Roche Pharma Day 2019

Late Stage Pipeline Oncology

Sandra Horning | Chief Medical Officer and Head Global Product Development

Late stage pipeline update

Topics covered in presentations and break-out sessions

1. **Hematology franchise** (1)
   - CLL: Venclexta Gazyva
   - DLBCL: Polivy, Venclexta
   - NHL, DLBCL: mosunetuzumab, CD20xCD3
   - AML: Venclexta, idasanutlin
   - MM: Venclexta

2. **Breast Cancer franchise** (2)
   - HER2+: Kadcyla, Perjeta, FDC SC, Tecentriq
   - TNBC: Tecentriq, ipatasertib
   - HR+: ipatasertib; PI3Kα inhibitor; SERD

3. **Lung Cancer franchise** (3)
   - NSCLC: Tecentriq
   - ALK+: Alecensa
   - ROS1+/NTRK+: Rozlytrek

4. **GU franchise** (4)
   - mUC: Tecentriq
   - CRPC: ipatasertib

5. **Pan tumor** (5)
   - NTRK+ tumors: Rozlytrek

6. **Other oncology** (6, 7, 8)
   - Melanoma: Tecentriq, Cotellic, Zelboraf
   - OC: Tecentriq, Avastin
   - HCC: Tecentriq, Avastin

6. **Hemophilia A**
   - Hemlibra

7. **Neuroscience** (9, 10, 11, 12, 13, 14)
   - MS: Ocrevus update
   - SMA: risdiplam
   - NMOSD: satralizumab
   - Huntington's disease: HTT-ASO
   - Autism: balovaptan
   - Parkinson's disease: prasinezumab

9. **Immunology** (15, 16, 17, 18)
   - Lupus nephritis: Gazyva
   - Ulcerative colitis: etrolizumab
   - Crohn's disease: etrolizumab
   - Food allergy: Xolair
   - Nasal polyps: Xolair

8. **Infectious diseases** (19)
   - Influenza A/B: baloxavir marboxil

6. **Ophthalmology** (20, 21, 22, 23)
   - DME, nAMD: faricimab
   - AMD: Port Delivery System
   - GA: ASO factor B
   - Choroideremia: Gene therapy

Oncology / Hematology
Neuroscience
Ophthalmology
Infectious diseases
Immunology

1 Topics main presentations
1 Topics break-out sessions

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 18 results presentation appendix or visit the IR homepage

Oncology: Progress since late 2018

12 pivotal studies addressing needs of >800k patients reading out soon

Lead in Hematology

NHL: Rituxan, Gazyva, Venclexta, Polivy, mosunetuzumab, CD20xCD3

CLL: Venclexta, Gazyva

AML: Venclexta, idasanutlin

MM: Venclexta

Hemophilia A: Hemlibra

High medical need in later lines, aNHL and AML

Lead in Breast Cancer

HER2+ BC: Herceptin, Perjeta, Kadcyla, H+P FDC SC

TNBC: Tecentriq, ipatasertib

HR+ BC: ipatasertib, PI3Kα inhibitor (RG6114); SERD (RG6171)

> 80% patients in adjuvant

Growth in Lung

ALK+/ROS1+/NTRK+: Alectinib, Rozlytrek

SCLC: Tecentriq

NSCLC: Tecentriq, Avastin

>70% still metastatic

Establish presence (with Tecentriq and combos)

mUC: Expand in 1L; Move into adjuvant

HCC: Potential new SOC

CRPC: Potential new SOC

OC: Potential new SOC

RCC and CRC: Explore opportunities

= Significant progress since last Pharma Innovation Day (September 2018)

Roche significantly advancing patient care

26 BTD's reflecting the quality of our research

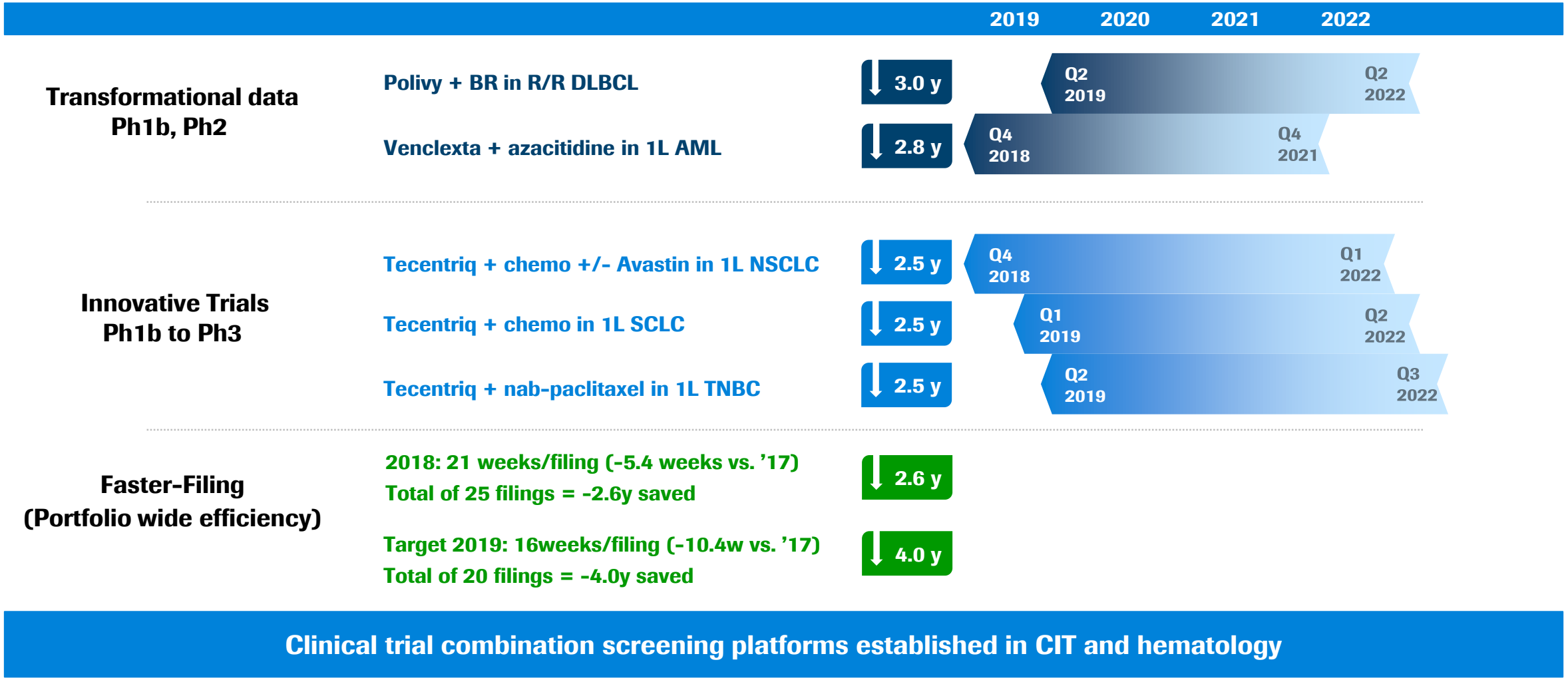
Year	Molecule	Indication	
2019	**Venclexta + Gazyva**	*1L unfit CLL*	✓
	Kadcyla	*Adjuvant HER2+ BC*	✓
2018	**satralizumab**	*NMOSD*	
	Xolair	*Food allergies*	
	Tecentriq + Avastin	*HCC*	
	Hemlibra	*Hemophilia A non-inhibitors*	✓
	Rozlytrek	*NTRK+ solid tumors*	✓
	balovaptan	*Autism spectrum disorders*	
2017	**Polivy + BR**	*R/R DLBCL*	✓
	Venclexta + LDAC	*1L unfit AML*	✓
	Zelboraf	*BRAF-mutated ECD*	✓
	Rituxan	*Pemphigus vulgaris*	✓
2016	**Actemra**	*Giant cell arteritis*	✓
	Alecensa	*1L ALK+ NSCLC*	✓
	Ocrevus	*PPMS*	✓
	Venclexta + HMA	*1L unfit AML*	✓
	Venclexta + Rituxan	*R/R CLL*	✓

Year	Molecule	Indication	
2015	**Actemra**	*Systemic sclerosis*	
	Tecentriq	*NSCLC*	✓
	Venclexta	*R/R CLL 17p del*	✓
	Hemlibra	*Hemophilia A inhibitors*	✓
2014	**Esbriet**	*IPF*	✓
	Lucentis	*Diabetic retinopathy*	✓
	Tecentriq	*Bladder*	✓
2013	**Alecensa**	*2L ALK+ NSCLC*	✓
	Gazyva	*1L CLL*	✓

