Roche Pharma Day 2020

Late Stage Pipeline Oncology & Non-malignant Hematology

Levi Garraway, M.D., Ph.D. | Executive Vice President, Head of Global Product Development and Chief Medical Officer

Late stage pipeline update

1. **Hematology franchise**
   - DLBCL: Polivy, glofitamab, mosunetuzumab
   - FL: mosunetuzumab, glofitamab, Polivy
   - AML: Venclexta
   - MM: Venclexta
   - MDS: Venclexta

2. **Breast Cancer franchise**
   - TNBC: Tecentriq, ipatasertib
   - HR+: SERD (RG6171), PI3Kαi (RG6114)
   - HER2+: Tecentriq

3. **Lung Cancer franchise**
   - NSCLC: Tecentriq, tiragolumab
   - SCLC: Tecentriq, tiragolumab
   - ALK+: Alecensa
   - ROS1+/NTRK+: Rozlytrek
   - RET+: Gavreto
   - KRAS *G12C*+: GDC-6063

4. **Other oncology**
   - CRPC: ipatasertib
   - Thyroid cancer: Gavreto
   - Esophageal cancer: tiragolumab
   - Melanoma: Tecentriq, Cotellic, Zelboraf

5. **Non-malignant hematology**
   - Hemophilia A: Hemlibra
   - Hemophilia A: Factor VIII Gene Therapy
   - PNH: crovalimab

6. **Neuroscience**
   - MS: Ocrevus; fenebrutinib
   - SMA: Evrysdi
   - NMOSD: Enspryng
   - AD: gantenerumab, anti-Tau, brain shuttle
   - Huntington's disease: tominersen
   - DMD: Micro-dystrophin Gene Therapy
   - Parkinson's disease: prasinezumab

7. **Immunology**
   - IPF: rhPentraxin-2, Esbriet
   - Myelofibrosis: rhPentraxin-2
   - Lupus nephritis: Gazyva
   - Crohn's disease: etrolizumab

8. **Ophthalmology**
   - nAMD, DME, DR: Port Delivery System
   - nAMD, DME, RVO: faricimab

9. **Infectious diseases**
   - HBV: TLR7 agonist, CpAM, RG6346, RG6084
   - Influenza A/B: Xofluza
   - SARS-CoV2: Actemra
   - SARS-CoV2: REGN-COV2

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

Oncology / Hematology
Neuroscience
Ophthalmology
Infectious diseases
Immunology

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 20 results presentation appendix or visit the IR homepage

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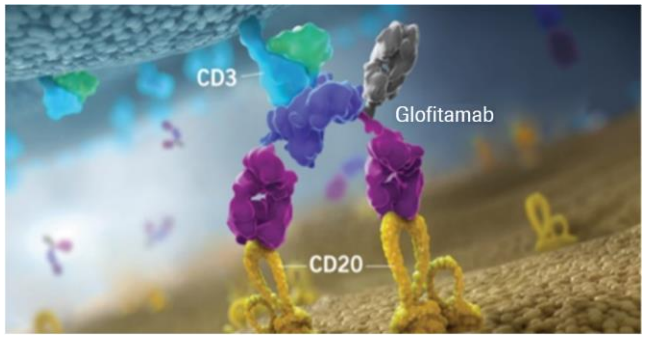
Hematology: Glofitamab in NHL

Potential for early filing in R/R DLBCL

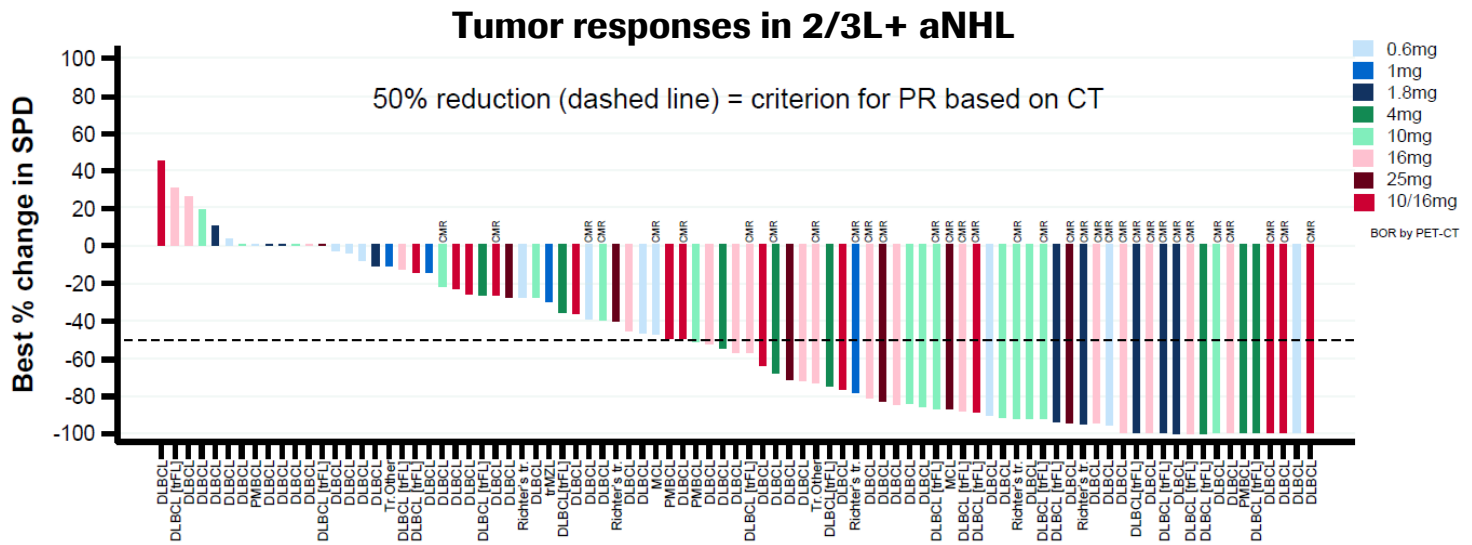
CD20 x CD3 program



Combination	Indication	Ph1	Ph2	Ph3
glofi+GemOx	2L+ DLBCL			
glofi	R/R DLBCL/FL			
glofi+G/R+CHOP	1L DLBCL			
glofi+T	R/R DLBCL/FL			
glofi+G	R/R FL			
glofi+P	R/R DLBCL			

- ~1000 Patients have been treated in the CD20xCD3 program (glofit and mosun)
- Initial registration potential for glofitamab in R/R DLBCL and for mosunetuzumab in R/R FL

Ph I (NP30179) dosing in R/R aNHL*



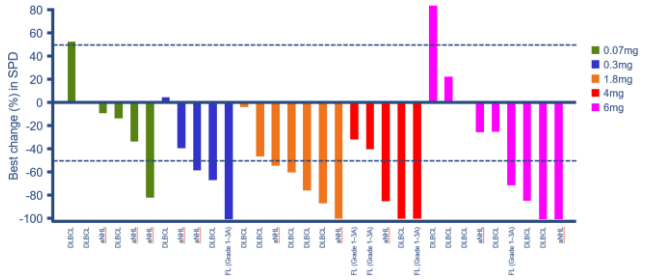
- The ≥10mg cohorts in R/R aNHL showed an ORR of 49.4% and a CR rate of 34.1%; CRs appeared durable with the mDOR not reached after a median follow up of 10.2m
- Good safety profile with manageable CRS confined to cycle 1
- Combination development with R-CHOP and Polivy in DLBCL on-going
- Ph III safety run-in for glofitamab + GemOx in 2L+ DLBCL initiated

Dickinson. M.J. et al, EHA 2020; aNHL=agressive non-Hodgkin's lymphoma; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; glofit=glofitamab; GemOx=gemcitabine, oxaliplatin; G=Gazyva; R-CHOP=Rituxan, cyclophosphamide, doxorubicin, vincristine, prednisone; P=Polivy; ORR=overall response rate; CR=complete response; mDOR=median duration of response; CRS=cytokine release syndrome; *Aggressive NHL includes primarily DLBCL, some transformed FL, PMBCL, MCL, transformed MZL and Richter's transformation

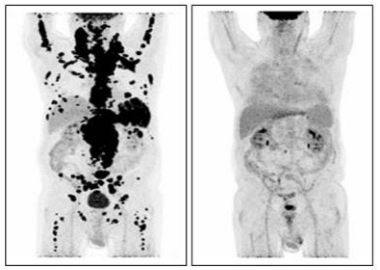
Hematology: Exploring feasible combinations

Initial efficacy and safety data show combination potential

Ph I results of glofitamab + Tecentriq in R/R NHL



3L R/R DLBCL patient

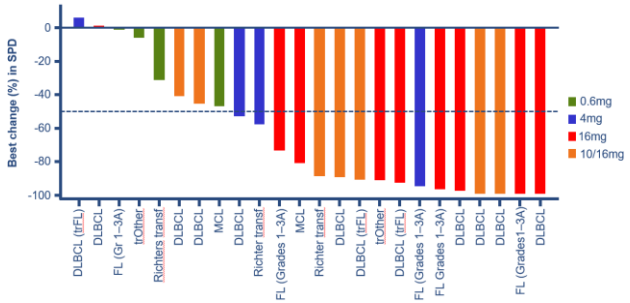


Baseline

CR after 2 doses glofitamab and 1 dose of Tecentriq

- T-cell activation observed consistent with the hypothesized MOA of the combination
- Trend towards increased response rate was observed starting at glofitamab doses ≥1.8mg
- Manageable safety in R/R NHL

Ph I results of glofitamab + Gazyva in R/R NHL



0.6mg and 4mg cohorts combined				
n(%)		aNHL (N=8)	DLBCL (N=2)	FL (N=2)
ORR		1 (12.5)	0	1 (50.0)
	CR	1 (12.5)	0	1 (50.0)
	PR	0	0	0
16mg and 10/16mg cohorts combined				
n(%)		aNHL (N=14)	DLBCL (N=9)	FL (N=4)
ORR		10 (71.4)	5 (55.6)	3 (75.0)
	CR	8 (57.1)	4 (44.4)	3 (75.0)
	PR	2 (14.3)	1 (11.1)	0

- Highly promising activity in heavily pre-treated patients
- ORR and CR rates by investigator assessment were 54% (15/28 pts) and 46% (13/28); CR appear durable
- Safety profile consistent with known safety profiles of the individual drugs

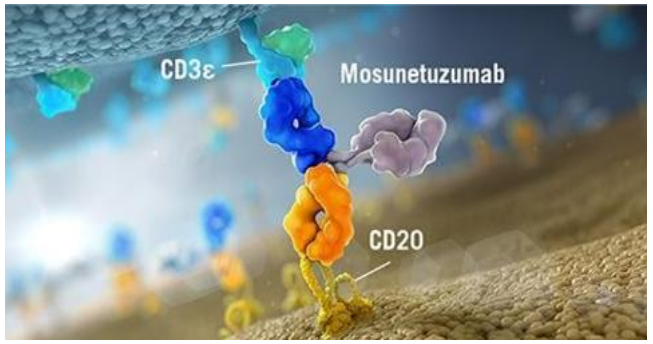
Further development work needed to identify most promising paths forward for chemo-free combinations

