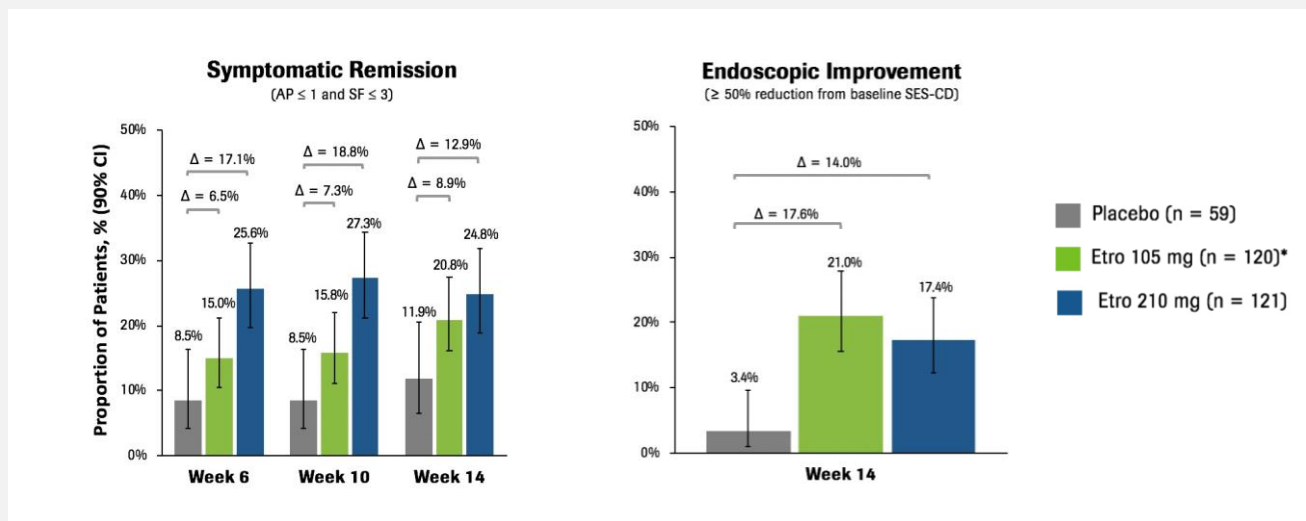
RG6287

- Preserves epithelial cell survival
- Ph1 on-going

IgG-IL-2 fusion protein

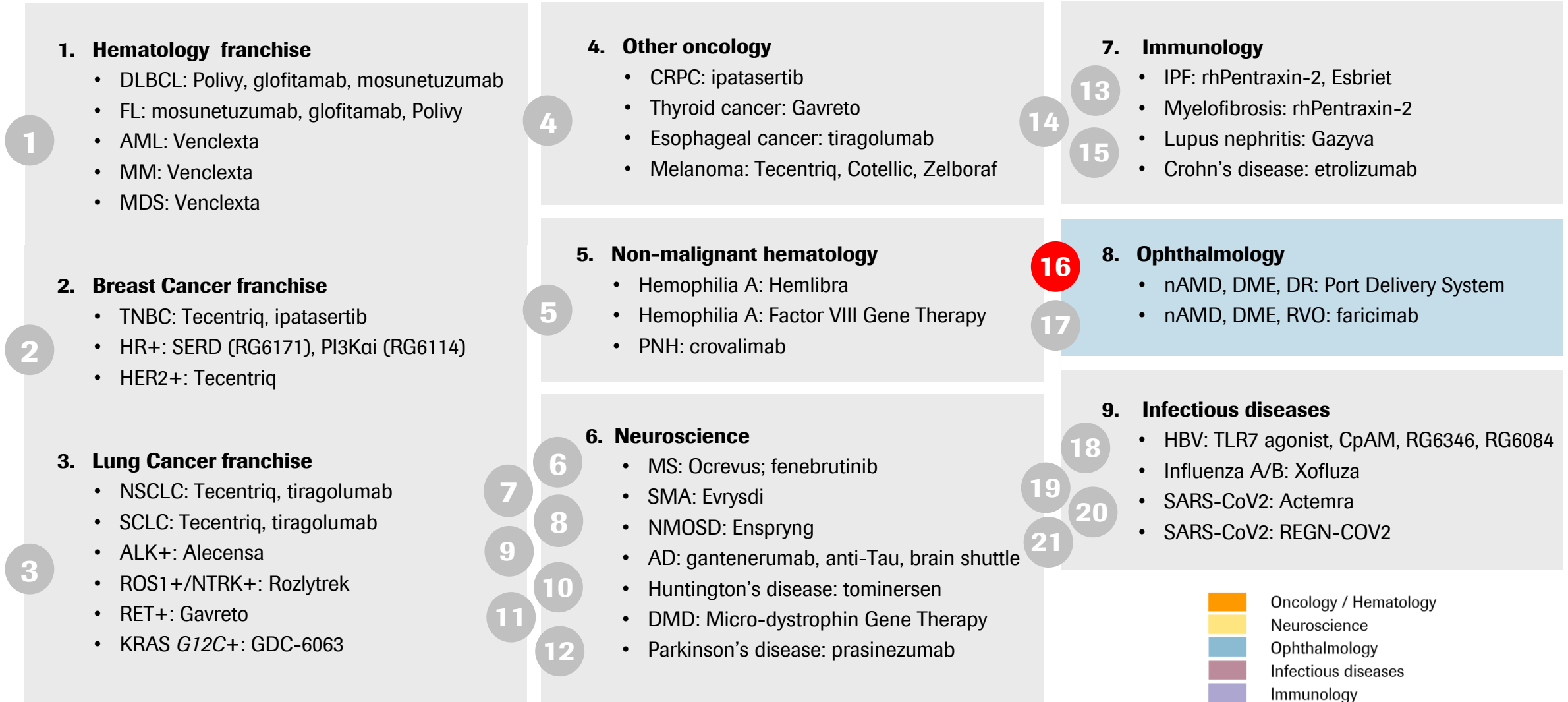
- Promotes regulatory T-cell proliferation
- Ph Ib on-going