✓ = approved

Acceleration of development timelines

Aiming for more faster



Clinical trial combination screening platforms established in CIT and hematology

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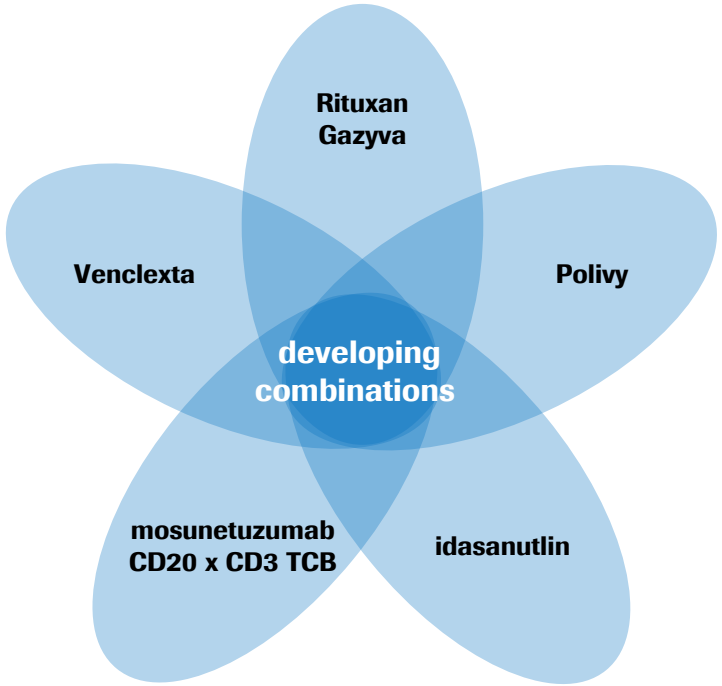
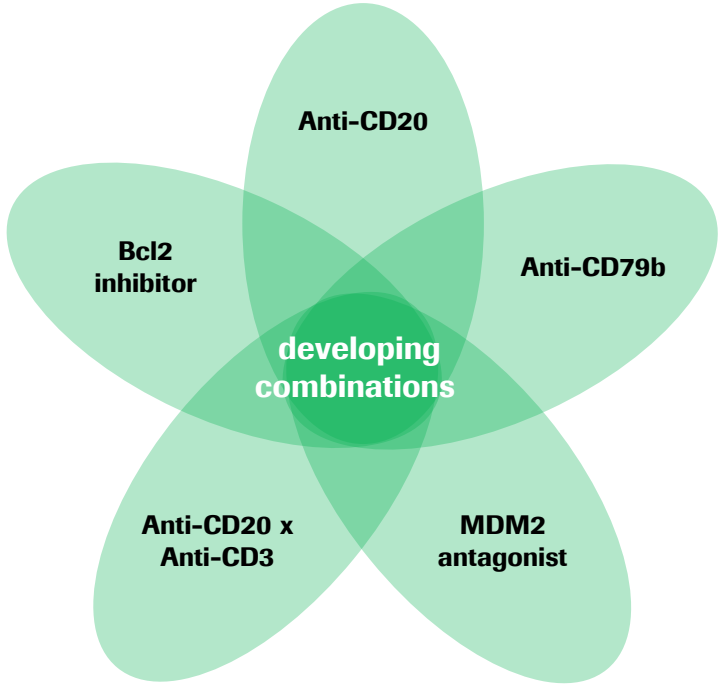
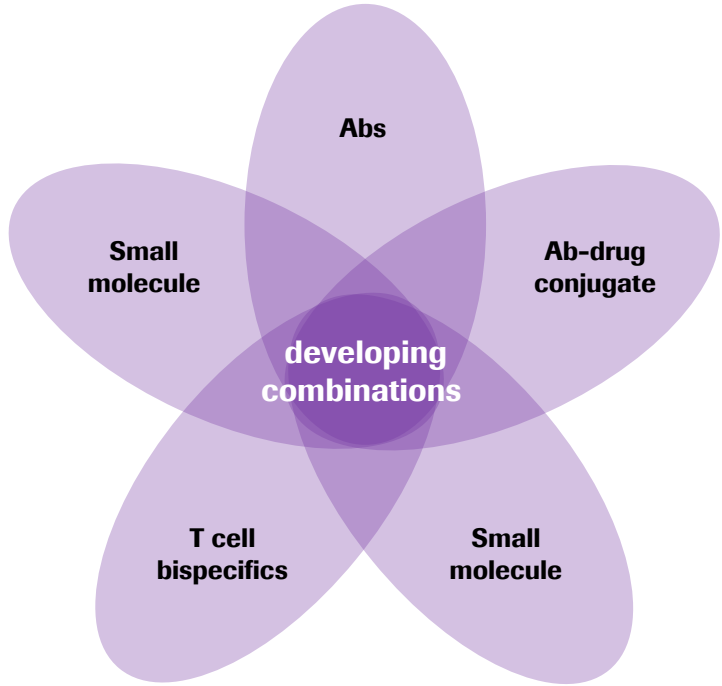
Uniquely positioned to improve SOC in hematology

Largest late stage portfolio allows to develop new combinations







7 molecules approved / late stage

5 different MOAs

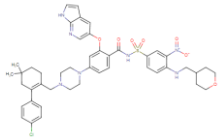
4 different platform technologies

Hematology: Venclexta + Gazyva in 1L unfit CLL

Fast track approval following outstanding PFS and MRD data

Venclexta progam

Bcl-2 inhibitor



	Combination	Indication	Ph1	Ph2	Ph3
NHL	V+R/G+CHOP	1L DLBCL (aNHL)			
	V+R	DLBCL			
	V+pola+G/R	R/R DLBCL/FL			
CLL	V+G	1L CLL			✓
	V+R	R/R CLL			✓
	V	R/R CLL 17p			✓
	V	R/R CLL after ibru/idel			
	V+G	1L and R/R CLL			
MM	V+dex	t(11;14) R/R MM			
	V+bor+dex	R/R MM			
AML	V+aza	1L AML			✓
	V+LDAC	1L AML			✓
	V+idasanutlin	R/R AML unfit			
	V+AMG176	R/R AML			
	V+gilteritinib	R/R AML			
MDS	V+aza	1L MDS			
	V+/-aza	R/R MDS			

Ph III (CLL14) results:

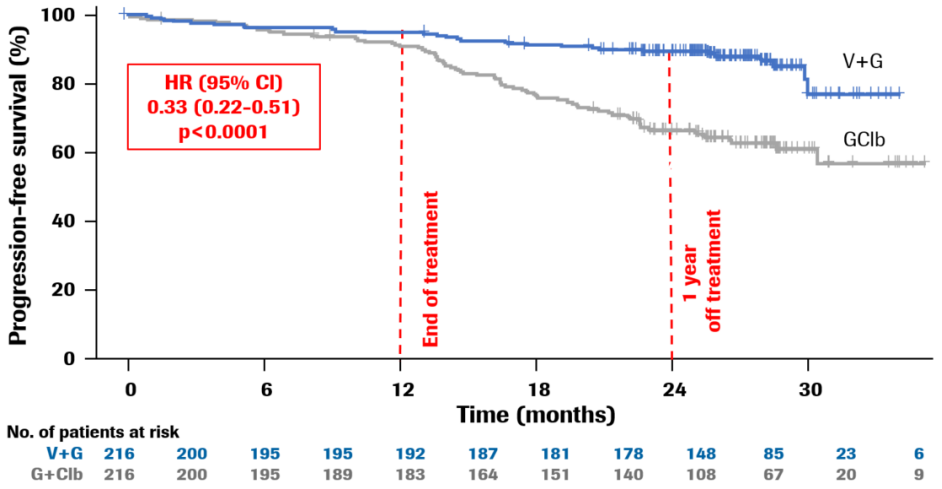
2019 ASCO ANNUAL MEETING

FDA BTD

Minimal residual disease

	V+G	G+Clb
MRD-negative, %, bone marrow (95%CI)	57 (50-64)	17 (12-23)
p-value	<0.0001	
MRD-negative, %, peripheral blood (95%CI)	76 (69-81)	35 (29-42)
p-value	<0.0001	

IRC assessed PFS



- PFS HR of 0.33 versus Gazyva + chlorambucil; mPFS not reached
- First fixed 12-month treatment, chemotherapy-free option
- Approval following 10 weeks after submission via the RTOR pilot program

Fischer K. *et al*., ASCO 2019; PFS=progression free survival; HR=hazard ratio; V=Venclexta; G=Gazyva; clb=chlorambucil; R=Rituxan; dex=dexamethasone; bor=bortezomib; T=Tecentriq; aza=azacitidine; LDAC=low dose cytarabine; RTOR=real-time oncology review; Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Cotellic in collaboration with Exelixis