Hutchings, M., et al, ASH 2019; Morschhauser, F., et al, ASH 2019; NHL=Non-Hodgkin's lymphoma; DLBCL=Diffuse large B-cell lymphoma; FL=Follicular lymphoma; MOA=mechanism of action; ORR=overall response rate; CR=complete response; CRS=cytokine release syndrome

Hematology: Mosunetuzumab in NHL

Potential for early filing in R/R FL; SC data to be presented at ASH

CD20 x CD3 program

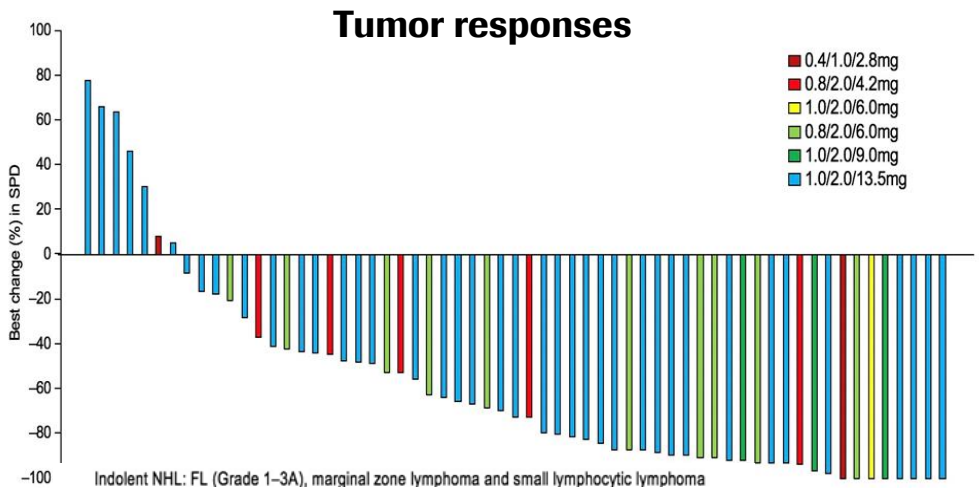


Combination	Indication	Ph1	Ph2	Ph3
mosun+len	R/R FL			
mosun+CHOP *	1L DLBCL			
mosun+CHP+P	1L DLBCL			
mosun *	R/R DLBCL/FL/MCL			
mosun *	1L/2L (unfit) DLBCL			
mosun	3L+ DLBCL/FL/ ibrutinib R/R MCL			
mosun+P	R/R DLBCL			
mosun+T	R/R DLBCL/FL			
mosun SC *	R/R DLBCL/FL			

* Data submitted to ASH 2020

Mosunetuzumab in 3L+ FL

FDA BTD



- Pooled data from 2.8mg to 13.5mg cohorts showed an ORR of 62.7% and CR of 43.3%; 82.8% patients remain in complete remission for up to 26m off initial treatment
- Overall CRS rate of 28.9% (predominantly fever Gr1) with only 1.1% CRS events of Gr≥3
- Ph III safety run-in for mosunetuzumab + lenalidomide in R/R FL initiated
- First Ph I data on mosunetuzumab SC to be presented at ASH 2020

Shuster, S.J., et al,, ASH 2019; NHL=non-Hodgkin's lymphoma; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; P=Polivy; T=Tecentriq; mosun=mosunetuzumab; ORR=overall response rate; CR=complete response; CRS=cytokine release syndrome; R/R=relapsed/refractory; mDOR=median duration of response; SC=subcutaneous

Hematology: Venclexta in CLL, AML, MM, MDS

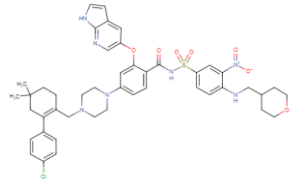
Ph III studies to be initiated in various indications

VENCLEXTA® venetoclax tablets 10mg, 50mg, 100mg — Roche

25TH EHA CONGRESS FRANKFURT, GERMANY JUNE 11 - 14, 2020

Venclexta progam

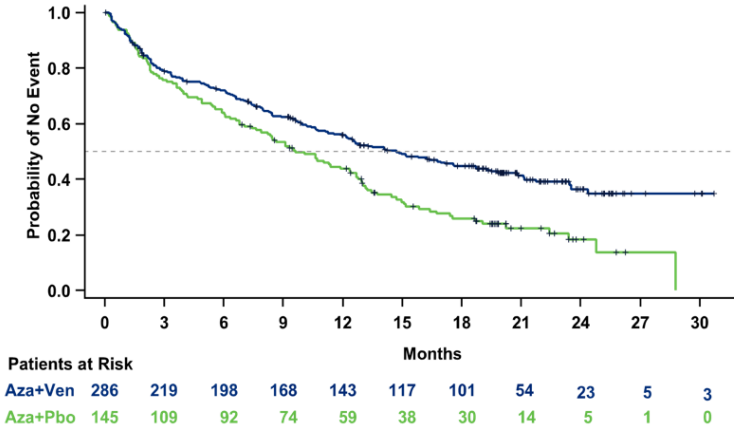
Bcl-2 inhibitor



	Combination	Indication	Ph1	Ph2	Ph3
NHL	V+P+G/R	R/R DLBCL/FL			
CLL	V+G	1L unfit CLL			✓
	V+R	R/R CLL			✓
	V	R/R CLL 17p			✓
	V	R/R CLL after ibru/idel			
	V+G	1L fit CLL			
MM	V+dex	t(11;14) R/R MM			
	V+carfilzomib+dex	t(11;14) R/R MM			
AML	V+aza	1L AML			✓
	V+LDAC	1L AML			✓
	V+AMG176	R/R AML			
	V+gilteritinib	R/R AML			
MDS	V+aza	1L MDS			
	V+/-aza	R/R MDS			
HR+BC	V+fulvestrant	2L+ HR+			

Ph III (VIALE-A) results in 1L unfit AML

Overall survival



No. of events/No. of patients (%)	Median duration of study treatment, months (range)	Median overall survival, months (95% CI)
161/286 (56)	7.6 (<0.1 – 30.7)	14.7 (11.9 – 18.7)
109/145 (75)	4.3 (0.1 – 24.0)	9.6 (7.4 – 12.7)

Hazard ratio: 0.66 (95% CI: 0.52 – 0.85), p<0.001

- Ph III (Viale-A) results in 1L unfit AML filed in US (RTOR) and EU
- Ph III (Viale-M) in 1L fit AML initiated
- Ph III (CristaLLo) in 1L fit CLL with MRD as primary endpoint started in Q2 2020
- Additional Ph III studies in AML and MDS planned

DiNArdo C.D. et al., EHA 2020; NHL=non-Hodgkin's lymphoma; CLL=chronic lymphoid leukemia; AML=acute myeloid leukemia; MM=multiple myeloma; MDS=myelodysplastic syndrome; mOS=median overall survival; HR=hazard ratio; V=Venclexta; P=Polivy; G=Gazyva; R=Rituxan; dex=dexamethasone; bor=bortezomib; aza=azacitidine; LDAC=low dose cytarabine; RTOR=real-time oncology review; Venclexta in collaboration with AbbVie

Late stage pipeline update

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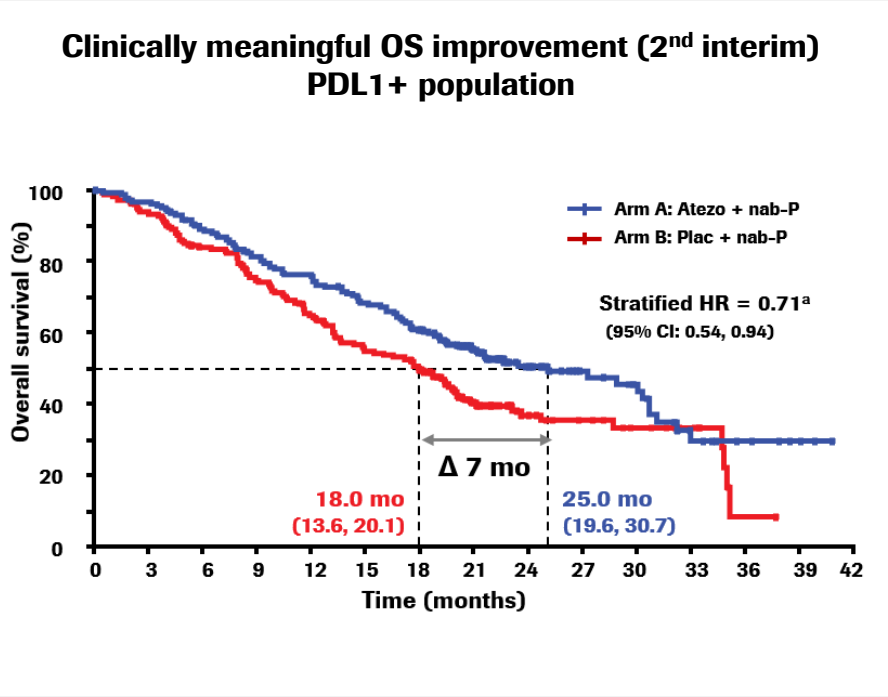
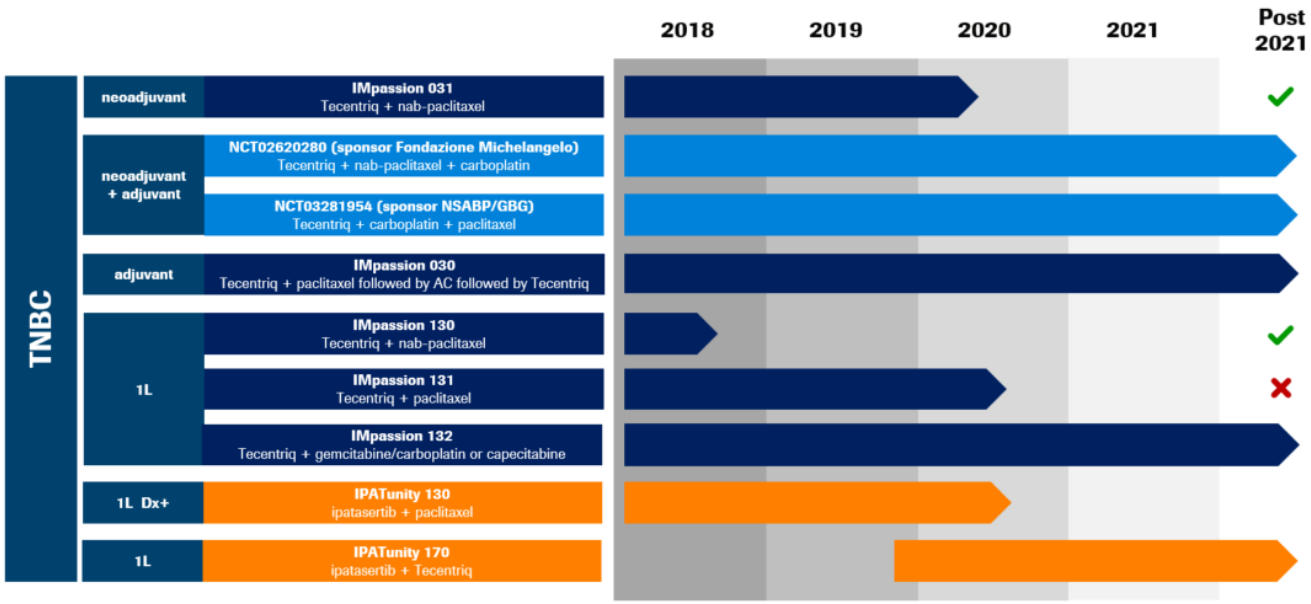
TNBC franchise: Tecentriq + nab-pac new SOC in 1L