Etrolizumab in CD: Ph III (BERGAMOT) interim results



- >70% of patients in cohort 1 were TNF IR, representing a population with high unmet need; symptomatic remission was seen at week 6 and observed through week 14; clinically meaningful endoscopic improvement was demonstrated
- Well tolerated; frequency of adverse events comparable to placebo
- Ph III enrolling with final data expected in 2021

Late stage pipeline update

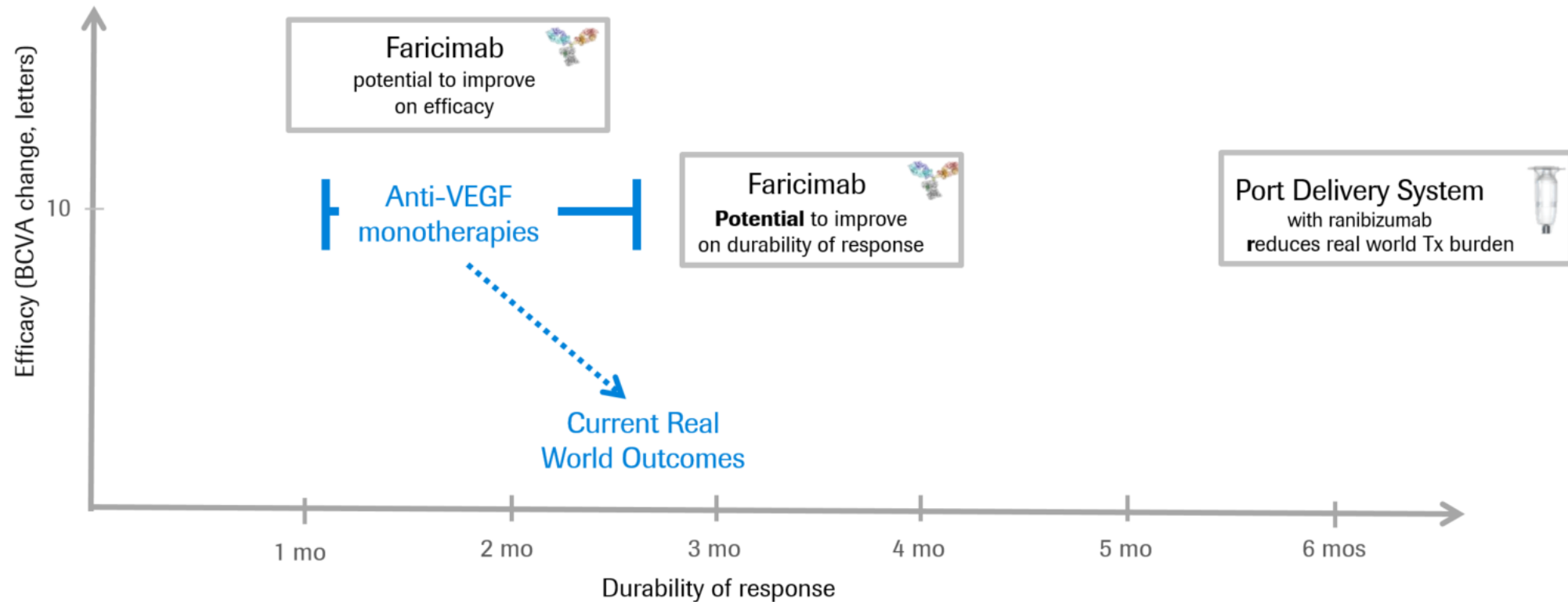