Hematology: Very strong US launch for Polivy

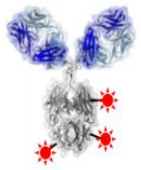
First approval for Polivy + BR in R/R DLBCL

POLIVY® polatuzumab vedotin

Roche

Polivy program

anti-CD79b ADC



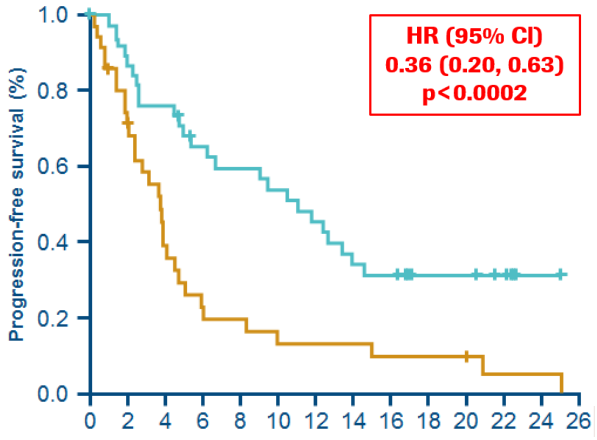
	Combination	Indication	Ph1	Ph2	Ph3
NHL	Polivy+R+CHP	1L DLBCL			
	Polivy+R+Gemox	R/R DLBCL			
	Polivy+G/R	R/R DLBCL/FL			
	Polivy+G/R+/-benda	R/R DLBCL/FL			✓
	Polivy+G/R+len	R/R DLBCL/FL			
	Polivy+G/R+V	R/R DLBCL/FL			
	Polivy+mosun	R/R DLBCL/FL			
	Polivy+mosun+CHP	R/R NHL			
	Polivy+mosun+CHP	1L DLBCL			

First and only pivotal randomized Ph II study with survival benefit [1]

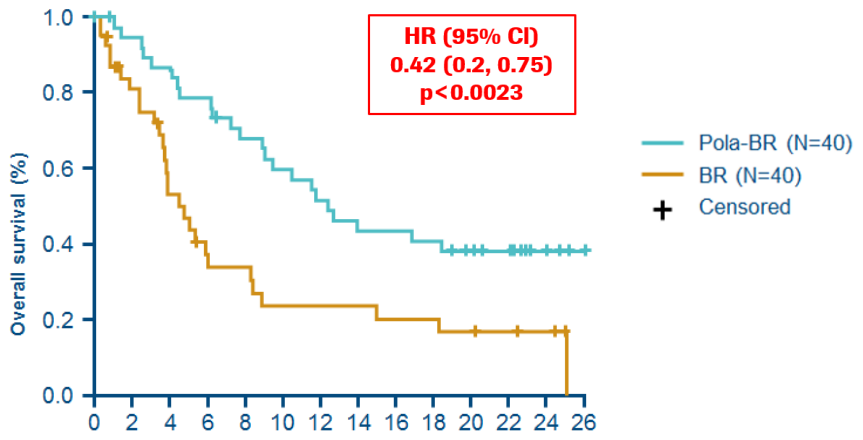
FDA BTD

EMA PRIME

PFS (IRC)



OS



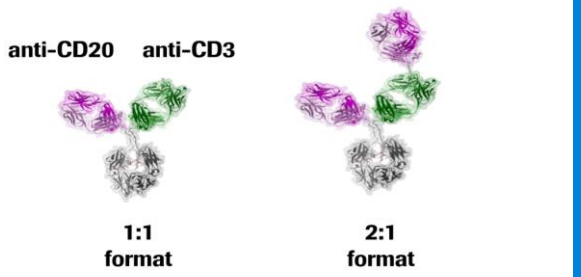
- Rapid uptake in R/R DLBCL following early US approval; EU approval expected in 2H
- Safely administered in combination with BR; also used as an off-the-shelf bridge therapy to consolidative therapies
- Ph III (POLARIX) in 1L DLBCL fully recruited ahead of schedule; Ph III (POLARGO) with additional chemo combinations in R/R DLBCL initiated

Sehn L. H. *et al*., ASH 2018; ADC=antibody drug conjugate; DLBCL=diffuse large B-cell lymphoma; PFS=progression free survival; OS=overall survival; HR=hazard ratio; BR=bendamustine+Rituxan;
1. In R/R DLBCL patients not candidates for transplant; Polivy in collaboration with Seattle Genetics

Hematology: CD20 x CD3 program in NHL

Strong durable efficacy and tolerable safety

CD20 x CD3 program



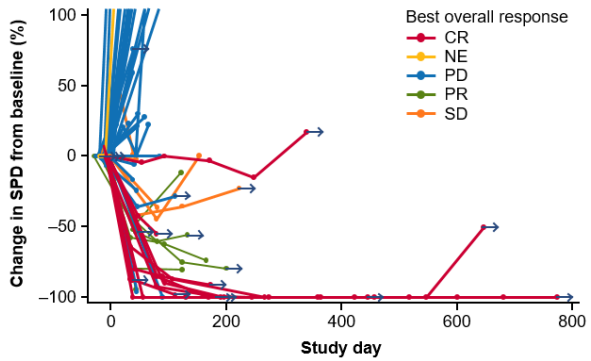
	Combination	Indication	Ph1	Ph2	Ph3
NHL	*mosun+CHOP*	1L DLBCL, R/R NHL			
	mosun+CHP+pola	1L DLBCL, R/R NHL			
	mosun	R/R DLBCL/FL/MCL			
	mosun+T	R/R DLBCL/FL/MCL			
	mosun+pola	R/R DLBCL/FL			
	mosun	1L unfit/elderly DLBCL			

	Combination	Indication	Ph1	Ph2	Ph3
NHL	*CD20xCD3*	R/R DLBCL/FL			
	CD20xCD3+R +CHOP	1L DLBCL			
	CD20xCD3+T	R/R DLBCL/FL			
	CD20xCD3+G/R +CHOP	R/R FL			
	CD20xCD3+G	R/R DLBCL/FL			

Mosunetuzumab (PhI dosing):

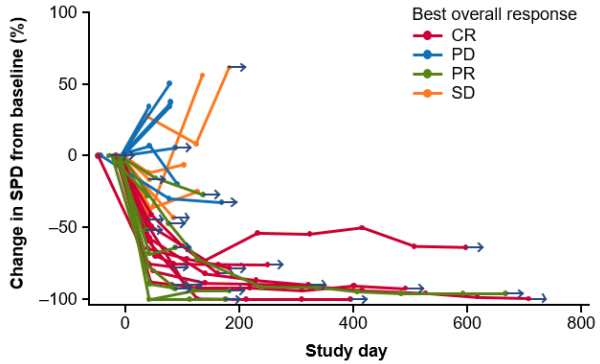
R/R aNHL*

- **Median duration of CR not reached**
- **Median CR fllow up: 298 days (46–816 days)**



R/R FL

- **Median duration of CR not reached**
- **Median CR fllow up: 330 days (54–788 days)**



- Induces durable CR in R/R indolent and aggressive NHL; CRs in patients refractory to R-CHOP and CAR-T
- Favorable safety profile: Cycle 1 step-up dosing appears to mitigate toxicity
- Dose optimization and combination trials with Tecentriq, Polivy and CHOP ongoing; Further efficacy update planned for H2 2019

Budde. L. et al, ASCO 2019; NHL=non-Hodgkin's lymphoma; mosun=mosunetuzumab; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; pola=polatuzumab; T=Tecentriq; G=Gazyva; R=Rituxan; CR=complete response; R/R=relapsed/refractory; SPD=sum of the product diameters; CAR T cells=chimeric antigen receptor; *includes R/R DLBCL/trFL