Positive Ph III results in neoadjuvant

Ph III (IMpassion130) results in 1L



TNBC program covering all lines of treatment*



- Positive Ph III (IMpassion031) results for Tecentriq+nab-pac in neoadjuvant TNBC announced; data to be presented

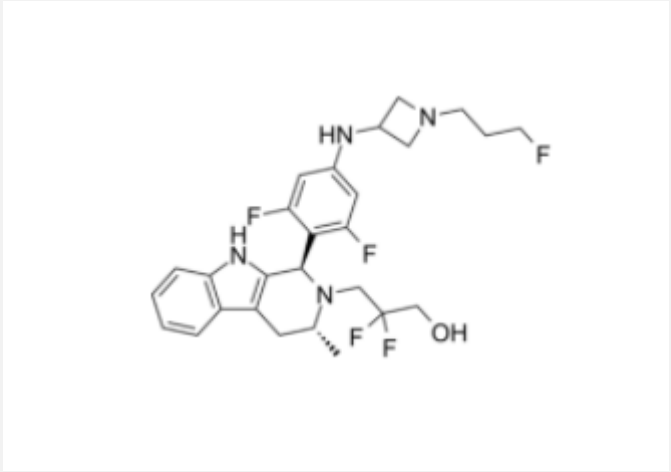
Schmid P, et al. ASCO 2019 (Data cutoff: January 2, 2019); Schmid P, et al. ESMO 2018; TNBC=triple negative breast cancer; nab-pac=nab-paclitaxel (Abraxane); HR=hazard ratio; OS=overall survival;
[a]Not formally tested due to pre-specified hierarchical analysis plan (data included in the EMA label); *Outcome studies are event-driven: timelines may change

HR+/HER2- franchise: Potentially best in class 3rd gen SERD

Strong efficacy as a single agent and in combination

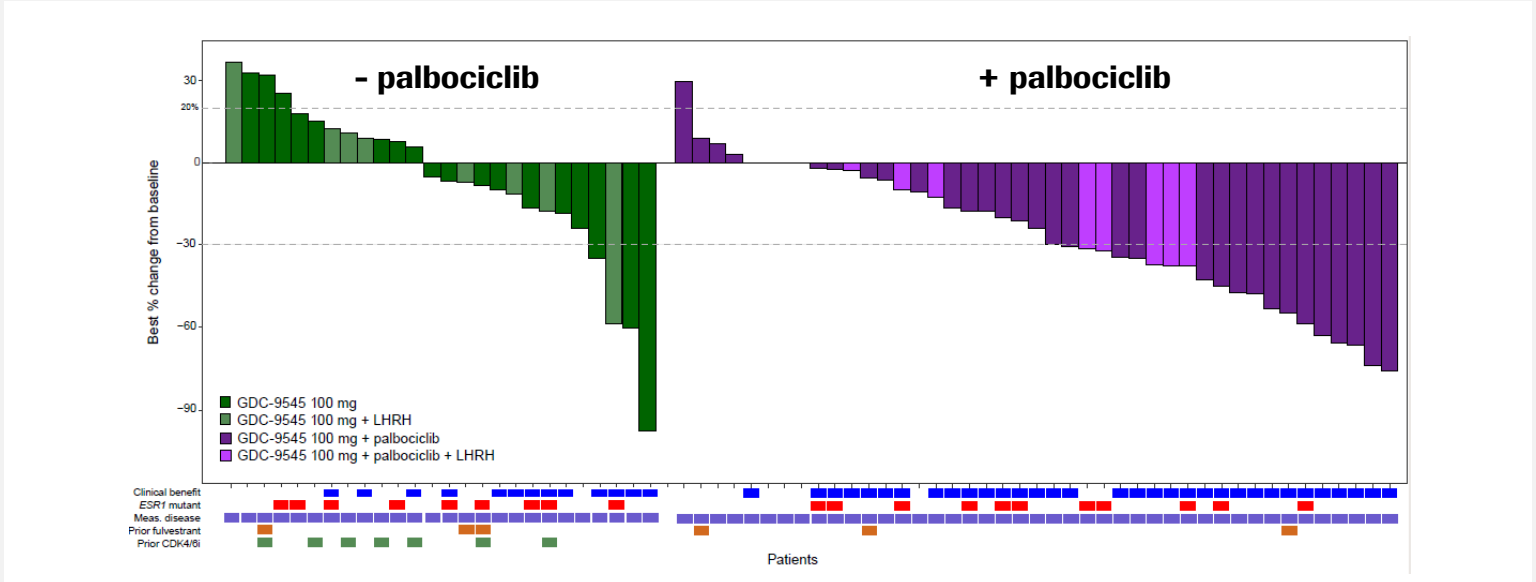
ASCO 20 Virtual

Selective ER degrader (SERD) RG6171 (GDC-9545)



- 3rd generation oral SERD
- Highly potent in vitro and improved efficacy in vivo versus previous SERDs
- High potency + minimal safety findings lead to wide nonclinical safety margins
- First SERD with positive combination data with a CDK4/6 inhibitor

Ph Ib results: Tumor responses RG6171 +/- palbociclib



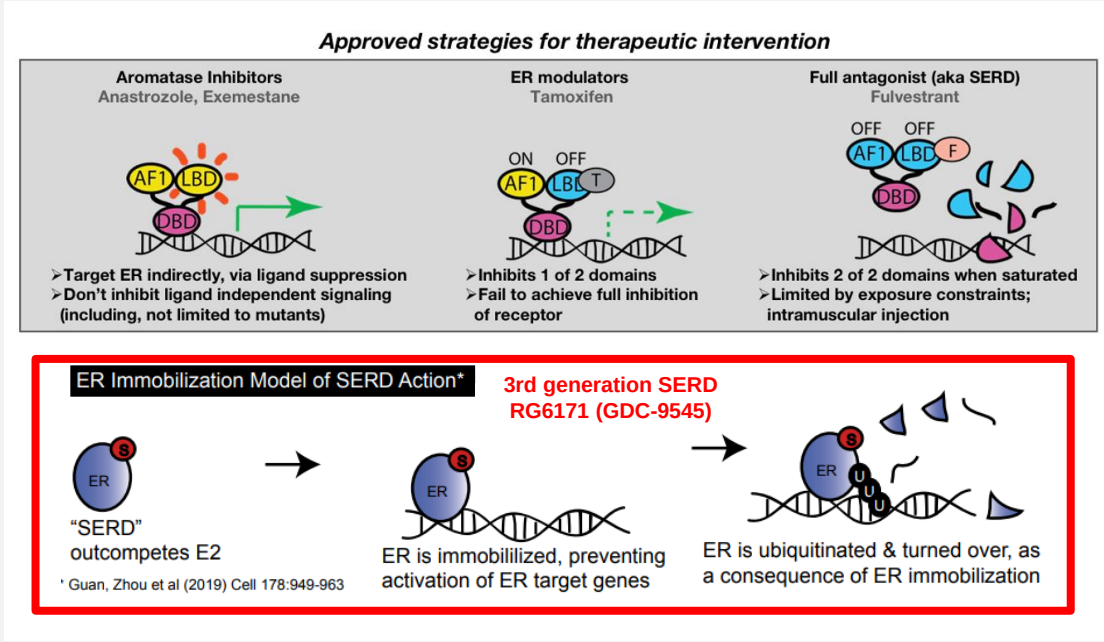
- Strong potentially best-in-class efficacy as single agent or in combination with a CDK4/6 inhibitor in pre-treated ER+ patients, regardless of ESR1 resistance mutations
- Well-tolerated up to doses of 100 mg daily
- Expansion cohort at 30 mg daily on-going given the promising efficacy with a clinical benefit rate of 50%*

Lim E. *et al*., ASCO 2020; Metcalfe C. *et al*., SABCS 2018; HR=hormone receptor; mBC=metastatic breast cancer; ER=estrogen receptor; LHRH=lutenizing hormone /releasing hormone; * At 30 mg no bradycardia events reported to date

HR+/HER2– franchise: Potentially best in class 3rd gen SERD

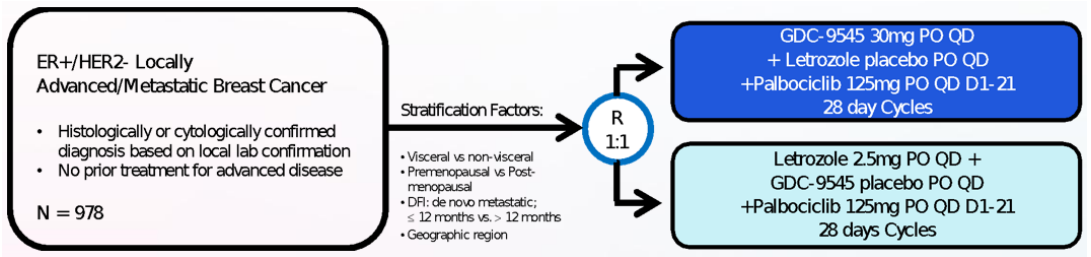
Ph III program in 1L+ and eBC initiated

3rd gen SERD: Overcoming fulvestrant limitations Improved MOA for a well established target



- RG6171 is a 3rd generation SERD with improved bioavailability and a novel MOA: Increased efficacy is due to "ER immobilization" which supressess transcriptional activity prior to ER degradation

Ph III trial design in 1L mBC



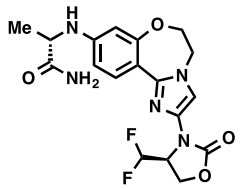
- Ph III RG6171 + palbociclib in 1L mBC to start in 2H 2020
- Ph II RG6171 + palbociclib in neoadjuvant started in Q3 2020; Ph III adjuvant study planned
- Pivotal Ph II RG6171 in 2/3L to start in Q4 2020; results expected in 2022

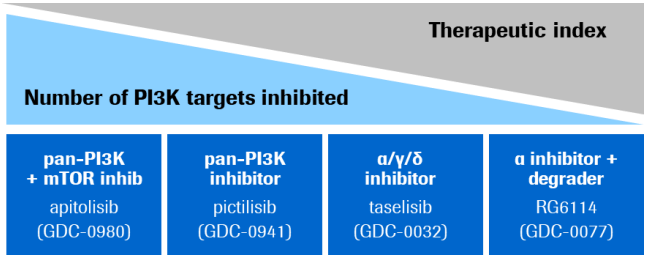
Guan J. and Zhou W. et al. (2019) Cell; HR=hormone receptor; mBC=metastatic breast cancer; ER=estrogen receptor; MOA=mechanism of action; L=line

