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Late Stage Immunology, Ophthalmology and Infectious Disease

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5. uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
6. increased government pricing pressures;
7. interruptions in production;
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9. litigation;
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### Strong short term news flow

**Diversifying the late stage pipeline and setting new standards of care**

<table>
<thead>
<tr>
<th>Product</th>
<th>Timing</th>
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<tbody>
<tr>
<td>risdiplam in SMA</td>
<td>Filed for Type 1/2/3</td>
</tr>
<tr>
<td>satralizumab in NMOSD</td>
<td>Filed</td>
</tr>
<tr>
<td>HTT-ASO in Huntington’s</td>
<td>Ph II &amp; III ongoing; filing latest 2022</td>
</tr>
<tr>
<td>Gazyva in lupus nephritis</td>
<td>initiating Ph III</td>
</tr>
<tr>
<td>etrolizumab in UC and Crohn's Disease</td>
<td>filing in UC in 2020</td>
</tr>
<tr>
<td>PDS in nAMD</td>
<td>fully recruited; filing in 2020</td>
</tr>
<tr>
<td>faricimab in DME/nAMD</td>
<td>recruitment ahead of plan; filing in 2021</td>
</tr>
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### Product Timing Table

<table>
<thead>
<tr>
<th>Product</th>
<th>Filing date</th>
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<tbody>
<tr>
<td>Tecentriq in 1L HCC</td>
<td>Filed</td>
</tr>
<tr>
<td>Tecentriq in neoadj TNBC</td>
<td>2020</td>
</tr>
<tr>
<td>Tecentriq in 1L melanoma</td>
<td>2020</td>
</tr>
<tr>
<td>Tecentriq in FL ovarian cancer</td>
<td>2020</td>
</tr>
<tr>
<td>idasanutilin in R/R AML</td>
<td>2020</td>
</tr>
<tr>
<td>Perjeta + Herceptin FDC-SC</td>
<td>Filed</td>
</tr>
<tr>
<td>ipatasertib 1/2L TNBC</td>
<td>2020</td>
</tr>
<tr>
<td>ipatasertib 1L+ HR+ (chemo treated only)</td>
<td>2020</td>
</tr>
<tr>
<td>ipatasertib in 1L mCRPC</td>
<td>2020</td>
</tr>
<tr>
<td>Polivy in 1L DLBCL</td>
<td>2020/21</td>
</tr>
<tr>
<td>Tecentriq in (neo)adj NSCLC</td>
<td>2021/22</td>
</tr>
</tbody>
</table>

Source: Roche/Genentech, incidence/prevalence in the major markets (US, FR, IT, ES, GB); 1 including China; SOC=standard of care; SMA=spinal muscular atrophy; NMOSD=neuromyelitis optica spectrum disorder; UC=ulcerative colitis; CD=Crohn's disease; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; HCC=hepatocellular carcinoma; TNBC=triple-negative breast cancer; FL=front line; R/R AML=relapsed/refractory acute myeloid leukemia; FDC=fixed dose combination; HR=hormone receptor; mCRPC=metastatic castration resistant prostate cancer; DLBCL= diffuse large B-cell lymphoma; NSCLC=non-small cell lung cancer; AC=all comers

Oncology

Neuroscience

Immunology

Ophthalmology
Creating new opportunities across therapeutic areas

**Immunology, Ophthalmology and Infectious Disease**

<table>
<thead>
<tr>
<th><strong>Etrolizumab</strong></th>
<th><strong>Gazyva</strong></th>
<th><strong>Xolair</strong></th>
<th><strong>Port Delivery</strong></th>
<th><strong>Faricimab</strong></th>
<th><strong>Xofluza</strong></th>
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</thead>
<tbody>
<tr>
<td>Gut-selective anti-β7 integrin with dual MoA inhibiting lymphocyte trafficking &amp; retention</td>
<td>Type II anti-CD20 provides enhanced B cell depletion</td>
<td>Xolair blocks IgE-mediated mast cell activation</td>
<td>Long-acting delivery of ranibizumab to reduce treatment burden</td>
<td>Bispecific antibody with potential to improve efficacy and durability</td>
<td>First “single dose” treatment for influenza that shortens flu symptoms</td>
</tr>
</tbody>
</table>