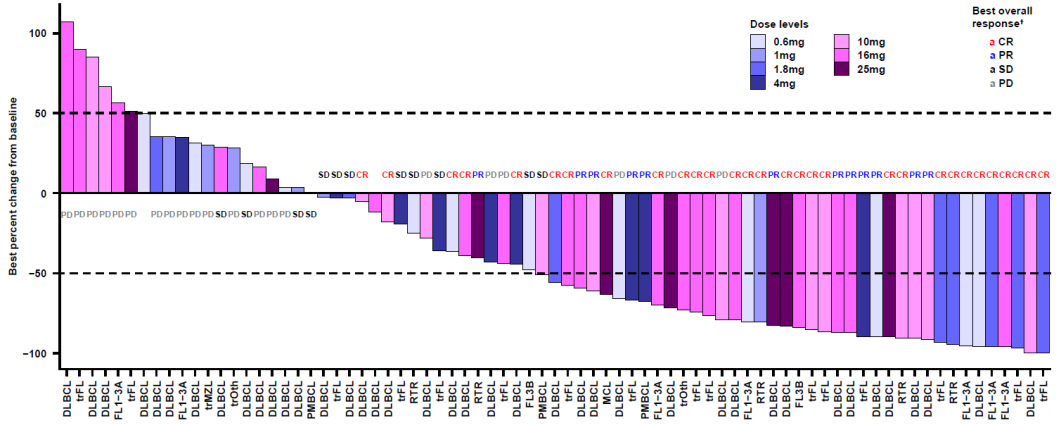
Hematology: CD20 x CD3 program in NHL

Strong efficacy and tolerable safety

15-ICML
15th International Conference on Malignant Lymphoma
Palazzo dei Congressi, Lugano, Switzerland, June 18-22, 2019

CD20 x CD3 (PhI dosing):

R/R aNHL*



10-16 mg cohorts*: ORR 19/33 (58%); CR 13/33 (39%)

Clinical case

- DLBCL patient with 6 prior lines: R-CHOP 21 (CR), R-DHAOX (SD), Selinexor (PD), GemOx-nivolumab (PD), lenalidomide plus RT (SD) and bromodomain inhibitor (PD)
- CR after 6 doses of CD20-TCB (16mg), surgical removal of necrotic PET-negative crust on Mar 14

- Continues to show highly encouraging OR and CR rates in R/R indolent and aggressive NHL
- 10-16mg dosing cohorts with ORR of 58% and a CRR of 39%
- Main safety signal is CRS: Mostly confined to cycle 1 and all but one patient was re-dosed at same dose level at cycle 2
- Overall low rate of AEs leading to discontinuation (1%)

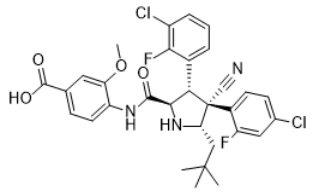
Dickinson, M., et al, ICML 2019; R/R=relapsed/refractory; NHL=non-Hodgkin's lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; R=Rituxan; OR=overall response; CR=complete response; SD=stable disease; PD=progressive disease; CRS=cytokine release syndrome; AE=adverse event; *aNHL includes FL Grade 3B, DLBCL, trFL, PMBCL, MCL, trMZL, RS and DLBCL/MCL

Hematology: Idasanutlin in AML

Promising activity in combination

Idasanutlin program

MDM2 antagonist



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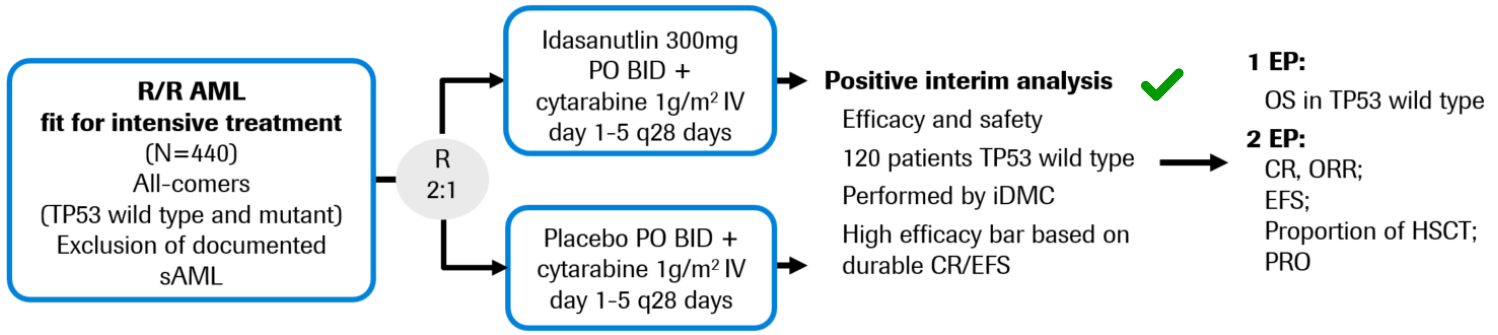
AML	idasanutlin +cytarabine	R/R AML			
	idasanutlin+V	R/R AML unfit for chemo			
	idasanutlin +cytarabine +daunorubicin	1L AML			
PV	idasanutlin	Hydroxyurea resistant/ intolerant PV			

Ph III (MIRROS) trial design



Responding patients may receive optional consolidation with up to 2 additional cycles

- Ph I in heavily pretreated AML patients: idasanutlin+cytarabine showed 29% cCR rate (all patients) and 42% cCR rate in patients dosed with Ph III dose with a mDoR >8m
- Ph II (NCT02670044): Venclexta+idasanutlin showed clinical activity (46% anti-leukemic RR and 33% CR+CRi+CRp rate at 600mg Venclexta + 150/200mg idasanutlin) in unfit R/R AML
- Ph III (MIRROS) in R/R AML is one of the largest R/R AML studies; NME filing possible in 2020

Martinelli G, et al., EHA 2016; Daver N. *et al.*, ASH 2018; OS=overall survival; cCR, leukemic RR (CR+CRp+CRi+MLFS); CR=complete remission rate; CRp=complete remission with incomplete platelet recovery; CRi=complete remission with incomplete count recovery, MLFS=morphologic leukemia-free state; mDoR=median duration of response; V=Venclexta; PV=polycythemia vera

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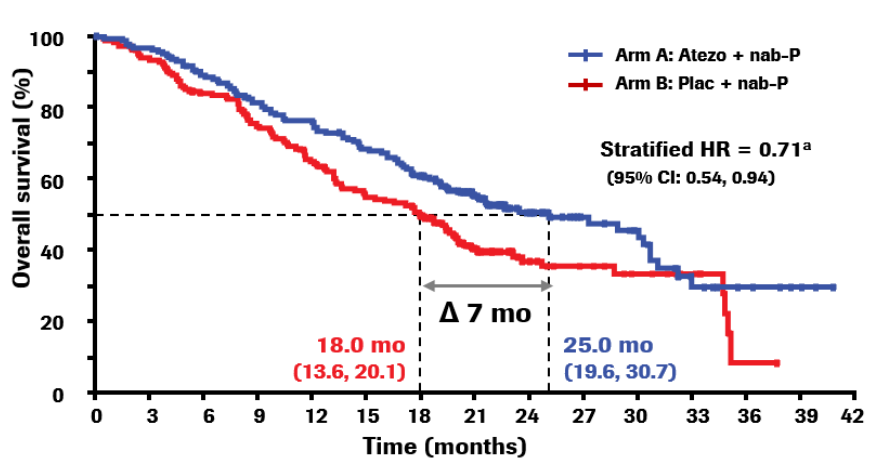
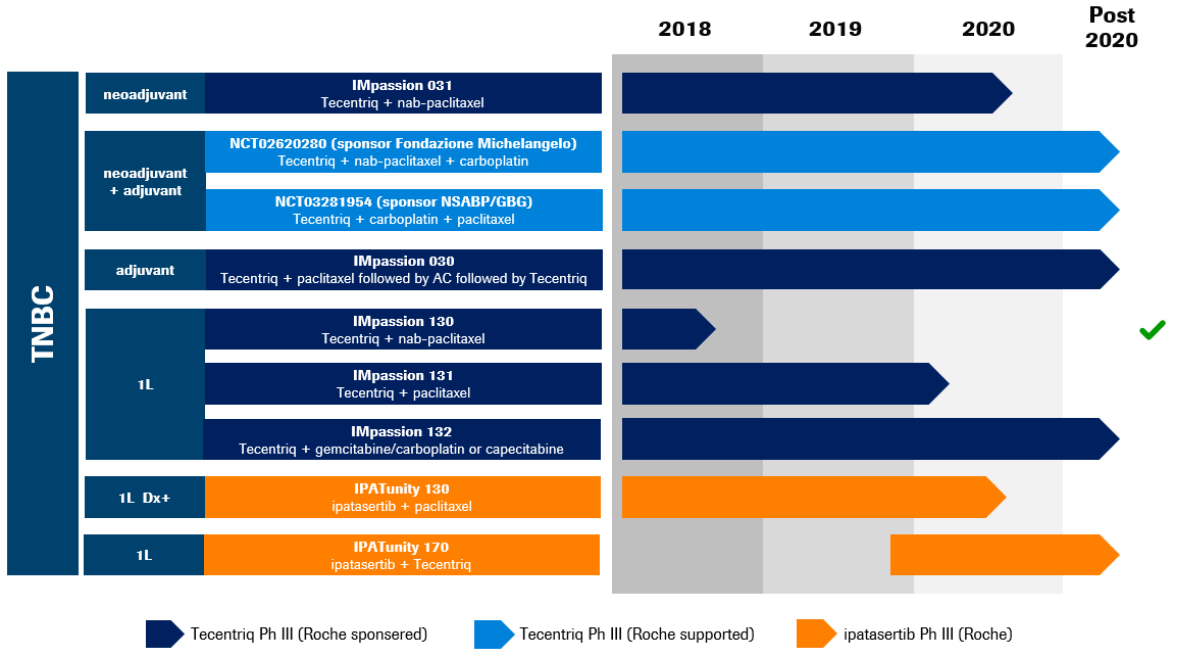
TNBC franchise: Tecentriq + nab-pac new SOC in 1L