HR+/HER2- franchise: PI3Kαi in *PIK3CA*-mutant tumors

Ph III for potentially best in class PI3Kα inhibitor started

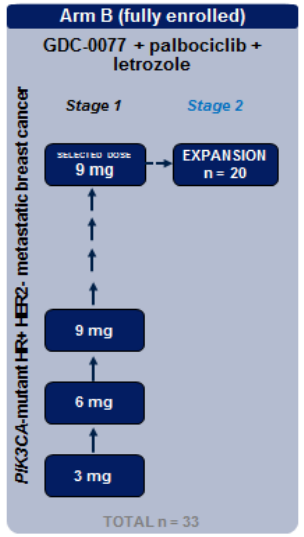
PI3Kα selective inhibitor + mutant PI3Kα degrader

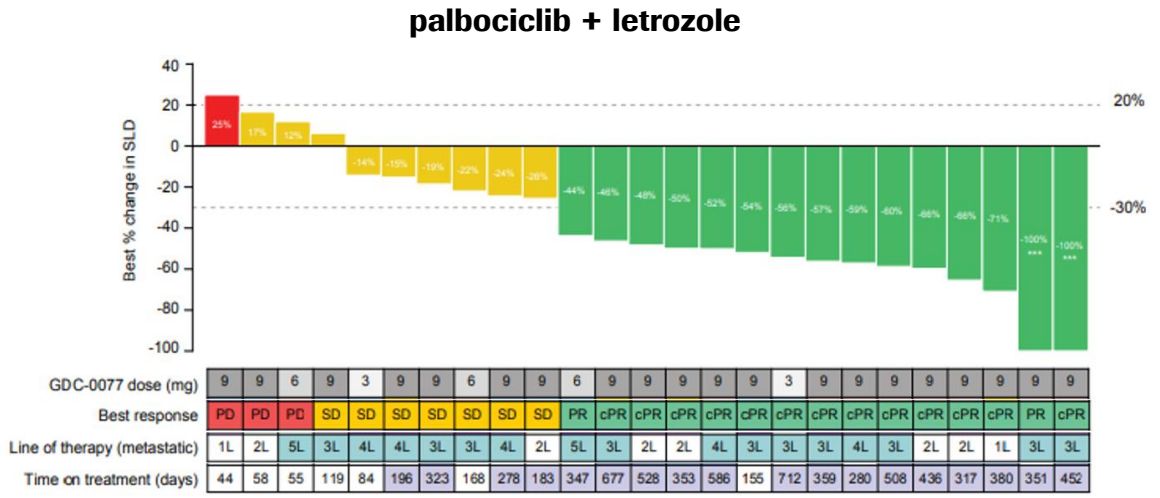




- Dual MOA: More potent and selective for PI3Kα + degrades mutant PI3Kα
- Greater safety margins
- Better in vivo efficacy
- Greater, more durable target inhibition
- Combinations with other therapies

Ph I (dose escalation and expansion cohort)





- Strong efficacy in on-going Ph I/Ib as single agent or as combo with ET (letrozole or fulvestrant) +/- palbociclib in patients with locally advanced or metastatic *PIK3CA*-mutant solid tumors
- Good safety as single agent or combined
- Ph III (INAVO120) RG6114* + palbociclib + fulvestrant in 1L *PIK3CA*-mutant HR+/HER2- mBC started in Q1 2020

Jhaveri, K., et al, SABCS 2019; Kalinsky K. et al., AACR 2020; ET=endocrine therapy; HR=hormone receptor; BC=breast cancer; ORR=overall response; * GDC-0077

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3. **Lung Cancer franchise**
   - NSCLC: Tecentriq, tiragolumab
   - SCLC: Tecentriq, tiragolumab
   - ALK+: Alecensa
   - ROS1+/NTRK+: Rozlytrek
   - RET+: Gavreto
   - KRAS *G12C*+: GDC-6063

4. **Other oncology**
   - CRPC: ipatasertib
   - Thyroid cancer: Gavreto
   - Esophageal cancer: tiragolumab
   - Melanoma: Tecentriq, Cotellic, Zelboraf

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   - Hemophilia A: Hemlibra
   - Hemophilia A: Factor VIII Gene Therapy
   - PNH: crovalimab

6. **Neuroscience**
   - MS: Ocrevus; fenebrutinib
   - SMA: Evrysdi
   - NMOSD: Enspryng
   - AD: gantenerumab, anti-Tau, brain shuttle
   - Huntington's disease: tominersen
   - DMD: Micro-dystrophin Gene Therapy
   - Parkinson's disease: prasinezumab

7. **Immunology**
   - IPF: rhPentraxin-2, Esbriet
   - Myelofibrosis: rhPentraxin-2
   - Lupus nephritis: Gazyva
   - Crohn's disease: etrolizumab

8. **Ophthalmology**
   - nAMD, DME, DR: Port Delivery System
   - nAMD, DME, RVO: faricimab

9. **Infectious diseases**
   - HBV: TLR7 agonist, CpAM, RG6346, RG6084
   - Influenza A/B: Xofluza
   - SARS-CoV2: Actemra
   - SARS-CoV2: REGN-COV2

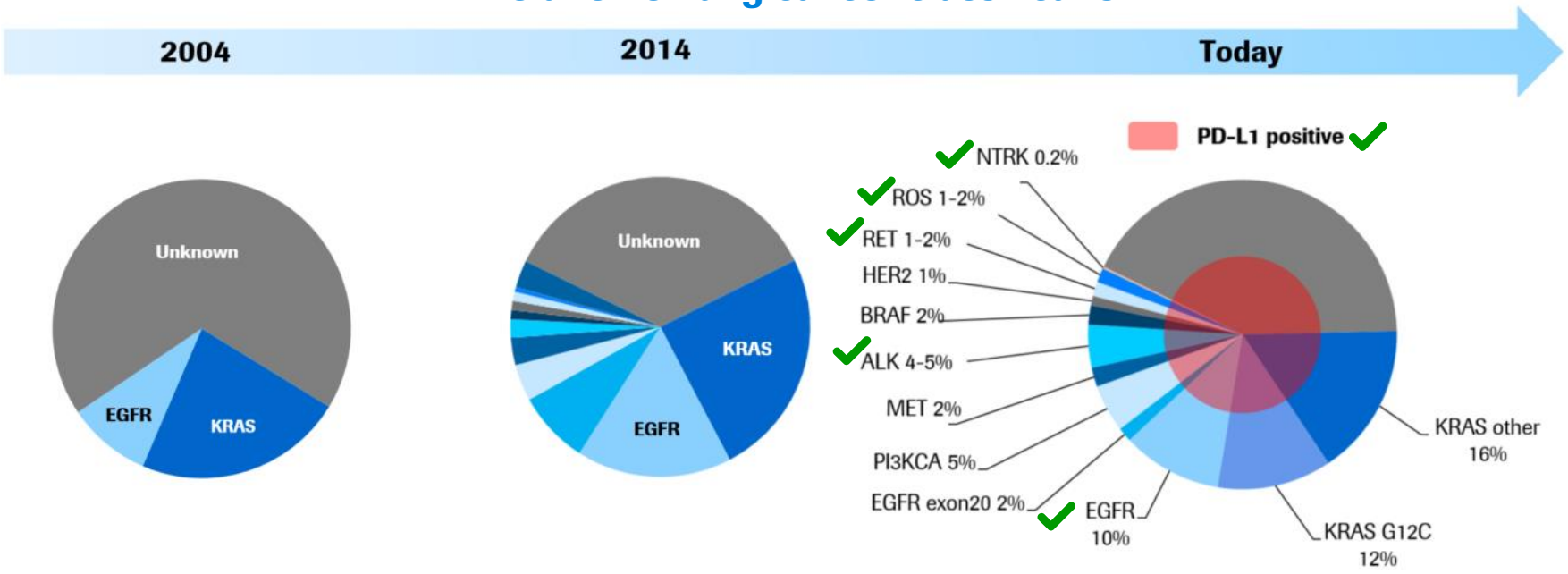
Oncology / Hematology
Neuroscience
Ophthalmology
Infectious diseases
Immunology

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 20 results presentation appendix or visit the IR homepage

Lung franchise

Integrated value proposition for patient classification & care

Evolution of lung cancer classification



- Roche uniquely positioned to establish integrated PHC solutions
- Develop rare mutation agents faster and cheaper leveraging B-FAST, FMI, Flatiron, PHC
- Multiple lung pilots focused on integrated offerings underway (Taiwan, Croatia, Australia)

FoundationOne®CDx

FoundationOne®Liquid CDx

NAVIFY®

ALECENSA alectinib

ENTRECTINIB

GAVRETO pralsetinib

Tarceva erlotinib

TECENTRIQ atezolizumab

AVASTIN bevacizumab

tiragolumab

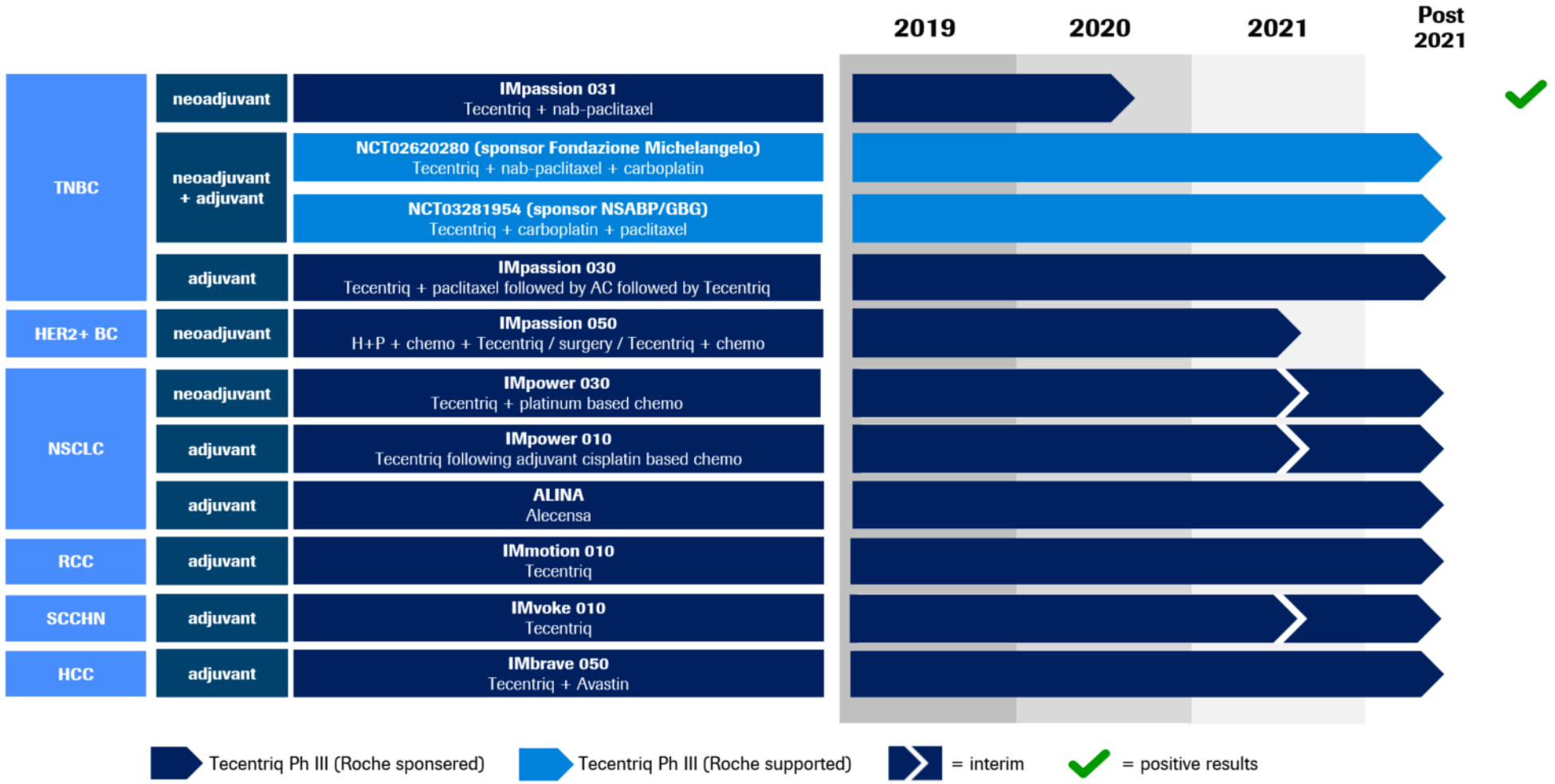
GDC-6036 (KRAS*G12C*)

PI3Kαi (RG6114)

Pao & Girard. Lancet Oncol 2011; Johnson, et al. ASCO 2013; FMI Database, Accessed November 2018 (all NSCLC).