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Late stage ophthalmology progressing rapidly

PDS and faricimab with the potential to address key unmet needs

Opportunity to differentiate on durability and improved efficacy

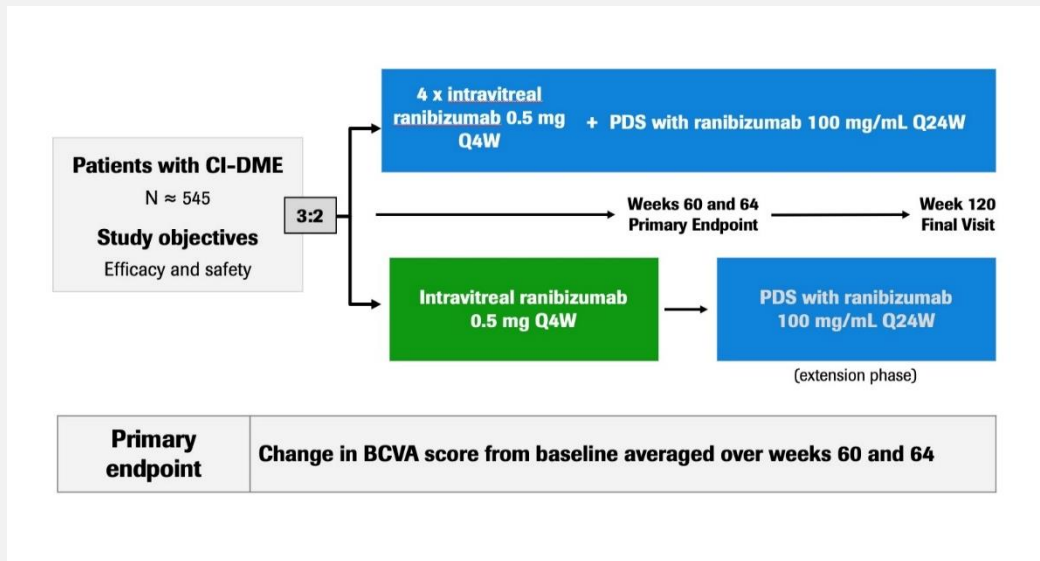


For illustrative purposes only

Port Delivery System (PDS) Platform

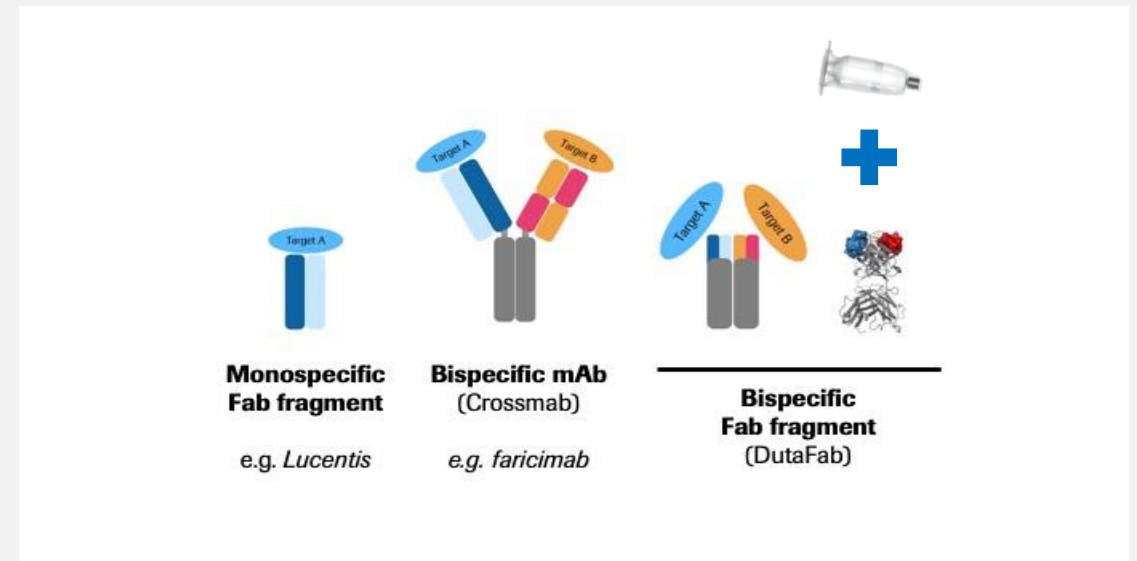
New indications and next generation bispecifics (DutaFabs)