Additional near-term read-outs in neoadjuvant and 1L

Tecentriq+nab-pac: Ph III (IMpassion130)



TNBC program covering all lines of treatment*



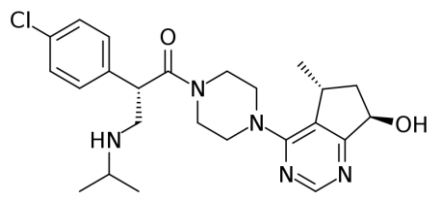
- 1L PDL1+TNBC: Tecentriq+nab-pac new SOC; PFS showed a HR=0.62 with mPFS improving from 5.0m to 7.5m
- Ph III (IMpassion131): Results for Tecentriq+paclitaxel in 1L expected early 2020
- Ph III (IMpassion031): Results for Tecentriq+nab-pac in neoadjuvant expected in 2020

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

Ipatasertib in TNBC and HR+ mBC

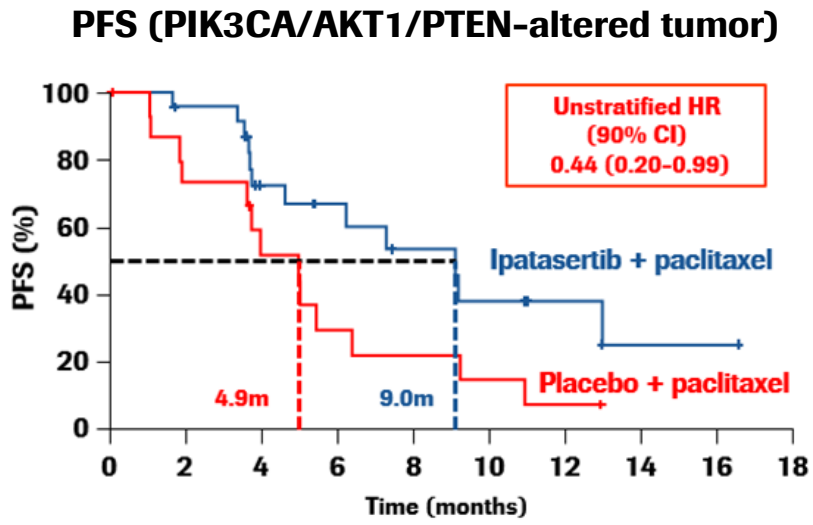
Strong PFS and OS benefit in 1L TNBC; New Ph III trials initiated

Highly selective AKT inhibitor



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

Phase II (LOTUS):



FMI NGS assay:

FOUNDATIONONE CDx™

- ***detects all classes of genetic alterations in 324 oncogenes + CIT biomarkers MSI and TMB***
- ***18 therapies currently approved for inclusion in the report***

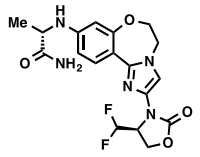
- PFS HR was 0.44 for Dx+ patients vs 0.6 for all-comers; OS trend with HR of 0.62 (all-comers)
- Positive Ph I data in 1L TNBC for ipatasertib+Tecentriq+chemo: 73% ORR in all-comers
- Ph III (IPATunity150) ipatasertib+fulvestrant+palbociclib in 1L HR+ mBC and Ph III (IPATunity170) ipatasertib+Tecentriq+chemo in 1L TNBC initiated
- Ph III (IPATunity130) results in Dx+ 1L TNBC and in Dx+ HR+/HER2- mBC expected in 2020

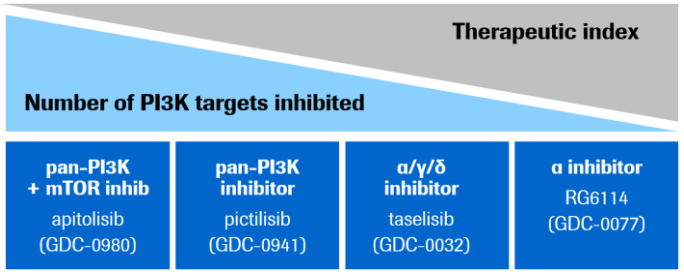
Dent R. *et al*., ASCO 2018; Schmidt P. et al, ACCR 2019; TNBC=triple negative breast cancer; HR=hormone receptor; BC=breast cancer; PFS=progression free survival; OS=overall survival; HR=hazard ratio; Ipatasertib in collaboration with Array BioPharma.

RG6114 in *PIK3CA*-mutant HR+/HER2- mBC

Potentially best in class PI3Kα inhibitor to go straight into Ph III

Highly selective PI3Kα inhibitor

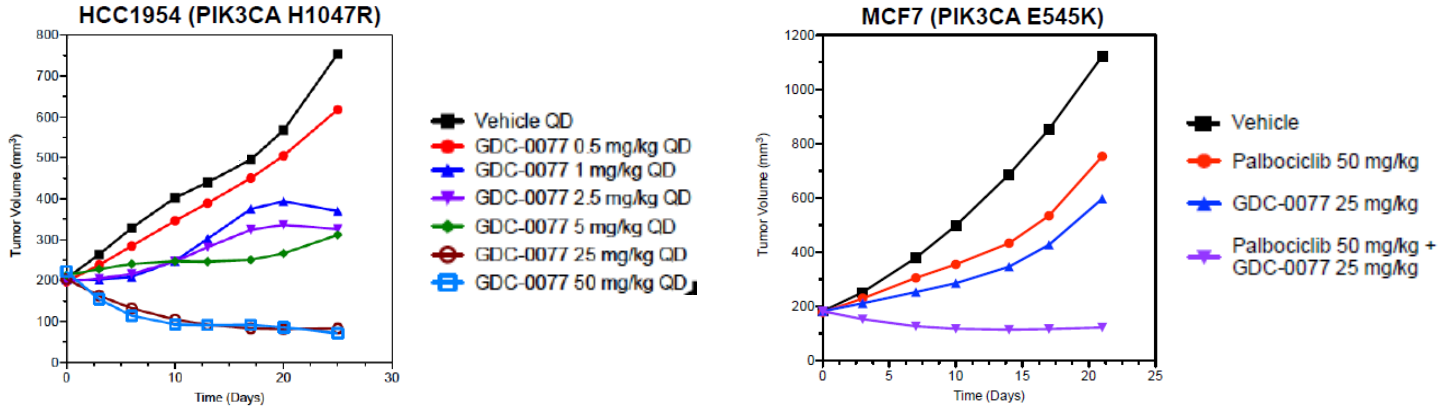




- Differentiation to previous PI3K inhibitors:
  - More selective for PI3Kα
  - Greater safety margins
  - Better in vivo efficacy
- Degrades mutant PI3Kα
- Greater, more durable target inhibition
- Combinations with standard therapies

Tumor growth inhibition as single agent or in combination

***PIK3CA*-mutant breast cancer xenograft mouse models**



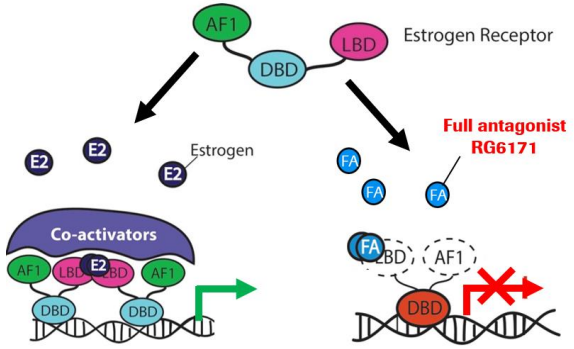
- On-going Ph I/Ib to evaluate RG6114 as single agent in patients with locally advanced or metastatic *PIK3CA*-mutant solid tumors and in combination with endocrine and targeted therapies in locally advanced or metastatic *PIK3CA*-mutant HR+/HER2- breast cancer
- First Ph I/Ib data to be presented at upcoming conference
- Ph III study in 1L *PIK3CA*-mutant HR+/HER2- mBC to start in 2019

