Roche Analyst Event
Tuesday, 08 June 2021
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Welcome
Karl Mahler, Head of Investor Relations and Group Business Planning

Early pipeline programs in focus
William Pao, M.D., Ph.D., Head of Roche Pharma Research and Early Development
Ira Mellman, Ph.D., Vice President, Cancer Immunology, Genentech Research & Early Development

Late-stage pipeline programs in focus
Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development

ASCO 2021 Highlight
Tecentriq in adjuvant NSCLC: Phase 3 IMpower010 primary results
Heather Wakelee, M.D., Prof. of Medicine, Stanford Univ Medical Center / Deputy Director Stanford Cancer Institute

Q&A
Karl Mahler | Head of Investor Relations and Group Business Planning
Reflecting the quality of research and development at Roche

### Breakthrough Therapy Designations (BTD) since 2013

<table>
<thead>
<tr>
<th>Year</th>
<th>Molecule</th>
<th>Indication</th>
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<tbody>
<tr>
<td>2020</td>
<td>tiragolumab + Tcq</td>
<td>1L PD-L1+ NSCLC</td>
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<tr>
<td></td>
<td>mosunetuzumab</td>
<td>3L+ FL</td>
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<tr>
<td></td>
<td>Tecentriq</td>
<td>unresectable or metastatic ASPS</td>
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<td></td>
<td>Esbriet</td>
<td>uILD</td>
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<td>2019</td>
<td>Gavreto</td>
<td>RET fusion-positive NSCLC</td>
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<tr>
<td></td>
<td>Gavreto</td>
<td>RET mutation-positive MTC</td>
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<td></td>
<td>Cotellic</td>
<td>Histiocytic neoplasms</td>
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<td></td>
<td>Gazyva</td>
<td>Lupus nephritis</td>
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<td></td>
<td>rhPentraxin-2</td>
<td>IPF</td>
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<tr>
<td></td>
<td>Venclexta + Gazyva</td>
<td>1L unfit CLL</td>
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<td></td>
<td>Kadcyla</td>
<td>Adjuvant HER2+ BC</td>
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<tr>
<td>2018</td>
<td>SPK-8011</td>
<td>Hemophilia A</td>
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<td>Enspryng</td>
<td>NMOSD</td>
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<td>Xolair</td>
<td>Food allergies</td>
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<td></td>
<td>Hemlibra</td>
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<td>Rozlytrek</td>
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<td>2017</td>
<td>Polivy + BR</td>
<td>R/R DLBCL</td>
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<td>Venclexta + LDAC</td>
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<td>Zelboraf</td>
<td>BRAF-mutated ECD</td>
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<td>Rituxan</td>
<td>Pemphigus vulgaris</td>
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### Approvals under Real-Time Oncology review (RTOR) since start of the first pilot program in 2018

<table>
<thead>
<tr>
<th>Year</th>
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**NEW application under RTOR**

- **Phase 3 IMpower010 interim analysis data**
- **Tecentriq in adjuvant NSCLC**
Our technology platforms in oncology

Roche pipeline includes differentiated therapeutic platforms

<table>
<thead>
<tr>
<th>Small molecules</th>
<th>Bi-specific mAb</th>
<th>Fusion protein</th>
<th>mAb</th>
<th>Antibody drug conjugate</th>
<th>Personalized neoantigen vaccine</th>
<th>Personalized T-cells</th>
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<td>[Image of small molecule]</td>
<td>2:1 format</td>
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<td>• giredestrant</td>
<td>• mosunetuzumab</td>
<td>• PD1-IL2v</td>
<td>• tiragolumab</td>
<td>• Polivy</td>
<td>• Autogene cevumeran²</td>
<td>• programmed T-cells⁵</td>
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<td>• belvarafenib</td>
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<td>• FAP-4-1BBL</td>
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<td>• KRAS G12C</td>
<td>• PD1xTIM3</td>
<td>• PD1xLAG3</td>
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<td>• HLA-A2 WT1xCD3</td>
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</tbody>
</table>

Target oncogenes, induce apoptosis, suppress tumor growth

Engage and activate T cells to kill tumour cells

Amplify immune response

Amplify immune response

Targeted toxic payload

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

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

Examples listed are highlighted during today’s presentation

In collaboration with ¹Hanmi ²Biontech; ³Vaccibody; ⁴Adaptive, ⁵SQZ Biotechnology
Early pipeline programs in focus

William Pao, M.D., Ph.D. | Head Roche Pharma Research & Early Development (pRED)
Roche pRED’s contributions to launching new medicines

Science and innovation have been keys to success

Newly launched Roche medicines since 2011

Molecules under full development

- glofitamab - NHL
- cibisatamab – MSS CRC
- gantenerumab – AD
- tominersen - HD
- crovalimab* – PNH
- SRP9001 – DMD
- AT-527 – COVID-19

Roche pRED supported development; *in collaboration with Chugai

NHL - Non-Hodgkin Lymphoma; MSS CRC - microsatellite stable colorectal cancer; AD - Alzheimer’s Disease; HD - Huntington’s Disease; PNH - paroxysmal nocturnal hemoglobinuria; DMD - Duchenne’s Muscular Dystrophy
pRED oncology focus areas
Covering a range of modalities in line with state of the art cancer biology

Molecular Targeted Therapy (MTT) – small molecules
- Cancer signaling
- Targeted protein degradation

Cancer Immunotherapy large molecules
- Direct T-cell engagers
- Generators of tumor selective immune cells
- Modulators of T-cell activity & innate immunity

‘Game Changing’ Innovation
- New targets, technologies, collaborations and partnerships

Cancer Immunotherapy small molecules
- Modulators of T-cell activity & innate immunity

Segment sizes are representative
Harnessing external innovation: 2018-2021

**In-licensing projects of high scientific quality and strategic fit**

- **Tusk Acquisition**
  - CD25 inhibitor (antibody) which entered clinical trial in 2019 (CIT)

- **Vividion**
  - 5 projects on covalent small molecules in early discovery (MTT)

- **Blueprint**
  - 2 programs in preclinical phase (MTT)

- **C4 Therapeutics**
  - 3 projects on targeted protein degradation in preclinical phase (MTT)

- **Idorsia collaboration**
  - EP2/4 small molecule inhibitor in preclinical phase (CIT)

- **University Lausanne & EPFL**
  - Strategic collaboration in cancer immunotherapy (CIT)

**Multiple strategic partnerships with biotech and academia**

- **Orano Med**
  - Pre-targeted radiotherapy using alpha-emitters (CIT)

- **SQZ Biotech**
  - Technology to manipulate antigen presenting cells (PBMCs) for vaccination (CIT)

- **Memorial Sloan-Kettering Cancer Center**

- **University of Zürich**

- **Harvard University**

- **ETH Zürich**

- **German Cancer Research Center**

- **ImaginAb**

- **VDI**

- **LUMC**

- **VHIO**

- **NIH**

**MTT** - Molecular Targeted Therapy; **CIT** - Cancer Immunotherapy
pRED Oncology development pipeline

<table>
<thead>
<tr>
<th>MTT</th>
<th>Cellular Signaling</th>
<th>Ph0</th>
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</table>

- Large Molecule
- Small Molecule
- Cell Therapy

MTT - Molecular Targeted Therapy; CIT - Cancer Immunotherapy; NME – new molecular entity
T-cell Bispecifics in early clinical development: Redirect T-cell attack
Utilizing novel 2:1 format for maximal efficacy