Ph III trial design (PAGODA) in DME



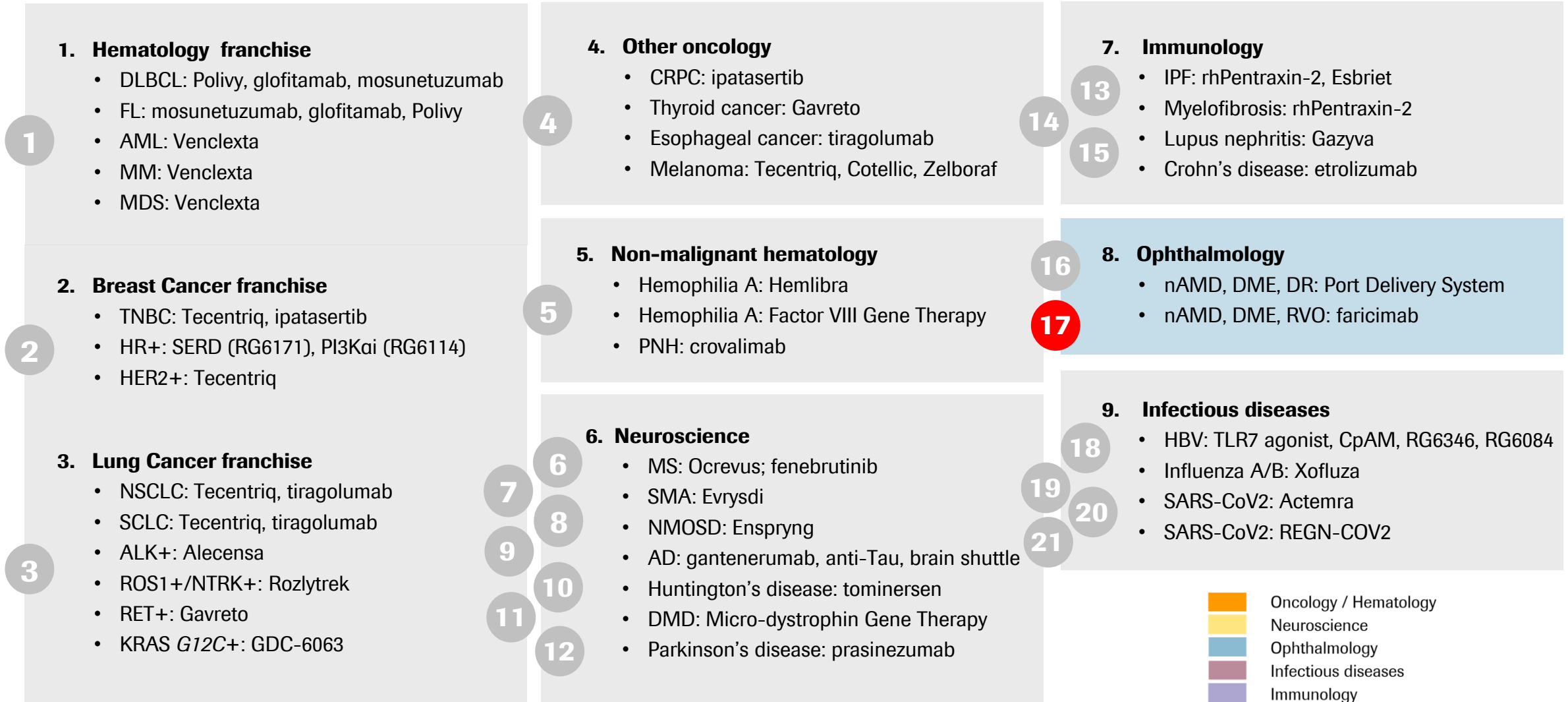
- In the US and EU diabetic eye disease (DME, DR) is the leading cause of vision loss in working age adults
- Ph III (PAGODA) results in DME expected in H1 2022
- Ph III (PAVILION) in DR started in Q3 2020