Edgar K. *et al.*, AACR 2017; HR=hormone receptor; BC=breast cancer

RG6171 in HR+/HER2- mBC

Potentially best in class SERD to go straight into Ph III

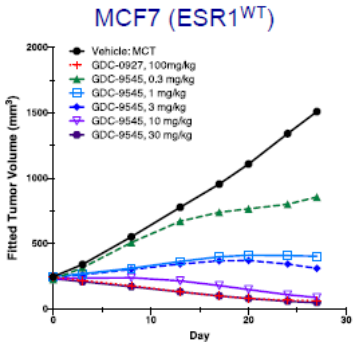
Selective ER degrader (SERD)

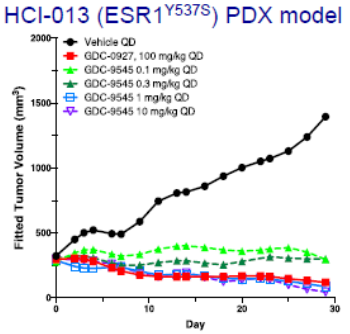


- 3rd generation molecule
- Highly potent in vitro and improved efficacy in vivo versus other SERDs
- Superior drug metabolism and PK results in efficacy at low doses in vivo
- High potency + minimal safety findings lead to wide nonclinical safety margins

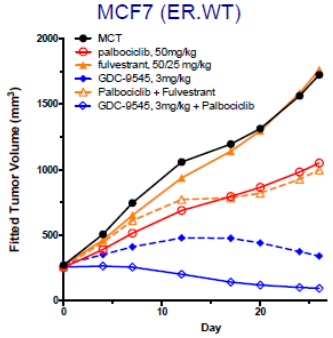
Tumor growth inhibition as single agent or in combination

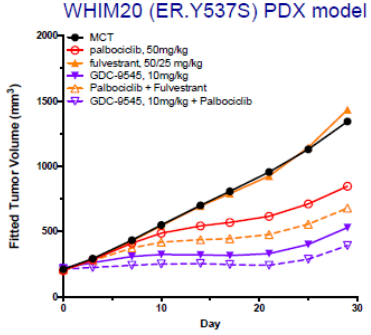
Tumor regression in wt and mutant ER+ xenograft mouse models





Increased tumor growth inhibition in combination with CDK4/6 inhibitors





- RG6171 causes ER degradation, tumor growth inhibition and enhances the efficacy of CDK4/6 inhibitors in xenograft mouse models
- Unlike tamoxifen and some previous SERDs no estrogenic activity in rodent uteri is seen
- Ph I/Ib data (+/-palbociclib or hormonal therapy) to be presented at upcoming conference
- Ph III combination studies in HR+/HER2- mBC to be initiated

Metcalfe C. *et al*., SABCS 2018; HR=hormone receptor; BC=breast cancer; ER=estrogen receptor; PK=pharmacokinetics

Late stage pipeline update

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- NHL, DLBCL: mosunetuzumab, CD20xCD3
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- HER2+: Kadcyla, Perjeta, FDC SC, Tecentriq
- TNBC: Tecentriq, ipatasertib
- HR+: ipatasertib; PI3Kα inhibitor; SERD

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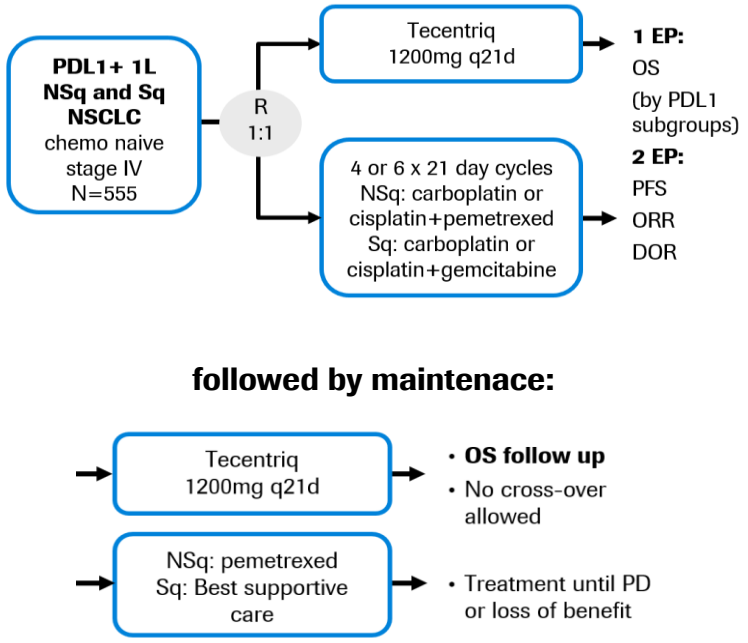
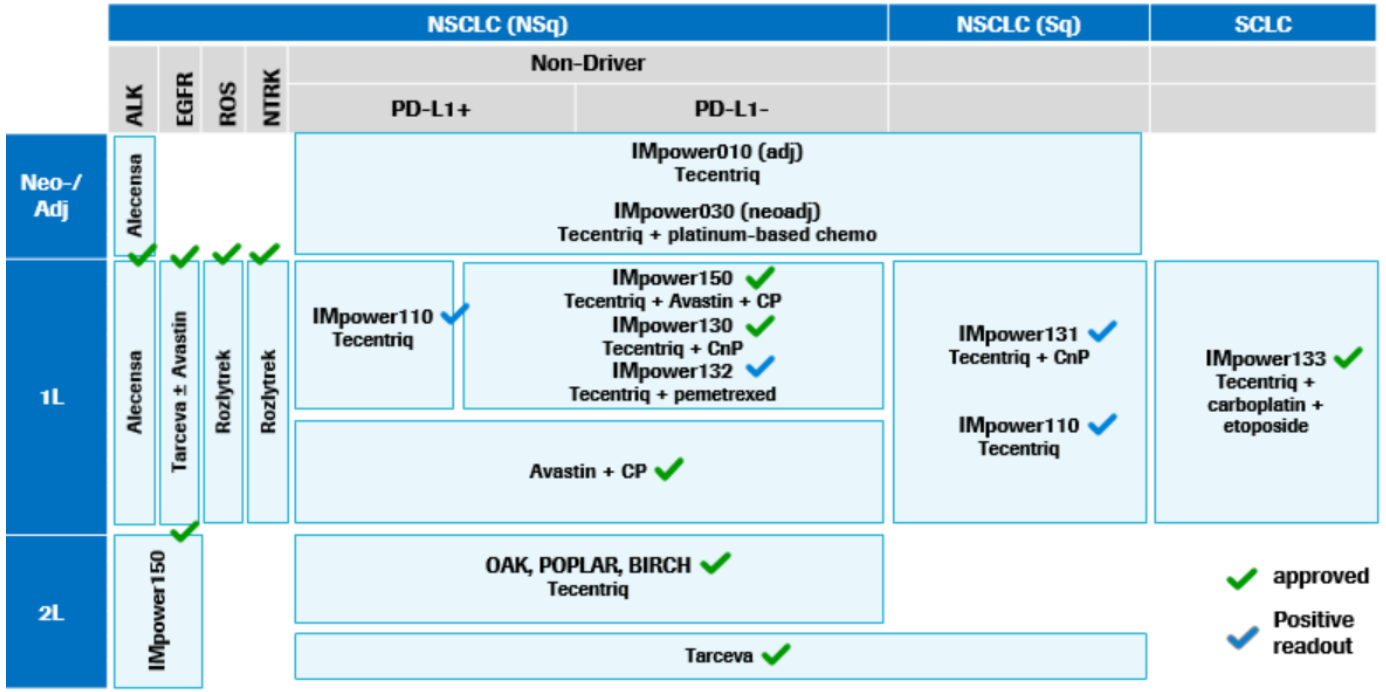
NSCLC franchise: Tecentriq in 1L PDL1+ NSCLC

Positive results for Tecentriq monotherapy

Ph III (IMpower110) trial design



NSCLC portfolio covering all segments



- Positive Ph III (IMpower110) results for Tecentrq monotherapy in 1L PDL1+NSCLC
- Data to be presented at ESMO