Late clinical development
- Cibisatamab – carcinoembryonic antigen; colorectal cancer
- Glofitamab – CD20; Non-Hodgkin lymphoma

Early clinical development
- NME 1 – malignant hematology
- NME 2 – solid tumors
- TYRP1 x CD3 (RG6234) – melanoma

Early clinical development – TCR-like
- HLA-A2 WT1 (RMF peptide) – AML/ALL and solid tumors
- NME 3 – solid tumors

Preclinical development
- Enhance specificity and safety of TCBs by masking the anti-CD3 Fab fragment

Glofitamab: Flexibility to combine with anti-CD20 mAbs

**Glofitamab 2:1 format: Option to combine with Rituxan (R) and Gazyva (G)**

1:1 bispecific

1 CD20 binder cannot readily displace combined strength of 2 CD20 binders of R/G

2:1 bispecific

2 CD20 binders can compete equally with R/G and displace them due to similar avidity

R or G

- CD20 antigen
- R/G
- 1:1 CD20xCD3
- 2:1 CD20xCD3

**Glofitamab + Gazyva:**

Strong efficacy demonstrated in preclinical and clinical studies

**OCI-Ly18/hu-mice DLBCL model**

Anti-tumor activity observed in almost all evaluable patients

Morschhauser, F. et al. ASH 2019, P-1584

- Bivalent binding of glofitamab on B-cell allows equal competition with bivalent aCD20s due to similar functional affinity for CD20
- CD20 B-cell occupancy by CD20 x CD3 only 2% for maximum efficacy

- Dual CD20-targeted therapy with concurrent glofitamab and Gazyva shows promising clinical activity and manageable safety in relapsed or refractory B-cell NHL in Ph Ib
- Comprehensive clinical development program in NHL as single-agent and in combinations
Assessing the potential of rapid non-invasive whole-body monitoring of patients with r/r NHL treated with glofitamab*

Preclinical studies with novel CD8 T-cell PET tracer using CEA TCB as proof of concept

- CEA-4-1BBL/CEA-TCB combination induced the strongest tumor regression

- PET distribution images 40 h post-injection showed homogenous signals throughout tumor borders and tumor center in CEA-TCB-treated and CEA-4-1BBL/CEA-TCB combo groups, respectively

• High sensitivity of $^{89}$Zr-Df-IAB22M2C tracer for the detection of intra-tumoral CD8+ T-cell infiltrates as promising monitoring tool for patients’ early response to cancer immunotherapy

• *FPI in sub-study of ongoing Phlb to assess potential of rapid non-invasive whole-body monitoring of patients with r/r NHL treated with glofitamab May 2021

*Glofitamab + $^{89}$Zr-Df-IAB22M2C PET-Tracer combination, Phlb in r/r NHL, NCT03533283; in collaboration with ImaginAb
Glofitamab in combination with CD19-4-1BBL (RG6076)
Potential for off-the-shelf alternative to 2nd generation CD19-CAR-T-cell

- Signal 1: NK or T-cell activation delivered by glofitamab
- Signal 2: CD19-4-1BBL leads to enhanced NK and T-cell activation and promotes a durable immune response

• CD19-4-1BBL enhances in vivo effector function of T or NK cells in the presence of CD19+ tumor targets in combination with glofitamab as well as obinutuzumab
• Ph I of CD19-4-1BBL in combination with glofitamab in r/r NHL ongoing

Umaña, P., AACR 2021
HLA-A2 WT1 x CD3 (RG6007) targeting intracellular oncoprotein WT1 TCR receptor-like T-cell bispecific for heme and solid tumors

- Targets intracellular proteins via peptide MHC complexes (pMHC) and CD3 T-cells
- High specificity for tumor cells sparing healthy cells
- Potential for development in hematology and solid tumors, Ph I single agent dose escalation of RG6007 in AML ongoing

PD1 mAbs in early clinical development

Enhancing activity of standard of care checkpoint inhibitors

**PD1-LAG3/RG6139**
- LAG-3
- PD-1
- PGLALA-Fc

**PD1-TIM3/RG7769**
- TIM-3
- PD-1
- PGLALA-Fc

**PD1-IL2v/RG6279**
- Bivalent high avidity binding to PD-1
- IL-2 variant fused to Fc region
- PGLALA-Fc

- Ph 1 dose expansion cohorts in solid tumors ongoing
- Randomized Ph 2 start vs anti-PD1 exp. 2021

- Ph 1 dose expansion cohorts in solid tumors ongoing
- Randomized Ph 2 start vs anti-PD1 exp. 2021

- Ph 1 dose escalation cohorts in solid tumors ongoing, data presented at AACR 2021
PD1 mAbs in early clinical development
Enhancing activity of standard of care checkpoint inhibitors

- PD1-LAG3/RG6139
  - Bivalent high avidity binding to PD-1
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- PD1-IL2v/RG6279
  - IL-2 variant fused to Fc region
  - Ph 1 dose escalation cohorts in solid tumors ongoing, data presented at AACR 2021
PD1-IL2v (RG6279): Delivering IL2 variant to PD-1+ T-cells

IL2v preferentially activates effector T cells

- IL2v engineered to eliminate binding to IL-2Rα (CD25), inducing only IL-2Rβγ agonism, thereby avoiding binding on endothelial cells and preferential expansion of Tregs

IL2v delivery to PD-1+ T cells

- PD1-targeting increases IL2v potency towards PD-1+ cells

Superior approach to exploit tumor-specific T-cells vs. CPI alone

- PD1-IL2v treatment leads to greater expansion of proliferative and cytotoxic effector cells compared to non-PD-1-targeted IL2v and anti-PD-1

CPI – Check point inhibition

1. Umaña, P., AACR 2021; 2. Wullschleger, S., AACR 2021
Encouraging preclinical activity of cis-targeted PD1-IL2v (RG6279)

**PD1-IL2v: Superior efficacy vs. aPD-1 and aPD-1 + FAP-IL2v**

- Ph1 dose escalation with RG6279 in solid tumors ongoing (NCT04303858)

**PD1-IL2v: Enhanced efficacy in combination with aPD-L1**

- **Orthotopic Panc02-H7 model**

1. Umaña, P., AACR 2021; 2. Wullschleger, S., AACR 2021
Anti-CD25 (RG6292)
Selective regulatory T-cell depletion without affecting IL-2 signaling

- RG6292-mediated Treg depletion leads to redistribution of IL-2 to effector T-cells

Solomon et al., Nature Cancer volume 1, 1153–1166 (2020), Amann AACR 2020
Anti-CD25 (RG6292)
Selective regulatory T-cell depletion without affecting IL-2 signaling

- Preliminary single agent dose escalation data indicate good tolerability with manageable skin toxicity being the most frequent AE
- PhI dose escalation as single agent (NCT04158583) and in combination with Tecentriq (NCT04642365) in solid tumors ongoing

**Preferential binding of RG6292 to iTregs in vitro**

- isotype control
- CDB T cells
- nTreg
- iTreg

**RG6292 induces dose dependent blood Treg depletion in patients**

- Consistent trend of Treg depletion observed from 2mg cohort onwards with > 75% Treg depletion from baseline

**RG6292 induced an inflamed tumor type in patients**

- Immune cell relocation and conversion of tumors to a CD8 inflamed phenotype

nTreg: naive/resting Treg; iTreg: induced/activated Treg; AE: adverse event

Kolben, AACR 2021
Increasing the therapeutic index of T-cell Bispecifics via novel protein engineering

Enhancing specificity and safety of TCBs by masking the anti-CD3 Fab fragment

- Protease-activation using anti-idiotypic masks enables tumor specificity of a T-cell bispecific allowing for optimized on-target activity while minimizing off-tumor activity.