DutaFabs: A new PDS compatible bispecific format



- DutaFabs are a novel bispecific Fab format significantly smaller than traditional full sized bispecific antibodies
- DutaFabs are compatible with the PDS technology, potentially enabling increased durability beyond Q6M
- 3 DutaFabs with novel dual MOAs in development

Late stage pipeline update

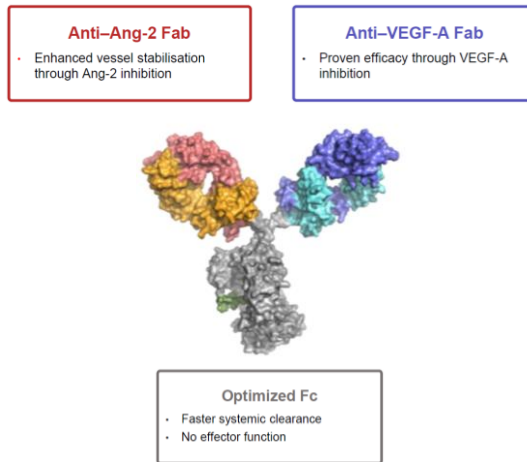


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Faricimab in nAMD

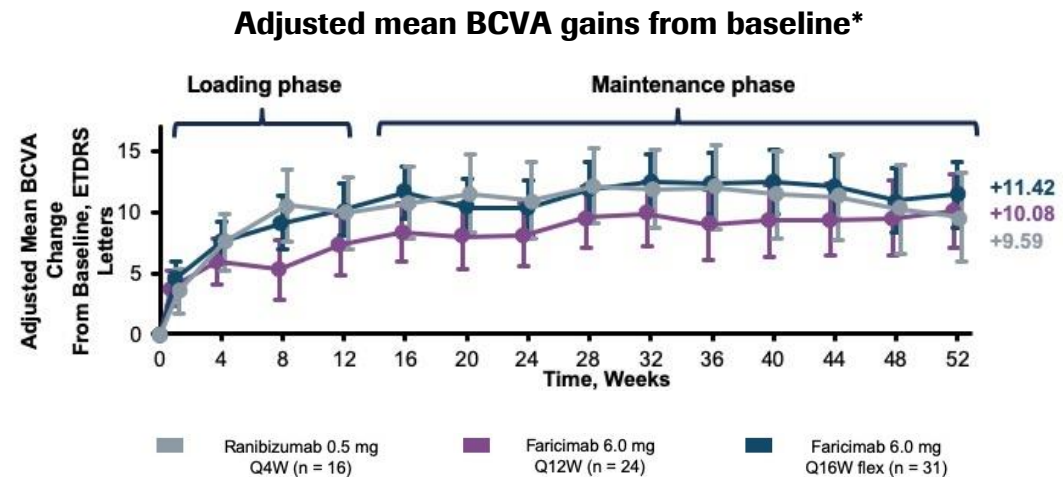
Potential to stabilize retinal vasculature and improve treatment durability

Anti-VEGF/Ang2 bispecific mAb



- First bispecific Ab in ophthalmology binding simultaneously to VEGF and Angiopoietin2 (Ang2)
- Ang2 inhibition may improve vascular stability and reduce retinal inflammation