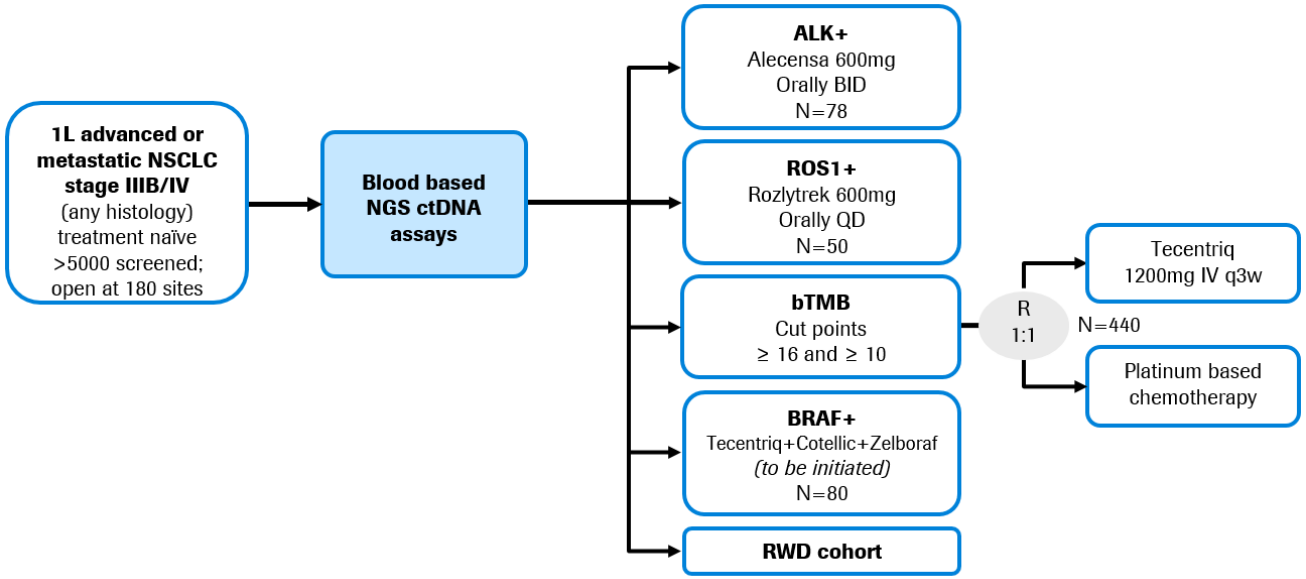
NSq=non-squamous; Sq=squamous

NSCLC franchise: 1L ALK+/ROS1+/bTMB high NSCLC

Patient selection based on blood-based NGS ctDNA assays

FDA Breakthrough device designation

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



- Potential to address diagnostic limitations as 30% of NSCLC patients have insufficient tissue for testing; Allows for serial liquid biopsy testing to follow tumor evolution and resistance
- RWD cohort paired with NGS testing provides additional natural history & epidemiological data
- First prospective blood-enrolled patient data for the ALK+ cohort to be presented at ESMO

Blood based biomarkers:

FOUNDATIONONE®LIQUID

- ***Only 17ml blood needed***
- ***A single liquid biopsy test that detects the 4 main classes of genomic alterations (70 genes)***
- ***Comprehensive genomic profile including resistance mutations or fusions in NSCLC***
- ***Includes MSI status***
- ***Guides therapy selection and clinical trials***

Mok T. et al., WCLC 2017; NGS=next generation sequencing; ctDNA=circulating tumor DNA; RWD=real world data

NSCLC franchise: Rozlytrek in ROS1+ mNSCLC

Strong responses in patients with brain metastases

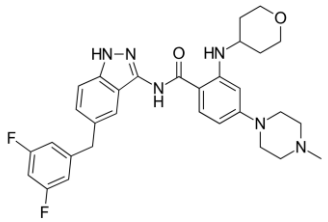
ROZLYTREK

Roche

Selective NTRK/ROS1 inhbitor

FDA BTD

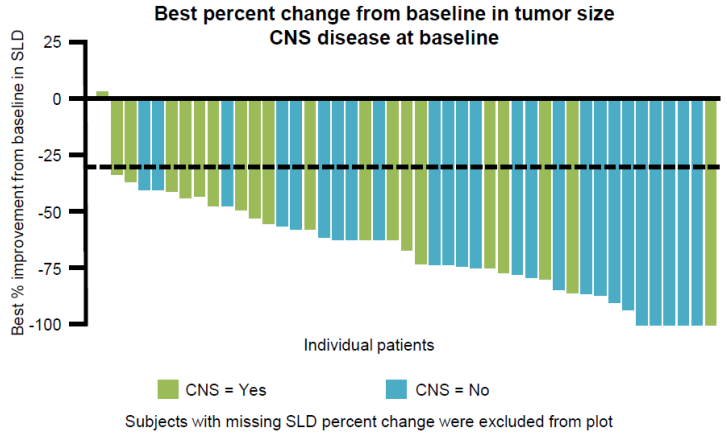
EMA PRIME



- Selective, CNS-active inhibitor of ROS1/NTRK/ALK tyrosine kinases
- Activating ROS1 rearrangements occur in 1-2% of NSCLC
- Activating rearrangements in TRK have been identified in >17 different solid tumors, including head and neck, thyroid, sarcoma and brain

Integrated Ph I/II (ALKA, STARTRK-1/2) results:

Pivotal, open-label, multicenter, global, basket study



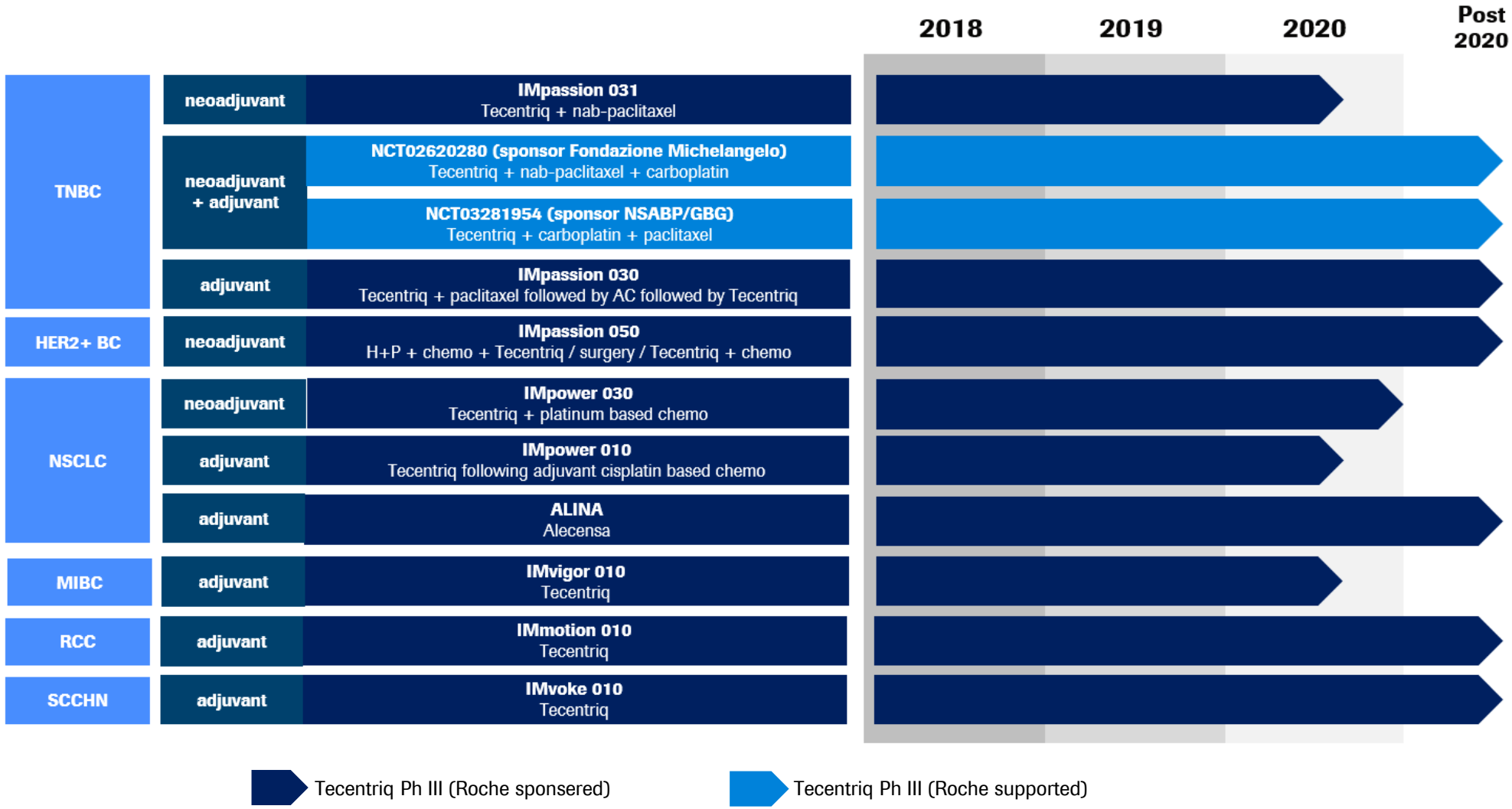
	Total n=53	CNS disease at baseline (n=23)	No CNS disease at baseline (n=30)
ORR (%) (95% CI)	**41 (77.4)** (63.8, 87.7)	**17 (73.9)** (51.6, 89.8)	**24 (80.0)** (61.4, 92.3)
Median DOR (months) (95% CI)	**24.6** (11.4, 34.8)	**12.6** (6.5, NE)	**24.6** (11.4, 34.8)
Median PFS (months) (95% CI)	**19.0** (12.2, 36.6)	**13.6** (4.5, NE)	**26.3** (15.7, 36.6)