1Geiger et al., Nat Commun. 2020 Jun 24;11(1):3196
Early pipeline programs in focus

Ira Mellman, Ph.D. | Vice President, Cancer Immunology, Genentech Research & Early Development (gRED)
Robust gRED oncology portfolio

**Targeted Therapy**

- *Anti-BCMA/CD16a
- Anti-HER2/CD3 TDB
- *belvarafenib
- cevostamab (FcRH5xCD3)
- *IL15/IL15-Ra-Fc
- *DNA vaccine
- KRAS G12Ci
- *MAGE-A4 ImmTAC
- CIT-NME-1
- CIT-NME-2
- *SHP2i

**Cancer Immunotherapy**

- *Autogene cevumeran
- *ipatasertib
- mosunetuzumab
- inavolisib (mPI3Kα inh)
- giredestrant (SERD)
- tiragolumab

* partnered/acquired programs
Ras-MAPK pathway in cancer

Due to pathway cross-talk and feedback mechanisms, combination strategies are required for optimal clinical effectiveness and to tackle resistance.
GDC-6036 (KRAS G12C inhibitor) in solid tumors

G12C driver mutations found in 12% of all NSCLC patients

- Highly potent irreversible covalent inhibitor of the KRAS G12C mutant protein, which becomes locked in an inactive state
- Minimal safety findings leading to wide nonclinical safety margins
- Ph I dose escalation and expansion in KRAS G12C+ solid tumors started in Q2 2020

NSCLC = non small cell lung cancer

In vitro cell line potency

Genentech unpublished results

The RAS pathway

- GDC-6036 as a key combination partner for our portfolio, both targeted and immunotherapeutics
- RAS pathway activation can promote resistance to immunotherapy by reducing expression of MHC class I and tumor neoantigen presentation
- Cancer immunotherapy established as standard of care in 1L NSCLC, but inhibition of KRAS G12C is expected to deepen activity and extend durability
Belvarafenib is a potent and selective RAF dimer inhibitor

**Selective inhibition of mutant RAF dimers**

- Inhibition of RAF dimers, including downstream of RAS signaling (e.g. NRAS)
- Exceptional CNS penetration in preclinical studies

**Promising efficacy in CPI-experienced NRAS melanoma**

- Responses in 5/13 patients (38.5%) including in 5/11 patients with prior CPI (45.5%)*
- Belvarafenib + cobimetinib showed acceptable tolerability
- Further studies ongoing in NRAS melanoma (~25% of melanoma pts)

* Belvarafenib in partnership with Hanmi, * 9 patients evaluable for response assessment; 4 non-evaluable patients at time of data cut; CPI=checkpoint inhibitor
Strategies to promote an antitumor immune response by phenotype

Target “rate limiting steps” associated with primary and secondary resistance

**IMMUNE DESERT**
- Generate/release/deliver antigens
- Enhance antigen presentation and T-cell priming
- Redirect and engage T cells

**IMMUNE EXCLUDED**
- Recruit T cells to tumour
- Address stromal barrier
- Redirect and engage T cells

**INFLAMED**
- Invigorate T cell response
- Redirect and engage T cells

---

Some patients may only require targeting of negative regulator (aPD-L1 monotherapy) to enable cancer immunity

Some patients will need two or more therapies to enable cancer immunity (e.g., to drive infiltration, boost MHC expression, etc)

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Multiple modalities and approaches to leverage T cell immunotherapy

- Monoclonal antibodies
- Bispecific antibodies
- Cytokines
- Neoantigen vaccines
- NeoT cell therapy
There are many T cell checkpoints to combine with PD-1/L1 blockade, why choose TIGIT?

**TIGIT is an inhibitory receptor discovered at Genentech**

- First checkpoint inhibitor to yield positive randomized data in NSCLC in combination with PD-1/L1
- Only negative regulator besides PD-1 expressed by T_{scm} cells, a key target of aPD-1/L1
- Convergence with PD-1-mediated regulation of CD226 and CD28 costimulation
- Possible antibody-mediated modulation of dendritic cells, T_{regs}, & NK cells

NK, natural killer
The convergence of the TIGIT and PD-1 pathways: CD226 and CD28 are both “clients” of PD-1

- TIGIT competes with CD226 for ligand binding
- PD-1 mediates dephosphorylation of both CD28 and CD226
- Optimal activation of costimulation requires coordinated inhibition of both TIGIT and PD-1
- TIGIT and PD-1 expressed on a likely target cell for PD-(L)1 therapy: T stem cell memory cells

X. Xu, E. Hui, J. Hagar, K. Banta, E. Chiang, I. Mellman, et al., in preparation
TIGIT activity may also reflect modulation of myeloid cells, CD226 suppression of Treg, NK cell activation

Modulation of myeloid (dendritic) cells creates proinflammatory tumor microenvironment

CD226 signaling may dampen Treg suppression, promote effector phenotype

TIGIT is also expressed by NK cells, unlike PD-1

Anti-TIGIT Fc:FcyR interaction may sequester TIGIT away from the synapse, and play a role in reprogramming of myeloid cells
gRED bispecific antibody portfolio

**Mosunetuzumab**
CD20 x CD3

**Cevostamab**
FcRH5 x CD3

**RG6296**
BCMA x CD16A

**RG6194**
HER2 x CD3
Cevostamab (FcRH5 x CD3)
Promising activity in heavily pretreated R/R MM patients

- Humanized IgG-based T-cell-engaging bispecific ab
- FcRH5 expressed exclusively in the B-cell lineage and across all maturation stages (elevated in myeloma cells and normal plasma cells vs normal B cells\(^1\))
- Expressed on myeloma cells with near 100% prevalence

1. Li et al. Cancer Cell 2017;31:383–95; Ig=immunoglobulin; MM=multiple myeloma; ab=antibody; CR = complete response; sCR=stringent CR; PR=partial response; VGPR=very good partial response; ORR=overall response rate

### Cevostamab Ph 1 dose escalation in R/R MM

![Graph showing response rate in ≥3.6/20mg cohorts]

- Responses in penta-drug refractory pts (7/17, ORR:41%) and patients with prior BCMA (5/8, ORR:63%)
- Responses observed across all FcRH5 expression levels (FcRH5 expression on myeloma cells detected in all patients)
- Manageable toxicities with step-up dosing (CRS most common in C1; nearly all grade 1-2; one patient with grade 3 CRS)
Autogene cevumeran, individualized neoantigen mRNA vaccine
Ph II studies underway in 1L melanoma

- Fully individualized vaccine: mRNA vectors provide patient specific therapy
- Novel algorithms predict neoantigens recognized by T cells
- On demand-production (highly iterated and reproducible with low failure rate)
- Liposomal formulation for systemic delivery IV
- Ph1 showed neoantigen-specific T cell responses in the majority of patients (AACR 2020)
DNA vaccine with distinct mechanism to activate immune response

Ph1 showed neoantigen-specific T cell responses in patients (SITC 2019)
NeoT: Personalized T cell therapy directed at neoantigens

In collaboration with Adaptive Biotechnologies

![Diagram of NeoT process]