Lung franchise: Overview adjuvant program

NSCLC, HER2+ BC, SCCHN reading out in 2021



Lung franchise: Tiragolumab + Tecentriq in NSCLC & SCLC

Pivotal Ph III study in stage III NSCLC initiated

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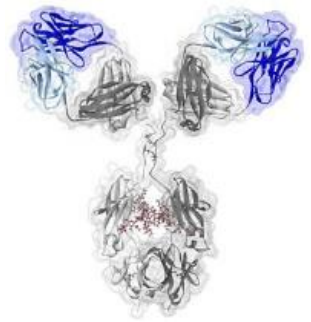
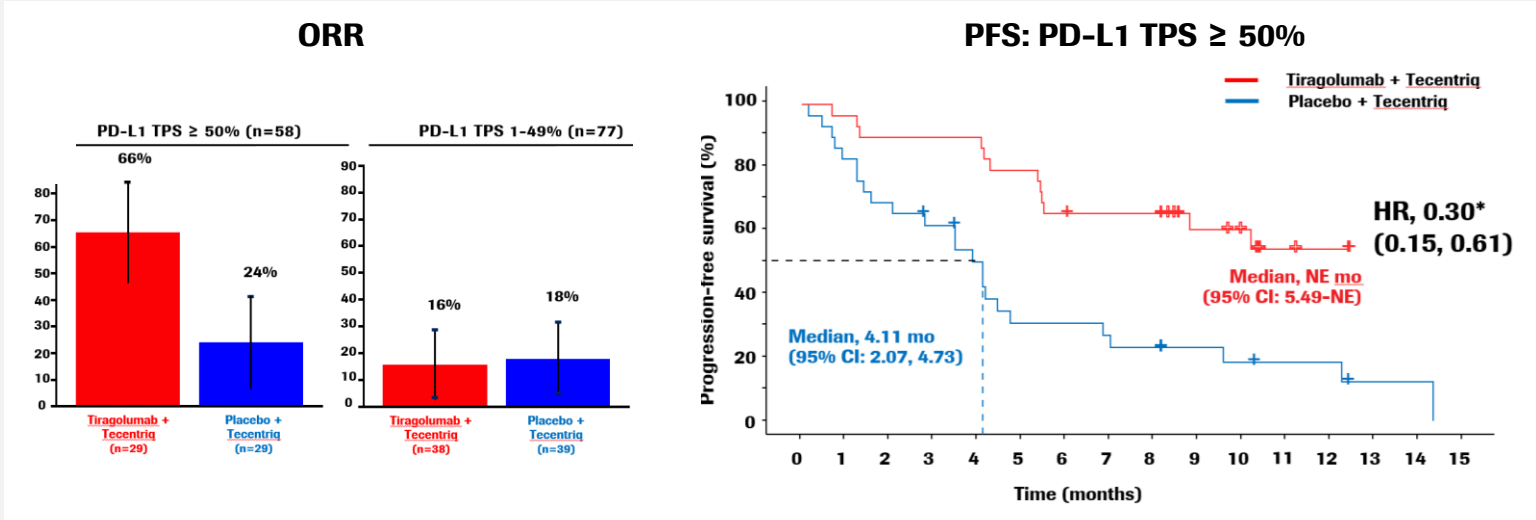
Anti-TIGIT mAb



- Fully human IgG1/kappa Ab with intact Fc region that blocks the binding of TIGIT to its receptor PVR
- Could restore anti-tumor response and could complement the activity of anti-PD-L1/PD-1 antibodies

Randomized Ph II (CITYSCAPE) in 1L NSCLC



- Tiragolumab + Tecentriq showed clinically meaningful improvement in ORR and PFS in the ITT population with a greater magnitude of improvement in the PD-L1 TPS ≥ 50% subgroup
- Tiragolumab + Tecentriq was well-tolerated with a safety profile similar to the control arm
- Ph III in 1L PDL1+ NSCLC (SKYSCRAPER-01), 1L ES-SCLC (SKYSCRAPER-02) and stage III NSCLC (SKYSCRAPER-03) on-going
- Ph II (CITYSCAPE) update including OS in 2021

Johnson et al. Cancer Cell 2014; Rodriguez-Abreu D. et al., ASCO 2020; Follow-up data cut-off: 02 December, 2019; Ab=antibodies; ORR=overall response rate; PFS=progression free survival; HR=hazard ratio; NE=non evaluable; ITT=intention-to-treat; TPS=tumor proportion score; ES-SCLC=extensive stage SCLC; OS=overall survival; * unstratified HR

Lung franchise: Gavreto new SOC in RET+ mNSCLC

Strong and durable responses including CNS disease control

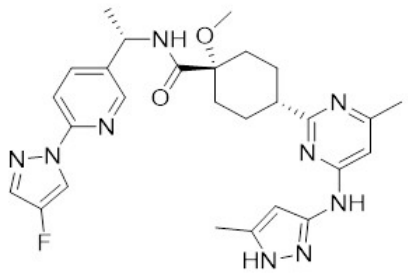
GAVRETO pralsetinib | Roche | blueprint MEDICINES

ASCO 20 Virtual

FDA approved

RET inhibitor

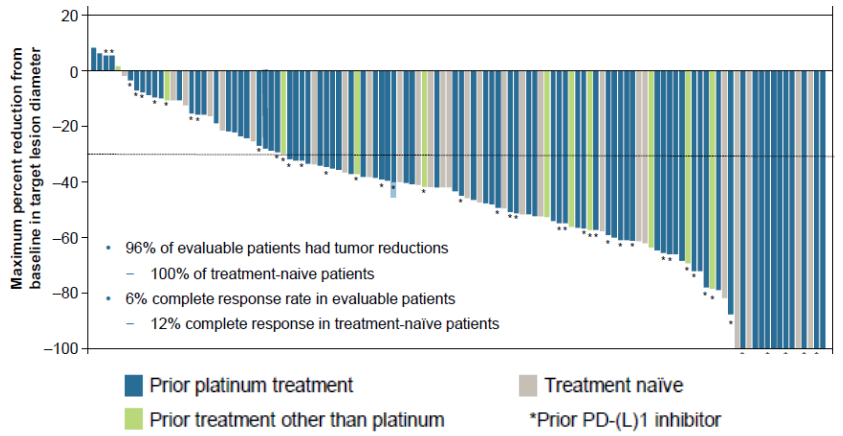
FDA BTD



- Oral small molecule kinase inhibitor
- Highly selective for RET fusions and mutations, including predicted resistence mutations
- Brain penetrant and CNS active
- ~1-2% of NSCLC patients with RET fusions, thereof ~40% with brain metastases

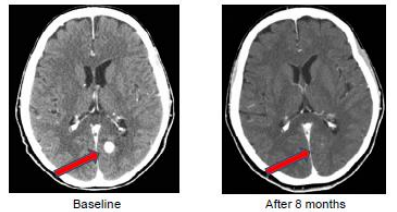
Ph I/II (ARROW) results in RET fusion+ mNSCLC

Tumor responses

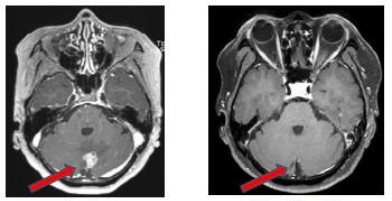


Gainor J. F. et al, ASCO 2020

CNS responses



(Courtesy of G. Curigliano)



(Courtesy of D.W Kim)

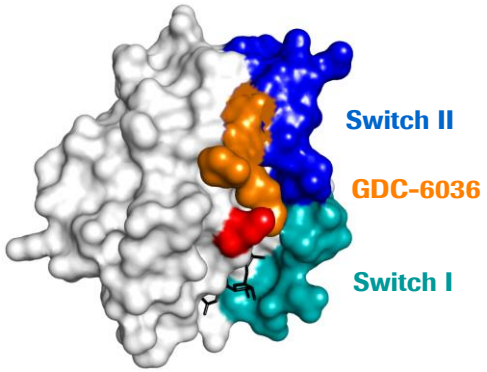
- 70% ORR in naive including 11% CR and 57% ORR in post-platinum patients including 6% CR*
- CNS ORR at 56% (n=9) including 33% CR; rapid and durable responses; mDOR not reached
- Well-tolerated across tumor types with most AEs of grade 1–2
- Ph III (AcceleRET Lung) in 1L advanced or metastatic RET+ NSCLC on-going
- US accelerated approval in RET+ mNSCLC achieved in Q3 2020; filed in the EU

Gainor J. F. et al, ASCO 2020; *Data in the label; SOC=standard of care; CNS=central nervous system; BTD=break through designation; mNSCLC=metastatic non small cell lung cancer; MTC=medullary thyroid cancer; ORR=overall response rate; CR=complete response; mDOR=median duration of response; AE=adverse events; Gavreto (pralsetinib) in collaboration with Blueprint Medicines; Gavreto, Blueprint Medicines and associated logos are trademarks of Blueprint Medicines Corporation; Gavreto was discovered by Blueprint Medicines

Lung franchise: GDC-6036 (KRAS G12C inhibitor) in solid tumors

G12C driver mutations found in 12% of all NSCLC patients

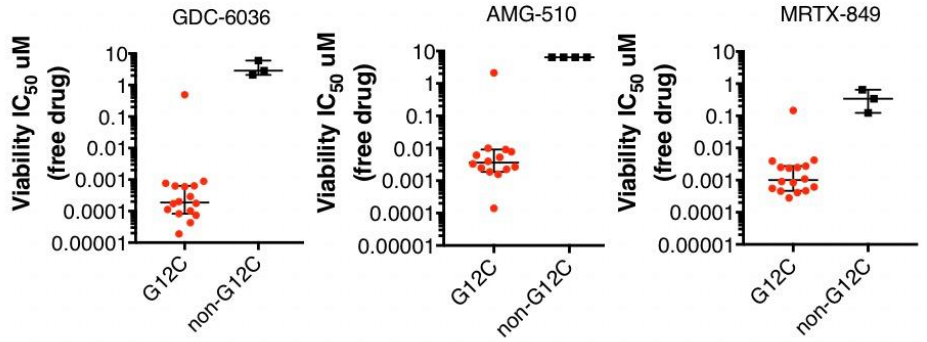
KRAS G12C inhibitor



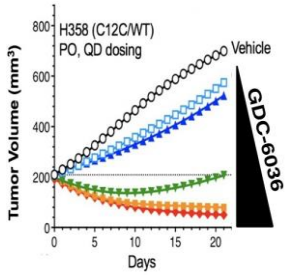
- Highly potent irreversible covalent inhibitor of the KRAS G12C mutant protein, which becomes locked in an inactive state
- Minimal safety findings leading to wide nonclinical safety margins