Ph II (STAIRWAY) results in nAMD

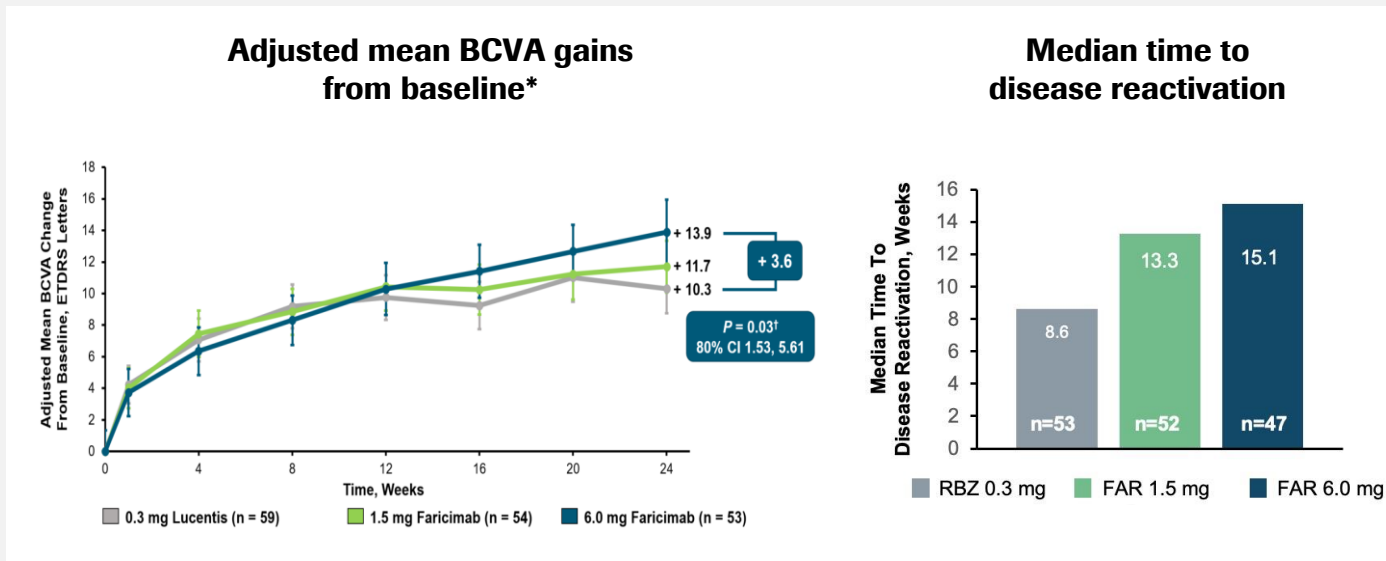


- BCVA gains with faricimab Q16W flexible dose and Q12W comparable with ranibizumab Q4W
- 12 weeks after last loading dose 65% of patients had no disease activity and could potentially benefit from Q16W dosing
- Ph III (TENAYA and LUCERNE) enrollment completed; results expected Q1 2021

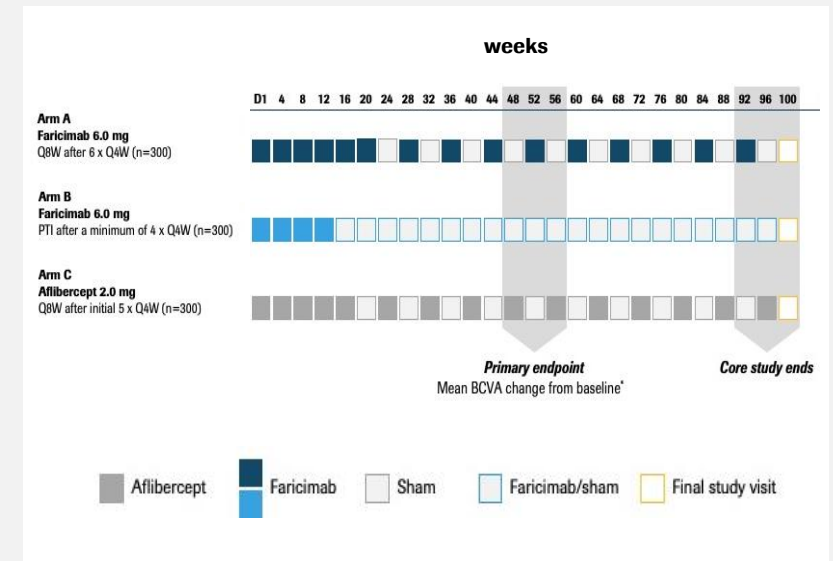
Faricimab in DME

Potential for improved efficacy and durability

Ph II (BOULEVARD) results in DME



Ph III trial design (YOSEMITE, RHINE)



- Robust BCVA efficacy gains with a mean of +13.9 letters from baseline
- Statistically significant gain of +3.6 letters over Lucentis
- Durability shown with median time to disease reactivation of 15.1 weeks for faricimab vs 8.6 weeks for Lucentis

- Primary endpoint: Mean BCVA Δ from baseline at 1yr; arm B to evaluate personalized treatment interval of Q12W or Q16W
- Ph III data expected in Q4 2020
- Ph III in RVO to start in 2021

Doing now what patients need next