TCR: T cell receptor, HLA: human leukocyte antigen; PBL: peripheral blood leukocytes
Late-stage programs in focus

Levi Garraway, M.D., Ph.D | Chief Medical Officer and Head of Global Product Development
## Significant near-term oncology news flow

### Key upcoming oncology news flow

<table>
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<tr>
<th>Product</th>
<th>Indication</th>
<th>Data/filing</th>
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<td>NSCLC adj</td>
<td>2021</td>
</tr>
<tr>
<td></td>
<td>SCCHN adj</td>
<td>2022</td>
</tr>
<tr>
<td></td>
<td>RCC adj</td>
<td>2022</td>
</tr>
<tr>
<td></td>
<td>1L mUC</td>
<td>2022</td>
</tr>
<tr>
<td></td>
<td>NSCLC neoadj</td>
<td>2022</td>
</tr>
<tr>
<td></td>
<td>HCC adj</td>
<td>2022</td>
</tr>
<tr>
<td>Alecensa</td>
<td>ALK+ NSCLC adj</td>
<td>2022</td>
</tr>
<tr>
<td>Polivy</td>
<td>1L DLBCL</td>
<td>2021</td>
</tr>
<tr>
<td>Venclexta</td>
<td>r/r MM t(11:14)</td>
<td>2022</td>
</tr>
<tr>
<td>mosunetuzumab</td>
<td>3L+ FL</td>
<td>2021</td>
</tr>
<tr>
<td>glofitamab</td>
<td>3L+ DLBCL</td>
<td>2021</td>
</tr>
<tr>
<td>tiragolumab</td>
<td>1L SCLC</td>
<td>2022</td>
</tr>
<tr>
<td>giredestrant</td>
<td>2L/3L ER+/HER2- mBC</td>
<td>2022</td>
</tr>
<tr>
<td>ipatasertib</td>
<td>1L CRPC</td>
<td>2022</td>
</tr>
<tr>
<td>inavolisib</td>
<td>P3K 1L HR+ BC</td>
<td>2022/2023</td>
</tr>
</tbody>
</table>

6 potential oncology NMEs with near-term pivotal data
Innovation for patients across solid tumors and hematology

Moving earlier in disease
- Curative potential for the largest number of patients
- Increasing screening, early detection technologies

Exploring rational combinations, new indications
- Combinations: tiragolumab+Tecentriq, Polivy+mosun/glofit
- New indications: MM (cevostamab), HR+/HER2- BC (giredestrant, inavolisib)

PHC 2.0
- Innovative trial design: TAPISTRY (tumor agnostic), AlphaT (decentralized)
- Building leading insights business

PHC = personalized healthcare; MM = multiple myeloma; HR+ BC = hormone receptor positive breast cancer
Earlier disease presents the opportunity for a cure
Need for high efficacy treatments that are well tolerated

**Chance for a cure**: development earlier in the course of disease is critically important to improving the cure rate

**Cost to society**: treatment initiated in earlier stages of cancer reduces cost vs. treatment initiated later

**Unmet need**: large population with continued unmet needs including opportunity to improve long-term OS

**Growing population**: early disease population is expected to grow with the rise of early detection technologies, increasing screening

---

1. National Cancer Institute, SEER database, literature review; OS= overall survival
Investing earlier in disease

### Lung / Rare

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecentriq</td>
<td>Adjuvant NSCLC</td>
<td>1Mpower010</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Neoadjuvant NSCLC</td>
<td>1Mpower030</td>
<td>✓</td>
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</tr>
<tr>
<td></td>
<td>Adjuvant SCCHN</td>
<td>1MVoke010</td>
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<tr>
<td>tiragolumab&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Stage III unres. NSCLC</td>
<td>SKYSCRAPER-03</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neoadj/Adj NSCLC</td>
<td>SKYSCRAPER-05</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Alecensa</td>
<td>Adjuvant ALK+ NSCLC</td>
<td>ALINA</td>
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</table>

### Breast / Gyn

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
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<tbody>
<tr>
<td>Tecentriq</td>
<td>Neoadj. TNBC&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1Mpassion031</td>
<td>✓</td>
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</tr>
<tr>
<td></td>
<td>Adj TNBC</td>
<td>1Mpassion030</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>giredestrant</td>
<td>Neoadj. HR+ BC</td>
<td>coopERA</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adjuvant HR+ BC&lt;sup&gt;3&lt;/sup&gt;</td>
<td>lidERA</td>
<td>✓</td>
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</table>

### GI / GU

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
</tr>
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<tbody>
<tr>
<td>Tecentriq</td>
<td>Adjuvant RCC</td>
<td>1Mmotion010</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adjuvant HCC</td>
<td>1Mbrave050</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR NMIBC</td>
<td>ALBAN</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ctDNA+ HR MIBC</td>
<td>IMvigor011</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>MSI-H CRC</td>
<td>ATOMIC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BCG unresp. NMIBC</td>
<td>SWOG S1605</td>
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<td></td>
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<tr>
<td>tiragolumab&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Locally adv. ESCC</td>
<td>SKYSCRAPER-07</td>
<td>✓</td>
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### Heme

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polivy</td>
<td>1L DLBCL</td>
<td>POLARIX</td>
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</tr>
<tr>
<td>Venclexa</td>
<td>1L fit AML</td>
<td>VIALE-M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glofit/Mosun&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1L DLBCL</td>
<td>Ph 1b</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. In combination with Tecentriq; 2. Positive for PCR, 3, +/- Polivy 4. Planned trial; NSCLC= non-small cell lung cancer; ESCC= esophageal squamous cell carcinoma; HCC= hepatocellular carcinoma; TNBC = triple negative breast cancer; RCC = renal cell carcinoma; NMIBC = non-muscle invasive bladder cancer; DLBCL = diffuse large B-cell lymphoma; AML = acute myeloid leukemia; CRC = colorectal carcinoma; ctDNA = circulating tumor DNA

✓ = met primary endpoint
High unmet need in adjuvant NSCLC

Tecentriq filed with FDA under RTOR

High unmet need in early NSCLC

5-year OS by disease stage

- Many patients with Stage I-III NSCLC continue to have disease recurrence/progression post-surgery

Adjuvant NSCLC treatment is still evolving

**Screening:** Early detection technologies expected to increase diagnosis at early stage

**Testing:** Increasing with adjuvant development for EGFR+, PD-L1+, ALK+ patients

**Systemic therapy:** Adjuvant treatment rates expected to increase with new therapeutic options

1. Chansky, et al Journal of Thoracic Oncology (2017); NSCLC = non-small cell lung cancer; RTOR = real time oncology review
Tiragolumab (anti-TIGIT) development program: scientific and clinical rationale

Scientific / clinical evidence

<table>
<thead>
<tr>
<th>CITYSCAPE Ph 2 trial</th>
<th>SKYSCRAPER-01 (PD-L1+ NSCLC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS benefit observed on top of Tecentriq in randomized trial</td>
<td>• Confirm CITYSCAPE results</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ph 1b expansion cohorts</th>
<th>SKYSCRAPER-08 (ESCC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signal seeking across tumor types, with and without chemotherapy</td>
<td>• Early clinical data from Ph1b suggests Tecentriq+tira drives responses in ESCC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Biomarker data</th>
<th>SKYSCRAPER-02 (SCLC)</th>
</tr>
</thead>
</table>
| Building scientific rationale, defining inclusion criteria | • High expression of TIGIT ligand PVR in SCLC