In vitro and *in vivo* tumor growth inhibition

***In vitro* cell line potency**



Tumor regression in G12C mutant xenograft mouse models



- GDC-6036 causes tumor growth inhibition in multiple patient derived KRAS G12C+ cell lines and in xenograft mouse models
- GDC-6036 synergizes with multiple targeted therapies; strong scientific rationale for combining with medicines that act on other parts of RAS pathway to deepen responses, extend duration of disease control, and limit treatment resistance.
- Ph I dose escalation and expansion in KRAS G12C+ solid tumors started in Q2 2020

Genentech unpublished results

Lung franchise: Blood-based NGS ctDNA assays

30% of lung cancer patients with insufficient biopsy material

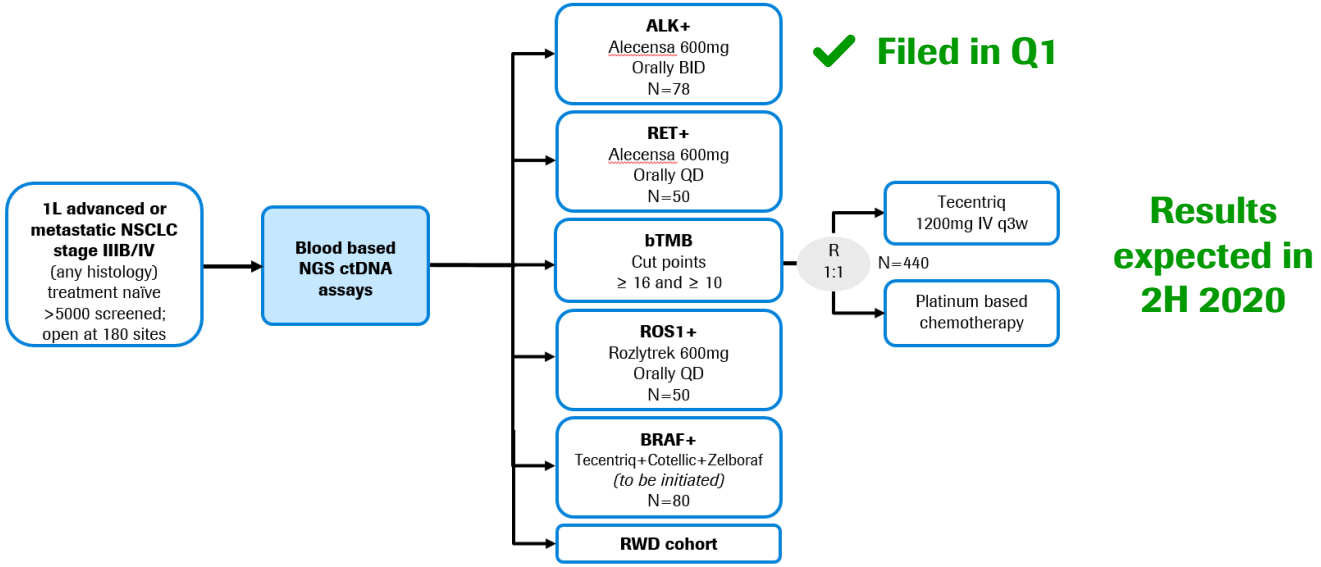
FOUNDATION MEDICINE

Roche

FDA Breakthrough device designation

FDA approved

Ph III trial design (B-FAST) for 1L treatment naive NSCLC



- Allows for serial liquid biopsy testing to follow tumor evolution and resistance
- RWD cohort paired with NGS testing provides additional natural history & epidemiological data
- Primary endpoint in the ALK+ cohort met; filed in Q1 2020

Blood based biomarkers

FoundationOne®Liquid CDx

- ***Liquid biopsy test that detects the 4 main classes of genomic alterations (324 genes), bTMB, MSI***
- ***Comprehensive genomic profiling including resistance mutations or fusions in NSCLC***
- ***Guides therapy selection and clinical trials***

Mok T. et al., WCLC 2017; NGS=next generation sequencing; ctDNA=circulating tumor DNA; RWD=real world data; bTMB=blood tumor mutational burden; MSI=microsatellite instability

Late stage pipeline update

1. **Hematology franchise**
   - DLBCL: Polivy, glofitamab, mosunetuzumab
   - FL: mosunetuzumab, glofitamab, Polivy
   - AML: Venclexta
   - MM: Venclexta
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Oncology / Hematology
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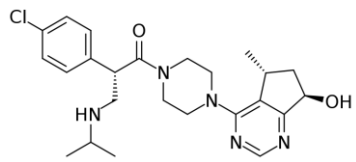
GU franchise: Ipatasertib in 1L mCRPC

Positive Ph III results for patients with PTEN loss

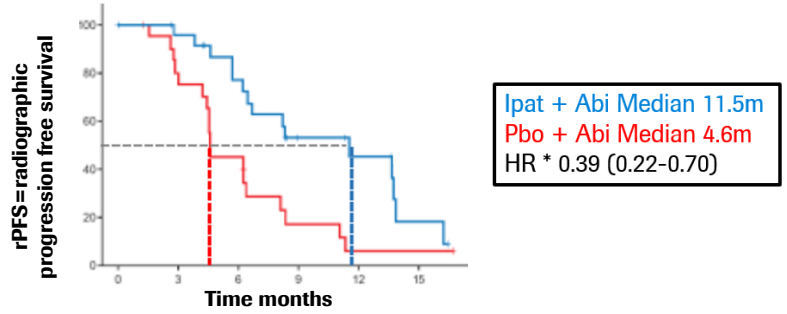
Highly selective AKT inhibitor



- Oral, highly specific inhibitor of all three activated isoforms of AKT and potentially preventing cancer cell growth and survival
- Clinical development in tumors with high frequency of PI3K/AKT pathway activation (CRPC, TNBC, HR+ mBC)

Ph II (A.MARTIN) results

rPFS (400mg dose) in PTEN loss patients



	ICR IHC		Ventana IHC		FISH		NGS	
	PTEN loss	PTEN non-loss	PTEN loss	PTEN non-loss	PTEN loss	PTEN non-loss	PTEN loss	PTEN non-loss
rPFS, mo								
Ipat	11.5	7.5	11.0	7.5	13.7	6.5	13.8	7.4
Pbo	4.6	5.6	4.6	5.7	6.5	5.6	6.2	4.5
rPFS HR [a]	0.39	0.84	0.50	0.74	0.67	0.77	0.24	0.52
90% CI	0.22-0.70	0.51-1.37	0.29-0.87	0.41-1.32	0.36- 1.24	0.50-1.20	0.10-0.60	0.25-1.13

Biomarker assay

Roche VENTANA PTEN (SP218)

- *IHC detection of PTEN protein loss in formalin-fixed, paraffin-embedded tissue*

FOUNDATION MEDICINE

- *Strong concordance to DNA technologies (NGS and FISH)*

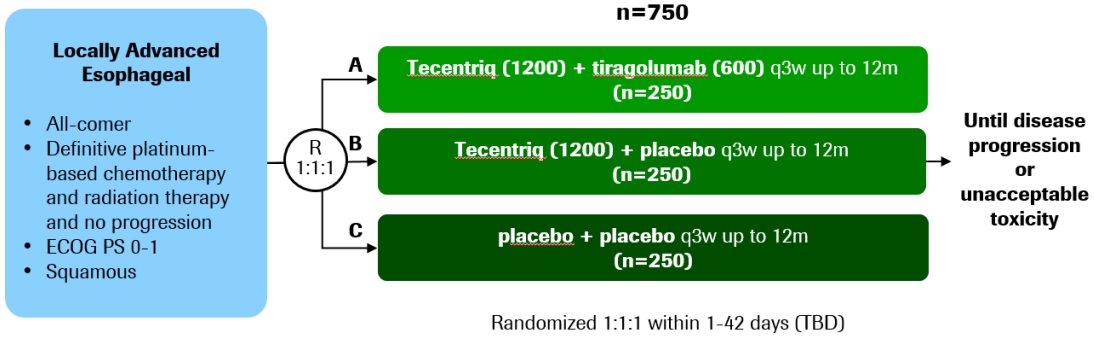
- Ph II: rPFS was prolonged in the ipatasertib 400 mg arm (8.2m vs 6.4m; HR=0.75); Dose-dependent improvement was observed in OS
- PTEN loss was associated with an improved rPFS outcome (HR of 0.39 at 400mg dose) as measured by NGS, FISH and IHC
- Ph III (IPATential150) met co-primary endpoint of rPFS in patients with PTEN loss

De Bono J.S. et al., ESMO 2016; mCRPC=metastatic castration resistent prostate cancer; rPFS=radiographic progression free survival; HR=hazard ratio; abi=abiraterone; OS=overall survival; NGS=next generation sequencing; FISH=fluorescence in situ hybridization; IHC=immunohistochemistry; * unstratified HR; 90% CI

GI franchise: Tiragolumab in esophageal cancer (EC)

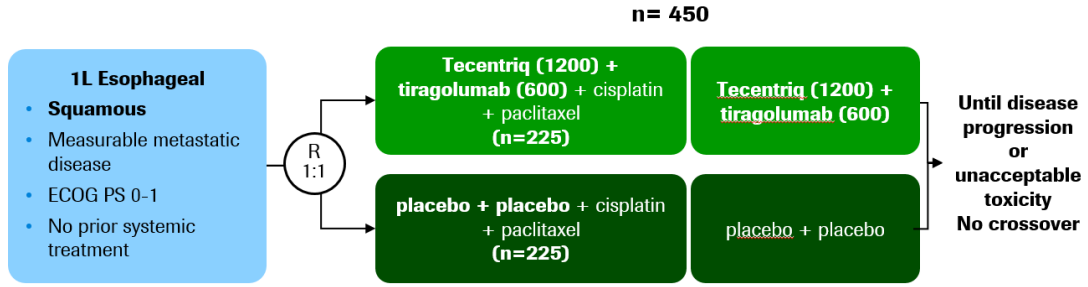
Pivotal Ph III studies initiated

Ph III trial design (SKYSCRAPER-07) in locally advanced EC



- 1EP: PFS A vs C; OS (hierarchical) A vs C; OS (hierarchical) B vs C
- 2EP: OS, PFS A vs B; PFS B vs C; ORR; DOR; safety; QoL

Ph III trial design (SKYSCRAPER-08) in 1L esophageal squamous cancers (ESCC)



- 1EP: OS; PFS
- 2EP: DOR; ORR; safety; QoL

- Preliminary Ph Ib safety and efficacy data in EC to be presented at upcoming conference
- Global development program with focus on Asia, especially China
- Ph III starts expected in 2020