- Extensive Ph III program in Ulcerative Colitis and Crohn’s Disease
- Efficacy in lupus nephritis in randomized Ph II trial
- Expanding into treatment of nasal polyps and food allergies
- Ph III program in nAMD and diabetic macular edema ongoing
- Ph III program in nAMD and diabetic macular edema ongoing
- CAP-dependent endonuclease inhibitor
There is significant unmet need for improved efficacy in moderate to severe IBD

- **Sustained remission**
  - Only 10-20% of patients remain in remission at 1 year

- **Rapid onset of action**
  - Onset of some agents are slow, taking up to 12 weeks

- **Disease modification**
  - Low rates of endoscopic healing and histological improvement

- **Non-immunosuppressive**
  - Current standard of care increases risk of serious infection and/or malignancy

- **Personalized therapy**
  - No current ability to personalize based on phenotype/biomarker

- **Safe and effective combo therapy**
  - Potential to raise the efficacy ceiling with a safe backbone to combine treatments

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Etrolizumab: First dual-action anti-integrin targeting α4β7/αEβ7
Targets two sources of inflammation – potential for best in class efficacy

### Etrolizumab Phase 3 Program in UC and Crohn’s Disease

*A landmark program designed to generate compelling claims*

#### Etrolizumab Phase 3 Development Program

<table>
<thead>
<tr>
<th>Ulcerative Colitis</th>
<th>Crohn’s Disease</th>
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<tbody>
<tr>
<td><strong>HIBISCUS I</strong></td>
<td>Induction trial comparing etro vs. adalimumab vs placebo in anti-TNF naïve patients</td>
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<tr>
<td><strong>HIBISCUS II</strong></td>
<td>Induction trial comparing etro vs. adalimumab vs placebo in anti-TNF naïve patients</td>
</tr>
<tr>
<td><strong>LAUREL</strong></td>
<td>Maintenance trial evaluating etro vs. placebo in anti-TNF naïve patients</td>
</tr>
<tr>
<td><strong>HICKORY</strong></td>
<td>Induction and maintenance; etro vs. placebo in anti-TNF incomplete responders</td>
</tr>
<tr>
<td><strong>GARDENIA</strong></td>
<td>Sustained remission evaluating etro vs infliximab in anti-TNF naïve patients</td>
</tr>
<tr>
<td><strong>COTTONWOOD</strong></td>
<td>Roll-over, open-label extension trial evaluating safety</td>
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</table>

| **BERGAMOT** | Induction and maintenance trial of etro vs. placebo in anti-TNF naïve and IRs |
| **JUNIPER** | Roll-over, open-label extension trial evaluating safety |

#### Comprehensive IBD Dataset

- **8 clinical studies**
  - 6 Ph3 trials, 2 open-label extension studies
  - TNF-naïve and TNF-IR
- Longitudinal dataset with clinical data, imaging, histology, multiomics, microbiome

#### Program of Firsts

- First *head-to-head comparisons vs. both Humira and Remicade (anti-TNFs)* in randomized, controlled pivotal studies in UC
- First to evaluate *endoscopic improvement* in Crohn’s disease
- First to use central endoscopy reading for patient eligibility and endpoint assessment
- Evaluating over 3,000 patients for induction and maintenance of disease remission

TNF IR is defined as patients who are refractory to or intolerant of TNF inhibitors

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7
Gazyva for Lupus Nephritis
A serious condition with high unmet medical need

Lupus nephritis

500k patients globally with lupus nephritis

- **Proliferative lupus nephritis (LN)** is characterized by:
  - Protein and blood in the urine, progressive loss of kidney function
  - Progressive loss of kidney function
- **Young women of color** at greatest risk
- **8x risk of death** vs. the general population, due to:
  - Uncontrolled disease, complication of treatment, dialysis, cardiovascular disease
  - Complications of treatment or dialysis
  - Cardiovascular disease
- **No approved therapies in U.S.**

Type II anti-CD20 region:
- Increased direct cell death
- Decreased CDC
- Reduced CD20 internalization

Gazyva (glycoengineered anti-CD20 Mab)
Greater b-cell depletion may improve efficacy