**Tiragolumab development program**

*First Ph 3 data reading out in 2022: SKYSCRAPER-02 (SCLC)*

### Nine Ph II/III trials of tiragolumab + Tecentriq initiated

<table>
<thead>
<tr>
<th>Lung Cancer</th>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L NSCLC: PD-L1 high</td>
<td>SKYSCRAPER-01</td>
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</tr>
<tr>
<td>1L ES-SCLC</td>
<td>SKYSCRAPER-02</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stage III unres. NSCLC</td>
<td>SKYSCRAPER-03</td>
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</tr>
<tr>
<td>Neoadj / Adj NSCLC</td>
<td>SKYSCRAPER-05</td>
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</tr>
<tr>
<td>1L NSq NSCLC</td>
<td>SKYSCRAPER-06</td>
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</table>

<table>
<thead>
<tr>
<th>Additional solid tumors</th>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Locally advanced ESCC</td>
<td>SKYSCRAPER-07</td>
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<tr>
<td>1L ESCC</td>
<td>SKYSCRAPER-08</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-L1+ Cervical Cancer</td>
<td>SKYSCRAPER-04</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1L SCCHN</td>
<td>SKYSCRAPER-09</td>
<td></td>
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</tr>
</tbody>
</table>

Additional trials ongoing in HCC, mUC, PDAC, TNBC, and hematology (MM, NHL)

**Development Strategy**

- **Build on Tecentriq**
- **Expand into early disease**
- **Compete in new indications**

NSCLC=Non-Small Cell Lung Cancer; ES-SCLC=extensive stage small cell lung cancer; ESCC=esophageal squamous cell carcinoma; HCC=hepatocellular carcinoma; mUC=metastatic urothelial carcinoma; PDAC= Pancreatic ductal adenocarcinoma; MM=multiple myeloma; NHL=non-hodgkins lymphoma
Giredestrant (SERD)

High unmet need remains across HR+/HER2- eBC and mBC

**ET is a mainstay of HR+ BC treatment**

20–50% of HR+ eBC patients stop treatment within 5-yrs due to safety/adherence issues1

10–30% of HR+ eBC patients become resistant to standard of care2

**Potential for best-in-class profile in HR+ BC**

- **Novel MOA**: immobilizes ER in the nucleus prior to degradation
- **High potency**: 7-15x more potent than other SERDs in development
- **Well tolerated** alone and in combination with CDK4/6i
- **Standardized dose**: 30mg once-daily selected for monotherapy/combo

**Ongoing / planned trials:**

- coopERA Ph 2
- lidERA* Ph 3
- persevERA Ph 3
- acelERA Ph 2

Neoadj ➔ Adjuvant ➔ 1L mBC ➔ 2L/3L mBC

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2. Ruhstaller, T. J Clin Oncol 2018

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* Planned trial; ET=endocrine therapy; HR+ BC=hormone receptor positive breast cancer; eBC=early breast cancer; mBC=metastatic breast cancer; SERD = selective estrogen receptor degraaer; ER = estrogen receptor
Giredestrant (SERD)
Promising activity across HR+/HER2- mBC and eBC

**HR+/HER2- mBC**

**Ph 1b: giredestrant monotherapy**

<table>
<thead>
<tr>
<th>Clinical activity</th>
<th>30mg (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR*</td>
<td>20%</td>
</tr>
<tr>
<td>CBR</td>
<td>55%</td>
</tr>
<tr>
<td>Prior fulvestrant</td>
<td>3/8 (38%)</td>
</tr>
<tr>
<td>Prior CDK4/6i</td>
<td>11/26 (42%)</td>
</tr>
<tr>
<td>ESR1 mut</td>
<td>13/17 (76%)</td>
</tr>
</tbody>
</table>

- Promising clinical activity in all patient subgroups including patients with ESR1 mutations
- Well tolerated at all doses, with no DLTs
  - No clinically relevant bradycardia or ocular toxicity
  - Low treatment discontinuation
- Pivotal Ph 2 trial in 2L/3L HR+/HER2- BC reading out in 2022

**Stage I-III neoadjuvant treatment**

**Window of Opportunity Study**

- Compelling pharmacodynamic effects observed in all dose cohorts (supportive of 30mg dose)
- Encouraging impact on proliferation (78% geomean reduction in Ki67); 55% of tumors exhibited complete cell cycle arrest (CCCA) at 2 weeks
- Ph 2 trial in neoadj HR+/HER2- BC reading out in 2021

*ORR in patients with baseline measurable disease; ET=endocrine therapy; HR+ BC=hormone receptor positive breast cancer; TNBC=triple negative breast cancer; eBC=early breast cancer; mBC=metastatic breast cancer; CCCA = complete cell cycle arrest, Ki67 ≤2.7%
Polivy readout in 1L DLBCL expected in 2021

Opportunity to establish Polivy as standard of care in curative setting

1L DLBCL treatment can be curative...

...however high unmet need remains in 1L DLBCL

- ~40% of patients not cured with R-CHOP in 1L
- Patients with R/R DLBCL have poor prognosis: mOS <2yrs
- No new 1L therapies approved since R-CHOP
- 3x more drug treated patients in 1L than 2L DLBCL

Polivy in collaboration with Seattle Genetics; R/R = relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; R-CHOP=Rituxan + cyclophosphamide + hydroxydaunorubicin + vincristine+ prednisone; mOS=median overall survival
Roche CD20 x CD3 bispecific portfolio can be tailored to address diverse patient and customer needs

**Mosunetuzumab**
Attractive profile for the outpatient setting and across a broad range of indications and settings

**Glofitamab**
Potential to offer CAR-T like efficacy “off-the-shelf”, for patients with aggressive disease

**Patients**
- FL/DLBCL/other histologies
- 1L or R/R disease
- Patient characteristics, including risk/prognostic factors
- Single agent vs combination

**Providers**
- Academic centers vs. community
- SC or IV administration
- Off-the-shelf administration

**Payers**
- Fixed duration vs. continuous

R/R = relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; SC=subcutaneous; IV=intravenous
Late line monotherapy
Pivotal cohorts reading out in 2021
• Mosun filing in 2021 in 3L+ FL
• Glofit filing in 2022 in 3L+ DLBCL

R/R NHL combinations
Randomized Ph 3 trials initiated
• Mosun + lenalidomide Ph 3 trial in R/R FL will begin enrolling soon
• Glofit + GemOx Ph 3 trial ongoing in 2L+ DLBCL

1L DLBCL
Developing in curative setting
• Exploring combinations with and without Polivy
• Intriguing early data for mosun in 1L elderly / unfit patients

R/R = relapsed/refractory; DLBCL = diffuse large B-cell lymphoma; FL = follicular lymphoma; NHL = non-Hodgkin Lymphoma; GemOx = gemcitabine + oxaliplatin; SOC = standard of care
Glofitamab

Potential for best-in-class efficacy with step-up dosing

- High and durable response rates in R/R aggressive NHL patients who have failed multiple lines of therapy
  - CR rate of 71.4% at RP2D (2.5/10/30mg)
- CRS was mostly low grade, and confined to cycles 1-2

<table>
<thead>
<tr>
<th>Responses, n (%)</th>
<th>All aNHL pts (n=28)</th>
<th>aNHL 2.5/10/30mg cohort (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOR</td>
<td>18 (64.3)</td>
<td>11 (78.6)</td>
</tr>
<tr>
<td>CR</td>
<td>16 (57.1)</td>
<td>10 (71.4)</td>
</tr>
</tbody>
</table>