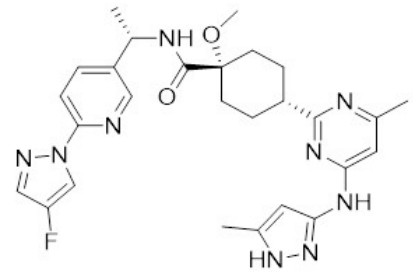
Ab=antibodies; ORR=overall response rate; TPS=tumor proportion score; PFS=progression free survival; NE=non evaluable; ITT=intention-to-treat; * unstratified HR

Thyroid cancer franchise: Gavreto in RET+ TC

Excellent efficacy and durability across thyroid cancer types

RET inhibitor

FDA BTD

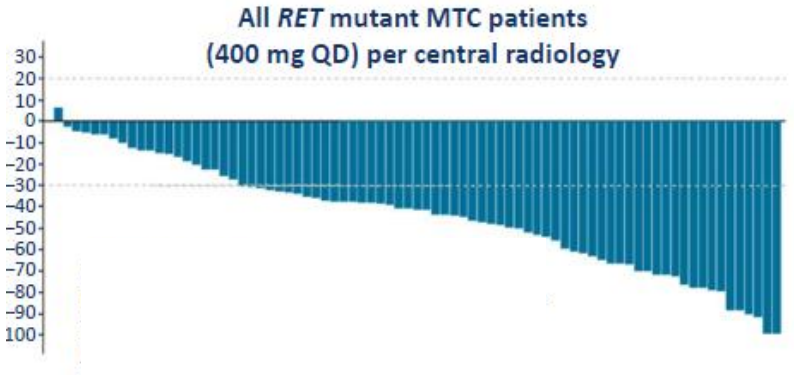


- Oral small molecule kinase inhibitor
- Highly selective for RET fusions and mutations, including predicted resistance mutations
- Brain penetrant and CNS active
- 90% of advanced MTC patients with RET activating mutations and ~10-20% of PTC patients with RET fusions

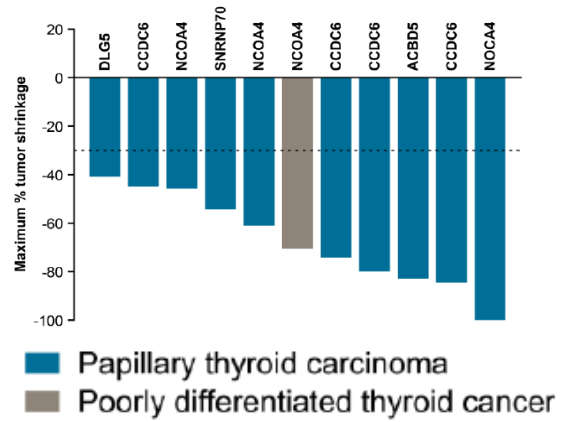
Ph I/II (ARROW) results

ASCO 20 Virtual

Tumor responses
RET mutation+ medullary TC (MTC)*



Tumor responses
other RET fusion+ TC



- RET+ MTC: ORR 74% in naive patients and 60% ORR in pretreated patients; mDOR not reached *
- RET+ TC: 91% ORR and 6-month DOR stands at 100%
- Registrational data on Ph I/II (ARROW) MTC results to be presented at ESMO
- Ph III (AcceleRET MTC) in MTC to start in H2 2020
- US priority review and RTOR for advanced or metastatic RET+ thyroid cancer on-going

* MTC data released by Blueprint Medicines on April 1, 2020; Subbiah V. et al, ASCO 2020; SOC=standard of care; TC=thyroid cancer; MTC=medullary thyroid cancer PTC=papillary thyroid cáncer; CNS=central nervous system; BTD=breakthrough therapy designation; RTOR=real time oncology review; ORR=overall response rate; mDOR=median duration of response; Gavreto (pralsetinib) in collaboration with Blueprint Medicines; Gavreto, Blueprint Medicines and associated logos are trademarks of Blueprint Medicines Corporation; Gavreto was discovered by Blueprint Medicines

Melanoma franchise: Tecentriq + Cotellic + Zelboraf

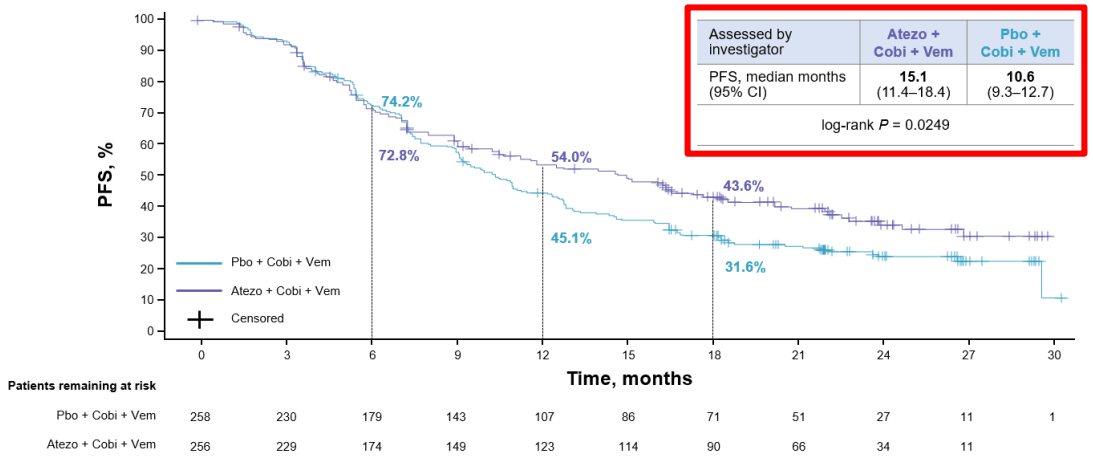
First CIT+targeted therapy in BRAF V600+ melanoma

AACR ANNUAL MEETING 2020
June 22 - 24, 2020
Virtual Meeting II, Sessions Available Online

FDA approved

Ph III (IMspire150/TRILOGY) results in BRAF+ melanoma

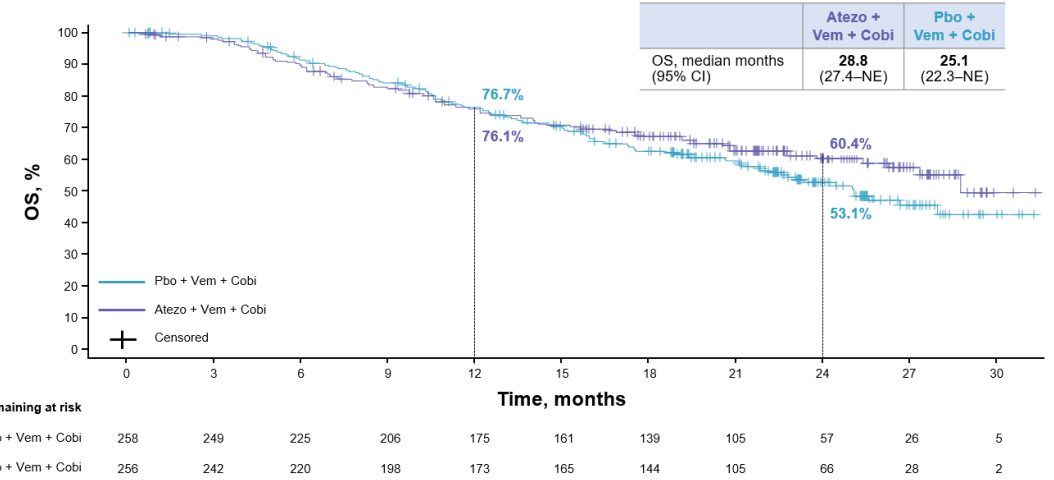
Investigator assesed PFS



Assessed by investigator	Atezo + Cobi + Vem	Pbo + Cobi + Vem
PFS, median months (95% CI)	**15.1** (11.4–18.4)	**10.6** (9.3–12.7)

log-rank $P = 0.0249$

Overall survival (OS)



	Atezo + Vem + Cobi	Pbo + Vem + Cobi
OS, median months (95% CI)	**28.8** (27.4–NE)	**25.1** (22.3–NE)

- Statistically significant and clinically meaningful improvement in investigator-assessed PFS (HR=0.78; 15.1m vs 10.6m) and clinically meaningful improvement in mDOR (21.0m vs 12.6m); no new safety signals were identified
- OS data not mature but favored triplet; next interim expected H1 2021
- FDA approval granted in Q2 2020 under priority review and being part of FDA's project Orbis

McArthur G.A. et al., AACR 2020; CIT=cancer immuno therapy; Atezo=atezolizumab (Tecentriq); CI=confidence interval; Cobi=cobimetinib (Cotellic); Pbo=placebo; Vem=vemurafenib (Zelboraf); PFS=progression free survival; Cotellic in collaboration with Exelixis; Zelboraf in collaboration with Plexxikon

Late stage pipeline update

1. **Hematology franchise**
   - DLBCL: Polivy, glofitamab, mosunetuzumab
   - FL: mosunetuzumab, glofitamab, Polivy
   - AML: Venclexta
   - MM: Venclexta
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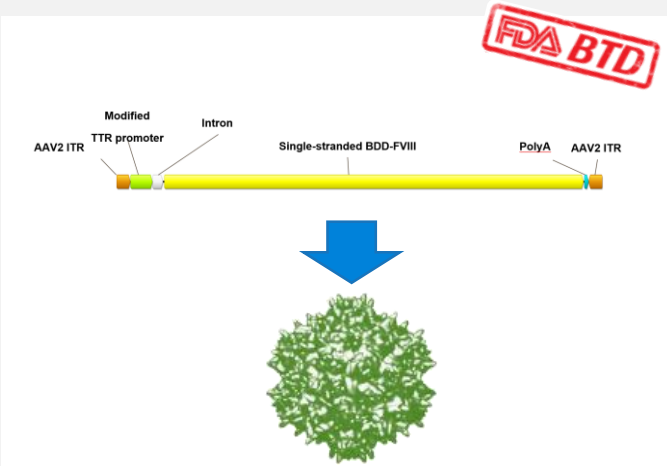
Non-malignant hematology: RG6357 (SPK-8011) in hem A

Early efficacy and safety data after 2 to 3.3 years of follow-up

Hemophilia A gene therapy

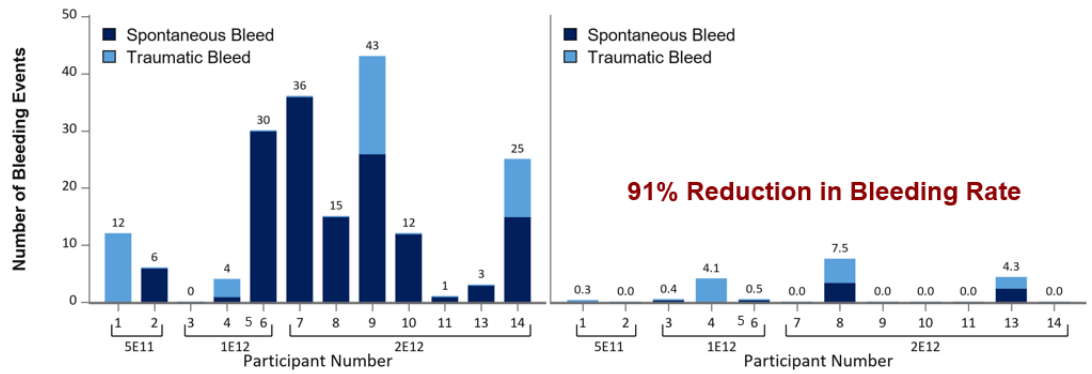


AAV-Spark200

- Bio-engineered adeno-associated viral (AAV) vector utilizing the AAV-LK03 capsid (Spark200)
- Contains a codon-optimized human factor VIII gene under the control of a liver-specific promoter