Glycoengineered Fc region:
- Higher FcγR affinity
- Enhanced ADCC/ADCP

**RBC casts in urine**

- Gazyva’s MOA shows greater potency than Rituxan in depleting peripheral and tissue-based B cell populations
- Recent studies suggest that tissue-based B cells play a role in lupus nephritis and that their complete depletion is needed
Gazyva - Type II anti-CD20
Positive Phase II results in lupus nephritis

Ph II (NOBILITY) results

Renal response endpoints

<table>
<thead>
<tr>
<th></th>
<th>Obinutuzumab + MMF</th>
<th>Placebo + MMF</th>
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<tbody>
<tr>
<td>Complete renal response (CRR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 52</td>
<td>35%</td>
<td>23%</td>
</tr>
<tr>
<td>Week 76</td>
<td>40%</td>
<td>18%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Obinutuzumab + MMF</th>
<th>Placebo + MMF</th>
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</thead>
<tbody>
<tr>
<td>Overall renal response (CRR or PRR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 52</td>
<td>56%</td>
<td>36%</td>
</tr>
<tr>
<td>Week 76</td>
<td>51%</td>
<td>29%</td>
</tr>
</tbody>
</table>

B-cell depletion in peripheral blood

<table>
<thead>
<tr>
<th>Percent with CD19+ count ≤ 5 cells/μL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obinutuzumab + MMF</td>
</tr>
<tr>
<td>Week 2</td>
</tr>
<tr>
<td>Week 4</td>
</tr>
<tr>
<td>Week 12</td>
</tr>
<tr>
<td>Week 24</td>
</tr>
<tr>
<td>Week 52</td>
</tr>
</tbody>
</table>

- Ph II (NOBILITY) met both primary and key secondary endpoints and provided clinically meaningful benefits through Week 76
- Rapid and complete peripheral b-cell depletion was achieved and sustained through Week 52 without increase in SAEs
- Ph III program expected to be initiated in 2020
### New Indications & Ease of Use

- **Food Allergy - high unmet need**  
  - Affects > 4.8 million children in US with no approved preventative treatments except avoidance

- **Nasal Polyps**  
  - Positive topline results in Q2 (data to be presented at ACAAI in November); U.S. filing in Q4 2019

- **Rapid IgE Point of Care Assay**  
  - 5-minute point-of-care (POC) test to determine total IgE and specific IgE levels to 5 major perennial allergens associated with allergic asthma

- **Home Use**  
  - European Commission approval granted in December 2018; U.S. submission planned

- **Autoinjector**  
  - Improves patient experience

### Food Allergy

- **Allergen avoidance is only partially effective**  
  - US: Every 3 minutes, someone goes to ER due to an adverse food reaction and ~40% of children with food allergy have experienced anaphylaxis

- **Xolair blocks IgE-mediated mast cell activation with data to support efficacy across multiple food allergens**

- **Phase III OUtMATCH Trial initiated Q3 2019**  
  - Designed to determine whether omalizumab can decrease or prevent allergic reactions to peanut and other food allergens (such as cow’s milk, egg, wheat, cashew, hazelnut etc.)

- **Unique collaboration between NIH, CoFAR and Genentech/Novartis**  
  - NIH-sponsored CoFAR (Consortium for Food Allergy Research) as the leading US academic food allergy research centers with established infrastructure and credibility

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2. United States Census Bureau Quick Facts (2015 estimates)
Real world outcomes have significant room for improvement in patients with neovascular AMD

nAMD treatment frequency in real world\(^1\)

Number of VEGF injections in 1\(^{st}\) Year

Number of injections correlates with vision improvement\(^1\)

1 Courtesy of T. Brogan/Vestrum Health, presented by Dr. D. Williams at ASRS 2018; Article in press. Ophthalmology Retina; nAMD=neovascular age-related macular degeneration
Ophthalmology franchise: Upcoming NME results in 2020

Opportunity to build a global business

Port Delivery System in nAMD, DME and DR

- Refillable intraocular implant using proprietary needle assembly
- Reduced treatment burden and potentially improved RW outcomes
- Sustained delivery platform to be combined with NMEs NMEs (VEGF Ang2 DuttaFab)

- Ph II: ~80% of nAMD patients with ≥6 months time to first refill; Median time to refill at 15 months
- Ph III (PAGODA) in DME using 6m dosing interval started in H2 19
- Ph III (PAVILLION) in DR to start in 2020
- Ph III (ARCHWAY) results in nAMD using 6m dosing interval expected mid 2020