R/R = relapsed/refractory; aNHL = aggressive non-Hodgkin Lymphoma; CR = complete response; BOR = best overall response; CRS = cytokine release syndrome
Rotemuzumab + Polivy
Novel combination with promising safety and efficacy

- Promising efficacy in patients with R/R NHL, including in post-CAR-T patients
- M-Pola has an acceptable safety profile with low Gr 1 (2/22, 9%) and no Gr ≥2 CRS events observed
- Ph 2 expansion cohort in R/R DLBCL ongoing, with no mandatory hospitalization

<table>
<thead>
<tr>
<th>Responses, n (%)</th>
<th>All pts (N=22)</th>
<th>aNHL pts (n=19)</th>
<th>Post-CAR-T pts (n=7)</th>
<th>FL grade 1–3A pts (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOR</td>
<td>15 (68.2)</td>
<td>12 (63.2)</td>
<td>4 (57.1)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>CR</td>
<td>12 (54.5)</td>
<td>9 (47.4)</td>
<td>2 (28.6)</td>
<td>3 (100)</td>
</tr>
</tbody>
</table>

Median prior therapies: 3

R/R = relapsed/refractory; DLBCL = diffuse large B-cell lymphoma; FL = follicular lymphoma; aNHL = aggressive non-Hodgkin Lymphoma; CR = complete response; BOR = best overall response; CRS = cytokine release syndrome
ASCO 2021 Highlight
Tecentriq in adjuvant NSCLC: Phase 3 IMpower010 primary results

Heather Wakelee, M.D | Prof. of Medicine, Stanford University Medical Center / Deputy Director Stanford Cancer Institute
IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC)

Heather A. Wakelee,1 Nasser Altorki,2 Caicun Zhou,3 Tibor Csőszi,4 Ihor O. Vynnychenko,5 Oleksandr Goloborodko,6 Alexander Luft,7 Andrey Akopov,8 Alex Martinez-Marti,9 Hirotsugu Kenmotsu,10 Yuh-Min Chen,11 Antonio Chella,12 Shunichi Sugawara,13 Fan Wu,14 Jing Yi,15 Yu Deng,15 Mark McCleland,15 Elizabeth Bennett,15 Barbara J. Gitlitz,15 Enriqueta Felip16

1Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; 2New York-Presbyterian Hospital, Weill Cornell Medicine, New York, NY, USA; 3Tongji University Affiliated Shanghai Pulmonary Hospital, Shanghai, China; 4Jasz-Nagykun-Szolnok Megyei Hetenyi Geza Korhaz-Rendelointezet, Szolnok, Hungary; 5Sumy State University, Regional Municipal Institution Sumy Regional Clinical Oncology Dispensary, Sumy, Ukraine; 6MI Zaporizhzhia Regional Clinical Oncological Dispensary Zaporizhzhia SMU Ch of Oncology, Zaporizhzhya, Ukraine; 7Leningrad Regional Clinical Hospital, St. Petersburg, Russia; 8Pavlov State Med Univ, St. Petersburg, Russia; 9Vall d’Hebron Institute of Oncology (VHIO), Vall d’Hebron University Hospital, Barcelona, Spain; 10Shizuoka Cancer Center, Shizuoka, Japan; 11Taipei Veterans General Hospital and National Yang Ming Chiao Tung University, Taipei, Taiwan; 12Azienda Ospedaliero Universitaria Pisana, Pisa, Italy; 13Sendai Kousei Hospital, Miyagi, Japan; 14Roche (China) Holding Ltd, Shanghai, China; 15Genentech, Inc., South San Francisco, CA, USA; 16Vall d’Hebron University Hospital, Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain
IMpower010: introduction

- Adjuvant platinum-based chemotherapy changed the standard of care for completely resected early-stage NSCLC (stage IB-IIIA) over 15 years ago\textsuperscript{1-4}
  - DFS HR, 0.84 (95% CI: 0.78, 0.91)
  - OS HR, 0.89 (95% CI: 0.82, 0.96)
  - Leads to 4%-5% OS improvement at 5 years vs observation
- Osimertinib provides substantial DFS benefit in patients whose tumors harbor \textit{EGFR} activating mutations,\textsuperscript{5} but there remains a high unmet need for improved adjuvant treatment in other patients with NSCLC
- IMpower010 evaluated the efficacy and safety of adjuvant atezolizumab vs best supportive care (BSC) after adjuvant chemotherapy in patients with completely resected NSCLC

**IMpower010: study design**

**Completely resected stage IB-IIIA NSCLC per UICC/AJCC v7**
- Stage IB tumors ≥4 cm
- ECOG 0-1
- Lobectomy/pneumonectomy
- Tumor tissue for PD-L1 analysis

**Stratification factors**
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status\(^a\): TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

**Primary endpoints**
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

**Key secondary endpoints**
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

Both arms included observation and regular scans for disease recurrence on the same schedule.
ECOG, Eastern Cooperative Oncology Group; IC, tumor-infiltrating immune cells; ITT, intent to treat; TC, tumor cells. \(^a\) Per SP142 assay.

Dr. Heather A. Wakelee
Presented By: IMpower010 Interim Analysis
https://bit.ly/33t6JJP

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IMpower010: statistical analysis plan

- The primary DFS endpoint was tested hierarchically in 3 primary analysis populations