Ph I/II (SPK-8011) results

Annualized bleed rate (ABR) of participants with sustained expression (n=12)*



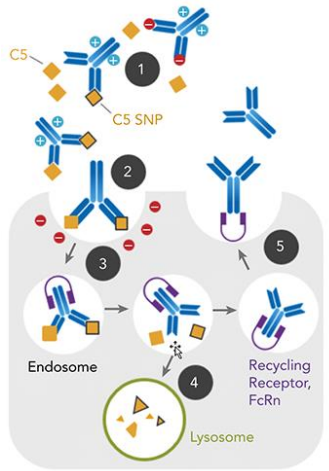
- Data from 5 participants in the $5x10^{11}$ and 1×10^{12} vg/kg dose cohorts and 7 participants in the $2x10^{12}$ vg/kg dose cohort showed a 91% ABR reduction and a 96 % reduction in FVIII infusions
- The 5 participants in the $5x10^{11}$ and $1x10^{12}$ vg/kg cohorts demonstrated durable and stable FVIII expression, had a clinically significant reduction in bleeding and factor use and showed an acceptable safety profile for 2 to 3.3 years of follow up
- Further dose optimization and selection of immunomodulatory regimen on-going
- Ph III to be initiated in 2021

George, L.A. et al, ISTH 2020; * Excludes 2 participants who lost expression

Non-malignant hematology: Crovalimab in PNH

Recycling Ab for maximal inhibition of C5

Anti-C5 mAb

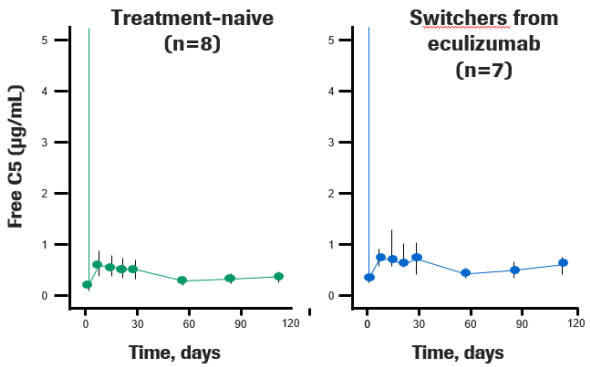


1. High affinity binding
2. Preferential Ab uptake of antigen-bound Ab (PI engineering)
3. Acid-sensitive antigen release
4. C5 degradation in the endosome
5. Ab recycling by FcRn engineering, protecting Abs from degradation

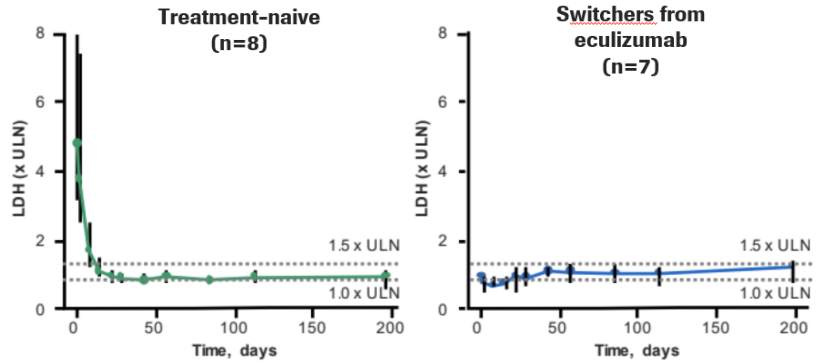
- Chugai engineered, anti complement component 5 (C5) recycling mAb[1–6]
- Engineered to enable maximal, long-lasting neutralization of C5 in complement mediated diseases
- Convenient SC Q4W dosing at home

Ph I/II (COMPOSER) results

Sustained low free C5 levels



Normalized LDH levels due to sustained hemolysis control

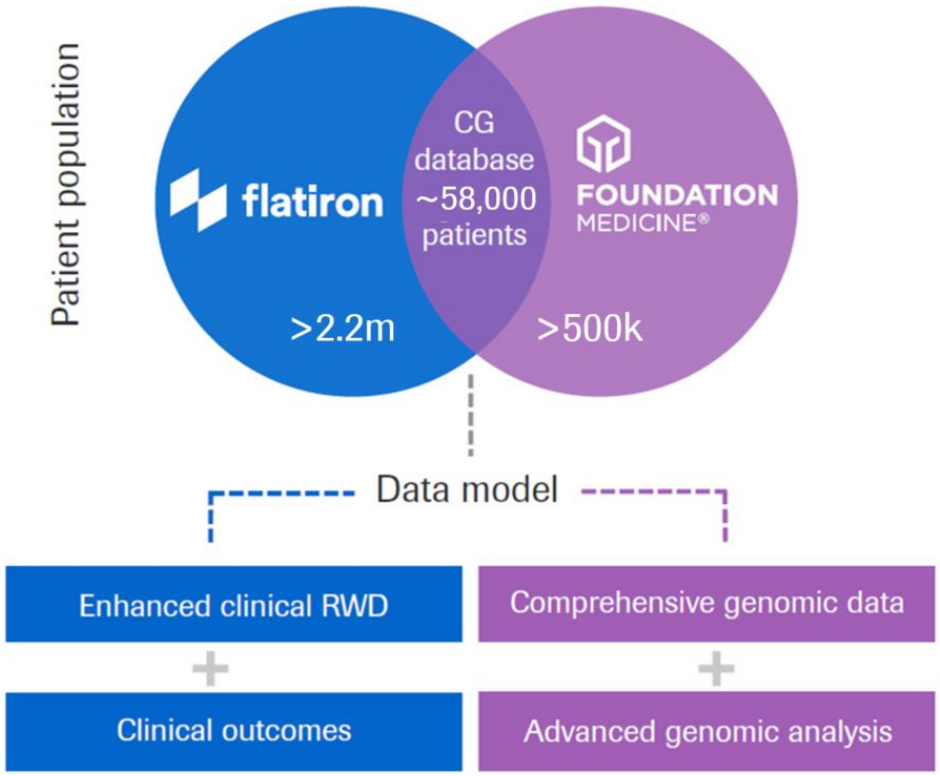


- Ph I/II (COMPOSER) results show complete complement inhibition and a well-tolerated safety profile in C5i-naive patients and eculizumab pre-treated patients[1]
- Efficacy was maintained over long-term treatment (44 patients treated for a median of 71 weeks) and breakthrough hemolysis events were infrequent[7]
- Ph III switch and naive studies (COMMODORE 1/2) in PNH to start in 2020
- Development in additional complement-mediated diseases is being explored

1. Röth A et al. Blood 2020;135:912–20; 2. Fukuzawa T et al. Sci Rep 2017;7:1080; 3. Sampei Z et al. PLoS One 2018;13:e0209509; 4. Röth A, Nishimura J. Centro Congressi Federico II 2019; 5. Röth A et al. ASH 2018; 6. Sostelly A et al. ASH 2019; 7. Röth A et al. EHA 2019; 8. Peffault de la Tour, R. et al. EHA 2020

Clinico-Genomic Database

Combining RWD and genomics drives R&D



Database R&D applications:

- Understanding genomics of rapidly progressive disease
- Natural history cohorts for defined populations (ALK, NTRK, EGFR, ROS-1, RET, KRAS, etc.), including patterns of metastatic spread
- Mechanisms of resistance
- Improved prognostic classifiers

Recent R&D examples:

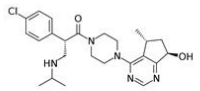
- Analysis found cumulative **incidence of brain metastases in patients with a certain mutation** is significantly higher than in patients with wild-type allele or other mutations; decision to develop brain-penetrant molecule as part of the broader development strategy
- Analysis of CGDB used to decipher a **molecular mechanism for checkpoint inhibitor resistance** and ultimately helped address a fundamental question that can potentially benefit many cancer immunotherapy projects

Linking advanced tumor genetics with clinical outcomes drives scientific hypothesis generation

RWD=real world data; CGDB=Clinico-Genomic Database

Our technology platforms keep expanding*

Small molecules

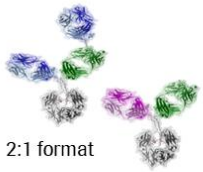


- Gavreto
- Alecensa
- ipatasertib
- RG6114
- RG6171
- KRAS G12C

Target oncogenes, induce apoptosis, supress tumor growth

- Evrysdi
- fenebrutinib
- ralmitaront
- TLR7 agonist
- GABA Aa5 PAM
- PTH1R agonist

Bi-specifics

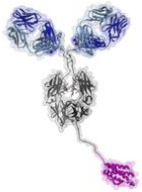


- mosunetuzumab
- glofitamab
- cibisatamab
- Her2 x CD3
- glypican-3 x CD3
- FcRH5 x CD3
- PD1 x TIM3
- PD1 x LAG3
- BCMA x CD16a

Engage and activate T cells to kill tumour cells

- Hemlibra
- faricimab
- FIXa x FX
- FGFR1 x KLB

Fusion protein



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

Amplify immune response

- brain shuttle gantenerumab
- IL22-Fc
- IgG-IL2

mAb

- tiragolumab
- CD25 mAb
- CD47 mAb
- selicrelumab
- codrituzumab

Amplify immune response

- Enspryng
- crovalimab
- gantenerumab
- prasinezumab
- semorinemab
- TLR4 mAb
- ST2 mAb
- REGN-CoV2

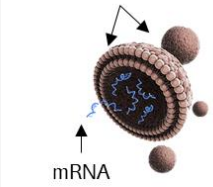
Antibody drug conjugate

- Polivy
- Kadcyla

Targeted toxic payload

- Anti-S.aureus TAC

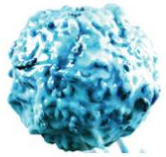
Personalized mRNA vaccine



- iNeST

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

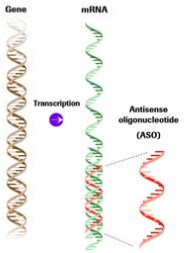
Personalized T cells



- programmed T cells

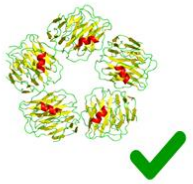
Patient's neo-antigens for anti-tumour immune response

RNA technologies



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

Recombinant proteins



- Activase
- Pulmozyme
- rhPentraxin-2

Gene therapy

- Luxturna
- SPK-8011
- SPK-8016
- SPK-7001
- SRP-9001
- 4D-R110

= Oncology

= Products approved

* List of pipeline and launched molecules shown is not complete; iNeST=Individualized Neoantigen-Specific Therapy

Doing now what patients need next