Faricimab in nAMD, DME and RVO

- First bispecific binding simultaneously to VEGF and Ang2 for intravitreal use
- Potentially improved vascular stability and reduced retinal inflammation

- Ph II (DME): BCVA gains of +13.9 letters, superior by +3.6 letters vs Lucentis at 6m, secondary endpoints including DRSS support superior efficacy
- Ph III (LUCERNE, TENAYA) in nAMD completed enrollment ahead of plan
- Ph III (YOSEMITE, RHINE) results in DME expected in late 2020
- RVO Ph III program to start in 2020

NME=new molecular entities; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; DR=diabetic retinopathy; RVO=retinal vein occlusion; RW=real world; Ang2=angiopoetin2; BCVA=best-corrected visual acuity; DRSS=Diabetic Retinopathy Severity Score
Faricimab and PDS address key unmet needs in nAMD and diabetic eye disease

Opportunity to differentiate on durability of response and efficacy

Faricimab potential to improve on efficacy

anti-VEGF monotherapies

Faricimab potential to improve on durability of response

Port Delivery System with ranibizumab reduces real world Tx burden

For illustrative purposes only
Xofluza - Unique MOA: Opportunity for broad development program

Single dose studied across variety of patient types and clinical settings

Unique MOA

Xofluza blocks viral mRNA transcription by inhibiting cap-dependent endonuclease activity

Broad Clinical Program

Continuing to advance the science and address the largest unmet needs in influenza:

- **Variety of patient types being studied:**
  - Otherwise Healthy Adults (CAPSTONE-1)
  - High-risk patients (CAPSTONE-2)
  - Pediatric patients (miniSTONE-1)
  - Pediatric patients (miniSTONE-2)
  - Hospitalized patients (FLAGSTONE)

- **Variety of clinical settings being studied**
  - Post-exposure prophylaxis (BLOCKSTONE)
  - Transmission prevention (CENTERSTONE)

- **Pandemic planning**

- **Xofluza** has been shown to have activity against oseltamivir-resistant and avian strains (H7N9, H5N1)

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- Annually **1 in 10 people are affected** by influenza, with millions hospitalized and up to **650,000 deaths** worldwide
- Currently approved antivirals have limitations in terms of efficacy, route of administration, convenience, & resistance

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Creating new opportunities across therapeutic areas

**Immunology, Ophthalmology and Infectious disease key data readouts**

<table>
<thead>
<tr>
<th>2019</th>
<th>2020</th>
<th>2021</th>
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<tbody>
<tr>
<td>Gazyva Lupus Nephritis</td>
<td>Etrolizumab UC</td>
<td>Xolair Food Allergy</td>
</tr>
<tr>
<td>Nobility</td>
<td>HICKORY, HIBISCUS I &amp; II</td>
<td>OUtMATCH</td>
</tr>
<tr>
<td>Xolair Nasal Polyps</td>
<td>Etrolizumab UC</td>
<td>Etrollzumab CD</td>
</tr>
<tr>
<td>POLYP 1 &amp; POLYP 2</td>
<td>LAUREL, GARDENIA</td>
<td>BERGAMOT</td>
</tr>
<tr>
<td>Xofluza PEP</td>
<td>Xofluza Hospitalized</td>
<td>Xofluza Transmission</td>
</tr>
<tr>
<td>BLOCKSTONE</td>
<td>FLAGSTONE</td>
<td>CENTERSTONE</td>
</tr>
<tr>
<td>Xofluza Pediatrics (1-12 yr)</td>
<td>Port Delivery System</td>
<td>Xofluza Pediatrics (0-1 yr)</td>
</tr>
<tr>
<td>miniSTONE-2</td>
<td>ARCHWAY</td>
<td>MiniSTONE 1</td>
</tr>
<tr>
<td></td>
<td>Faricimab DME</td>
<td>Faricimab AMD</td>
</tr>
<tr>
<td></td>
<td>YOSEMITE &amp; RHINE</td>
<td>TENAYA &amp; LUCERNE</td>
</tr>
</tbody>
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- Immunology
- Ophthalmology
- Infectious Diseases
Doing now what patients need next