**DFS in PD-L1 TC ≥1% stage II−IIIA population**
- 2-sided $\alpha=0.05$
- If positive:

**DFS in all-randomized stage II−IIIA population**
- 2-sided $\alpha=0.05$
- If positive:

**DFS in ITT population (stage IB−IIIA)**
- 2-sided $\alpha=0.05$
- If positive:

**OS in ITT population**
- 2-sided $\alpha=0.05$
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (N=1005)</th>
<th>PD-L1 TC ≥1% (SP263) (stage II-IIIa)</th>
<th>All randomized (stage II-IIIa)</th>
<th>ITT (stage IB-IIIa)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Atezolizumab (n=248)</td>
<td>BSC (n=228)</td>
<td>Atezolizumab (n=442)</td>
</tr>
<tr>
<td>Median (range) age, y</td>
<td>62 (26-84)</td>
<td>61 (34-82)</td>
<td>62 (26-84)</td>
<td>62 (26-84)</td>
</tr>
<tr>
<td>Age ≥65 y, n (%)</td>
<td>382 (38.0)</td>
<td>92 (37.1)</td>
<td>97 (42.5)</td>
<td>161 (36.4)</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>672 (66.9)</td>
<td>171 (69.0)</td>
<td>147 (64.5)</td>
<td>295 (66.7)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>738 (73.4)</td>
<td>162 (65.3)</td>
<td>166 (72.8)</td>
<td>307 (69.5)</td>
</tr>
<tr>
<td>Asian</td>
<td>242 (24.1)</td>
<td>78 (31.5)</td>
<td>56 (24.6)</td>
<td>121 (27.4)</td>
</tr>
<tr>
<td>Other</td>
<td>25 (2.5)</td>
<td>8 (3.2)</td>
<td>6 (2.6)</td>
<td>14 (3.2)</td>
</tr>
<tr>
<td>ECOG PS, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>556 (55.3)</td>
<td>140 (56.5)</td>
<td>125 (54.8)</td>
<td>239 (54.1)</td>
</tr>
<tr>
<td>1</td>
<td>446 (44.4)</td>
<td>107 (43.1)</td>
<td>102 (44.7)</td>
<td>201 (45.5)</td>
</tr>
<tr>
<td>Histology, non-squamous, n (%)</td>
<td>659 (65.6)</td>
<td>152 (61.3)</td>
<td>143 (62.7)</td>
<td>292 (66.1)</td>
</tr>
<tr>
<td>Stage, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB</td>
<td>123 (12.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>295 (29.4)</td>
<td>85 (34.3)</td>
<td>76 (33.3)</td>
<td>147 (33.3)</td>
</tr>
<tr>
<td>IIB</td>
<td>174 (17.3)</td>
<td>46 (18.5)</td>
<td>37 (16.2)</td>
<td>90 (20.4)</td>
</tr>
<tr>
<td>IIIA</td>
<td>413 (41.1)</td>
<td>117 (47.2)</td>
<td>115 (50.4)</td>
<td>205 (46.4)</td>
</tr>
<tr>
<td>Tobacco use history, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>222 (22.1)</td>
<td>51 (20.6)</td>
<td>41 (18.0)</td>
<td>100 (22.6)</td>
</tr>
<tr>
<td>Current/previous</td>
<td>783 (77.9)</td>
<td>197 (79.4)</td>
<td>187 (82.0)</td>
<td>342 (77.4)</td>
</tr>
<tr>
<td>PD-L1 by SP263, TC≥1%, n (%)</td>
<td>535 (54.6)</td>
<td>248 (100)</td>
<td>228 (100)</td>
<td>248 (57.8)</td>
</tr>
<tr>
<td>EGFR mutation status, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>117 (11.6)</td>
<td>23 (9.3)</td>
<td>20 (8.8)</td>
<td>49 (11.1)</td>
</tr>
<tr>
<td>Negative</td>
<td>527 (52.4)</td>
<td>123 (49.6)</td>
<td>125 (54.8)</td>
<td>229 (51.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>361 (35.9)</td>
<td>102 (41.1)</td>
<td>83 (36.4)</td>
<td>164 (37.1)</td>
</tr>
<tr>
<td>ALK rearrangement status, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>33 (3.3)</td>
<td>12 (4.8)</td>
<td>11 (4.8)</td>
<td>14 (3.2)</td>
</tr>
<tr>
<td>Negative</td>
<td>574 (57.1)</td>
<td>133 (53.6)</td>
<td>121 (53.1)</td>
<td>251 (56.8)</td>
</tr>
<tr>
<td>Unknown</td>
<td>398 (39.6)</td>
<td>103 (41.5)</td>
<td>96 (42.1)</td>
<td>177 (40.0)</td>
</tr>
</tbody>
</table>

Clinical cutoff: January 21, 2021. a 26 patients in the ITT population had unknown PD-L1 status as assessed by SP263. b For patients with non-squamous NSCLC, EGFR/ALK status was assessed locally or centrally. c 89.2% of patients with unknown EGFR status and 80.7% of patients with unknown ALK status had squamous NSCLC and were not required to undergo local or central testing.
IMpower010: DFS in the PD-L1 TC ≥1%<sup>a</sup> stage II-IIIA population (primary endpoint)

Clinical cutoff: January 21, 2021. CI, confidence interval; HR, hazard ratio; NE, not evaluable. <sup>a</sup> Per SP263 assay. <sup>b</sup> Stratified log-rank. <sup>c</sup> Crossed the significance boundary for DFS.

<table>
<thead>
<tr>
<th></th>
<th>Atezolizumab (n=248)</th>
<th>BSC (n=228)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median DFS (95% CI), mo</td>
<td>NE (36.1, NE)</td>
<td>35.3 (29.0, NE)</td>
</tr>
<tr>
<td>Stratified HR (95% CI)</td>
<td>0.66 (0.50, 0.88)</td>
<td>0.004&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>P value&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Median follow-up: 32.8 mo (range, 0.1-57.5)**
#IMpower010: DFS in key subgroups of the PD-L1 TC ≥1%\(^a\) stage II-IIIA population

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N</th>
<th>HR (95% CI)(^b)</th>
<th>Subgroup</th>
<th>N</th>
<th>HR (95% CI)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All patients</strong></td>
<td>476</td>
<td>0.66 (0.49, 0.87)</td>
<td><strong>All patients</strong></td>
<td>476</td>
<td>0.66 (0.49, 0.87)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td><strong>Stage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 y</td>
<td>287</td>
<td>0.67 (0.45, 0.96)</td>
<td>IIA</td>
<td>161</td>
<td>0.73 (0.43, 1.24)</td>
</tr>
<tr>
<td>≥65 y</td>
<td>189</td>
<td>0.64 (0.41, 1.01)</td>
<td>IIB</td>
<td>83</td>
<td>0.77 (0.35, 1.69)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td>IIBA</td>
<td>232</td>
<td>0.62 (0.42, 0.90)</td>
</tr>
<tr>
<td>Male</td>
<td>318</td>
<td>0.59 (0.43, 0.99)</td>
<td>Regional lymph node stage (pN)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>158</td>
<td>0.51 (0.38, 0.97)</td>
<td>N0</td>
<td>106</td>
<td>0.88 (0.45, 1.74)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td>N1</td>
<td>194</td>
<td>0.59 (0.36, 0.97)</td>
</tr>
<tr>
<td>White</td>
<td>326</td>
<td>0.63 (0.45, 0.89)</td>
<td>N2</td>
<td>176</td>
<td>0.66 (0.44, 0.99)</td>
</tr>
<tr>
<td>Asian</td>
<td>134</td>
<td>0.63 (0.37, 1.06)</td>
<td><strong>EGFR mutation status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ECOG PS</strong></td>
<td></td>
<td></td>
<td>Yes</td>
<td>43</td>
<td>0.57 (0.26, 1.24)</td>
</tr>
<tr>
<td>0</td>
<td>265</td>
<td>0.57 (0.40, 0.83)</td>
<td>No</td>
<td>248</td>
<td>0.67 (0.45, 1.00)</td>
</tr>
<tr>
<td>1</td>
<td>209</td>
<td>0.79 (0.51, 1.23)</td>
<td>Unknown(^c)</td>
<td>185</td>
<td>0.61 (0.38, 0.98)</td>
</tr>
<tr>
<td><strong>Tobacco use history</strong></td>
<td></td>
<td></td>
<td><strong>ALK rearrangement status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>92</td>
<td>0.63 (0.37, 1.10)</td>
<td>Yes</td>
<td>23</td>
<td>1.05 (0.32, 3.45)</td>
</tr>
<tr>
<td>Previous</td>
<td>309</td>
<td>0.54 (0.37, 0.78)</td>
<td>No</td>
<td>254</td>
<td>0.64 (0.44, 0.93)</td>
</tr>
<tr>
<td>Current</td>
<td>75</td>
<td>1.24 (0.58, 2.64)</td>
<td>Unknown(^c)</td>
<td>199</td>
<td>0.62 (0.39, 1.00)</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous</td>
<td>181</td>
<td>0.78 (0.47, 1.29)</td>
<td>Squamous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-squamous</td>
<td>295</td>
<td>0.60 (0.42, 0.84)</td>
<td>Non-squamous</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical cutoff: January 21, 2021. \(^a\) Per SP263 assay; \(^b\) Stratified for all patients; unstratified for all other subgroups. \(^c\) 89.2% and 80.7% of patients with unknown EGFR or ALK status, respectively, had squamous NSCLC and were not required to undergo local or central testing.

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IMpower010: DFS in the all-randomized stage II-IIIA population (primary endpoint)

Clinical cutoff: January 21, 2021.

Stratified log-rank: Crossed the significance boundary for DFS.

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IMpower010: DFS in key subgroups of the all-randomized stage II-IIIA population

Clinical cutoff: January 21, 2021.  

Stratified for all patients; unstratified for all other subgroups.

Atezolizumab better

BSC better

Dr. Heather A. Wakelee

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IMpower010: statistical analysis plan

- The significance boundary was not crossed at this DFS interim analysis in the ITT population (stage IB-IIIA) and testing will continue to the final DFS analysis in this population.

DFS in PD-L1 TC ≥1% stage II–IIIA population
2-sided α=0.05
If positive:
DFS in all-randomized stage II–IIIA population
2-sided α=0.05
If positive:
DFS in ITT population (stage IB–IIIA)
2-sided α=0.05
If positive:
OS in ITT population
2-sided α=0.05
IMpower010: DFS in the ITT population (stage IB-IIIA; primary endpoint)

Atezolizumab (n=507)  BSC (n=498)

Median DFS (95% CI), mo  NE (36.1, NE)  37.2 (31.6, NE)
Stratified HR (95% CI)  0.81 (0.67, 0.99)  0.04
P value

- DFS in the ITT population did not cross the significance boundary at this interim DFS analysis.

No. at risk
Atezolizumab  507 478 437 418 403 387 367 353 306 257 212 139 97 53 38 19 14 8 4
BSC  498 467 418 383 365 342 324 309 269 219 173 122 90 46 30 13 10 5 4

Clinical cutoff: January 21, 2021. \(^a\) Stratified log-rank. \(^b\) The statistical significance boundary for DFS was not crossed.
IMpower010: early OS data at interim DFS analysis

- OS data were immature at this pre-planned DFS interim analysis
  - OS in the ITT population was not formally tested
  - A trend toward OS improvement with atezolizumab was seen in the PD-L1 TC ≥1% stage II-IIIA population


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#ASCO21
## IMpower010: safety summary

### Clinical cutoff: January 21, 2021.

<table>
<thead>
<tr>
<th>Event</th>
<th>Atezolizumab (n=495)</th>
<th>BSC (n=495)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any-cause AE</td>
<td>459 (92.7)</td>
<td>350 (70.7)</td>
</tr>
<tr>
<td>Treatment-related AE</td>
<td>335 (67.7)</td>
<td>–</td>
</tr>
<tr>
<td>Grade 3-4 AE</td>
<td>108 (21.8)</td>
<td>57 (11.5)</td>
</tr>
<tr>
<td>Treatment-related grade 3-4 AE</td>
<td>53 (10.7)</td>
<td>–</td>
</tr>
<tr>
<td>Serious AE</td>
<td>87 (17.6)</td>
<td>42 (8.5)</td>
</tr>
<tr>
<td>Treatment-related serious AE</td>
<td>37 (7.5)</td>
<td>–</td>
</tr>
<tr>
<td>Grade 5 AE</td>
<td>8 (1.6)</td>
<td>3 (0.6)</td>
</tr>
<tr>
<td>Treatment-related grade 5 AE</td>
<td>4 (0.8)</td>
<td>–</td>
</tr>
<tr>
<td>AE leading to dose interruption of atezolizumab</td>
<td>142 (28.7)</td>
<td>–</td>
</tr>
<tr>
<td>AE leading to atezolizumab discontinuation</td>
<td>90 (18.2)</td>
<td>–</td>
</tr>
<tr>
<td>Immune-mediated AEs</td>
<td>256 (51.7)</td>
<td>47 (9.5)</td>
</tr>
<tr>
<td>Grade 3-4 immune-mediated AEs</td>
<td>39 (7.9)</td>
<td>3 (0.6)</td>
</tr>
<tr>
<td>Immune-mediated AEs requiring the use of systemic corticosteroids</td>
<td>60 (12.1)</td>
<td>4 (0.8)</td>
</tr>
</tbody>
</table>

---

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---

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### IMpower010: immune-mediated AEs

#### imAEs occurring in ≥1% of patients

<table>
<thead>
<tr>
<th>Atezolizumab (n=495)</th>
<th>BSC (n=495)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td><strong>Any grade</strong></td>
</tr>
<tr>
<td>Any immune-mediated AEs</td>
<td>256 (51.7)%</td>
</tr>
<tr>
<td>Rash</td>
<td>91 (18.4)</td>
</tr>
<tr>
<td>Hepatitis (diagnosis and laboratory abnormalities)</td>
<td>86 (17.4)</td>
</tr>
<tr>
<td>Hepatitis (laboratory abnormalities)</td>
<td>81 (16.4)</td>
</tr>
<tr>
<td>Hepatitis (diagnosis)</td>
<td>7 (1.4)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>86 (17.4)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>32 (6.5)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>19 (3.8)%</td>
</tr>
<tr>
<td>Infusion-related reaction</td>
<td>7 (1.4)</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>6 (1.2)</td>
</tr>
</tbody>
</table>

Clinical cutoff: January 21, 2021. a Data are from the safety population (all randomized patients who received ≥1 atezolizumab dose or for BSC, had ≥1 post-baseline assessment). b Includes 2 (0.4%) Grade 5 events. c Includes 1 (0.2%) Grade 5 event.

#### imAEs occurring in <1% of patients

<table>
<thead>
<tr>
<th>Atezolizumab (n=495)</th>
<th>BSC (n=495)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td><strong>Any grade</strong></td>
</tr>
<tr>
<td>Meningoencephalitis</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>Colitis</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>Myositis (myositis and rhabdomyolysis)</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Severe cutaneous adverse reaction</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Autoimmune hemolytic anemia</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>2 (0.4)c</td>
</tr>
<tr>
<td>Meningitis</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Guillain-Barre syndrome</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Ocular inflammatory toxicity</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Hypophysitis</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Nephritis</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>0</td>
</tr>
</tbody>
</table>

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IMpower010: conclusions

- IMpower010 is the first Phase III study of cancer immunotherapy to demonstrate DFS improvement in the adjuvant NSCLC setting after platinum-based chemotherapy
  - Adjuvant atezolizumab following complete resection and adjuvant chemotherapy showed statistically significant DFS benefit in the PD-L1 TC ≥1% stage II-IIIA (HR, 0.66; 95% CI: 0.50, 0.88) and all-randomized stage II-IIIA (HR, 0.79; 95% CI: 0.64, 0.96) populations, with enriched clinical benefit in patients whose tumors express PD-L1

- IMpower010 will continue for DFS and OS analyses in the ITT population
  - DFS in the ITT population, including patients with stage IB disease, did not cross the significance boundary at this interim DFS analysis
  - At this pre-planned interim DFS analysis, OS data were immature and not formally tested

- The safety profile of atezolizumab was consistent with prior experience of atezolizumab monotherapy across indications and lines of therapy

- Atezolizumab may be considered a practice-changing adjuvant treatment option for patients with PD-L1 TC ≥1% stage II-IIIA NSCLC
Acknowledgments

• The patients and their families
• The investigators and clinical study sites
• This study is sponsored by F. Hoffmann-La Roche Ltd
• Medical writing assistance was provided by Samantha Santangelo, PhD, of Health Interactions and funded by F. Hoffmann-La Roche Ltd

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Doing now what patients need next