- PhI/II results in ROS1+ mNSCLC: 77% systemic ORR with 74% ORR in patients with CNS disease at baseline
- mDOR of 24.6m and mPFS of 19.0m
- Updated Ph II (ALKA, STARTRK-1/2) data in NTRK+/ROS1+ tumors to be presented at ESMO

Doebele RC. et al., WCLC 2018; ORR=overall response rate; mDOR=median duration of response; mPFS=median progression free survival

Overview CIT adjuvant program

Lung, breast and bladder studies starting to read out in 2020



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- HR+: ipatasertib; PI3Kα inhibitor; SERD

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- Ulcerative colitis: etrolizumab
- Crohn's disease: etrolizumab
- Food allergy: Xolair
- Nasal polyps: Xolair

8. Infectious diseases
- Influenza A/B: baloxavir marboxil

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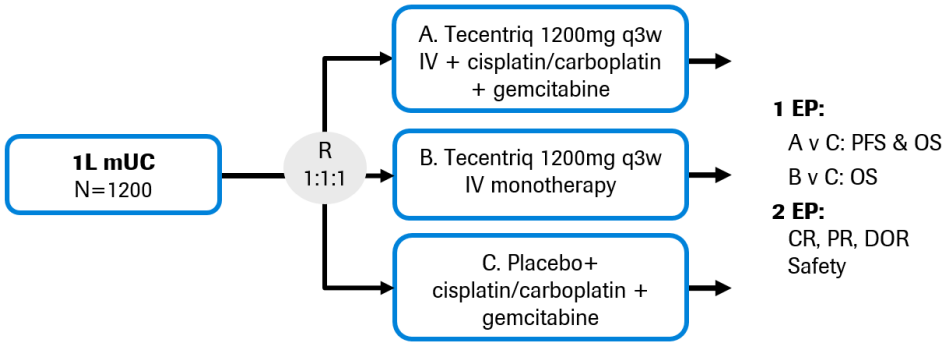
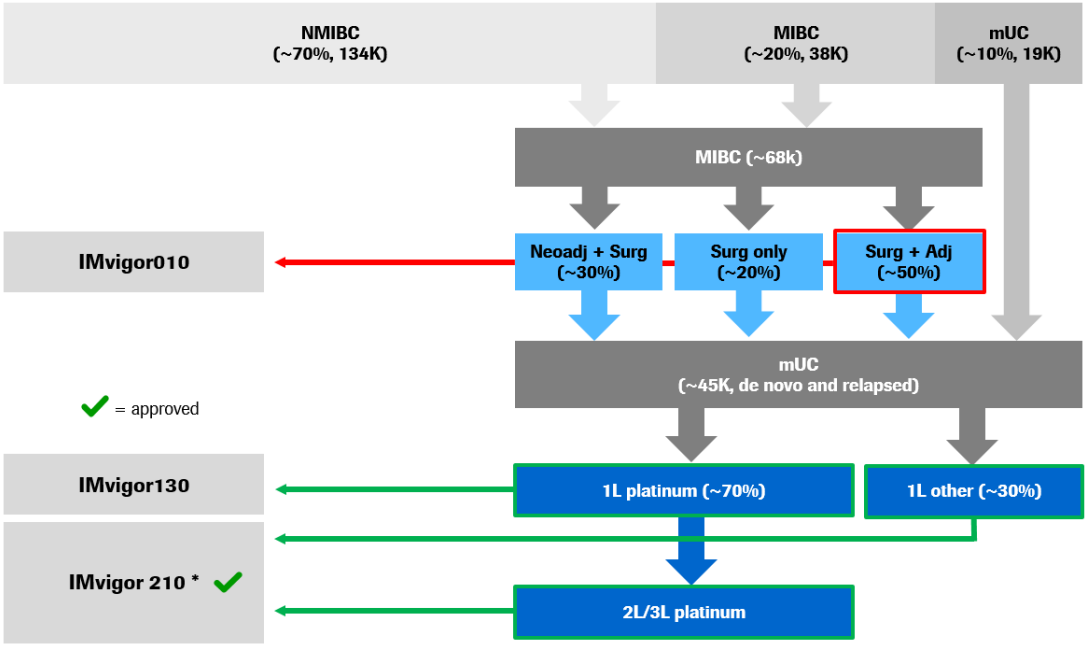
GU franchise: Tecentriq in bladder cancer

Positive results for Tecentriq + chemo in 1L; Adjuvant data in 2020

Ph III (IMvigor130) trial design



Standard of care evolution in the US



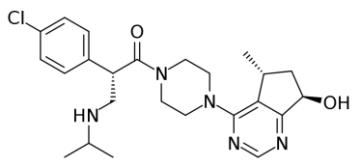
- Positive Ph III (IMvigor130) results for Tecentriq+gemcitabine/carboplatin+cisplatin in 1L mUC to be presented at ESMO
- Phase III (IMvigor010) results for Tecentriq monotherapy in the adjuvant setting expected in 2020

MIBC=muscle invasive bladder cancer; mUC=metastatic urothelial cancer; Patient numbers (US+EU-5): Roche internal estimates; *Current 1L approval is for cis-ineligible PD-L1+ (EU/US) and platinum-ineligible (US)

GU franchise: Ipatasertib in 1L mCRPC

Strong rPFS and OS benefit

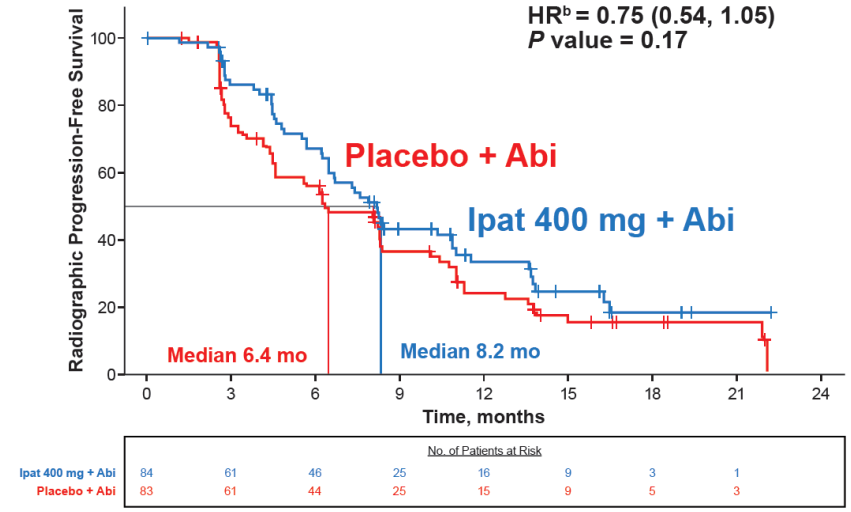
Highly selective AKT inhibitor



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

Phase II (A.MARTIN):

rPFS (400mg dose)



Assays:

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)***

- 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 (which leads to elevated PI3K/Akt pathway activation) was associated with an improved rPFS outcome as measured by NGS, FISH and IHC
- Ph III (IPATential150) results expected in 2020

De Bono J.S. et al., ASCO 2016; 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

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2. **Breast Cancer franchise** (2)
   - HER2+: Kadcyla, Perjeta, FDC SC, Tecentriq
   - TNBC: Tecentriq, ipatasertib
   - HR+: ipatasertib; PI3Kα inhibitor; SERD

3. **Lung Cancer franchise** (3)
   - NSCLC: Tecentriq
   - ALK+: Alecensa
   - ROS1+/NTRK+: Rozlytrek

4. **GU franchise** (4)
   - mUC: Tecentriq
   - CRPC: ipatasertib

5. **Pan tumor** (5)
   - NTRK+ tumors: Rozlytrek

6. **Other oncology** (6, 7, 8)
   - Melanoma: Tecentriq, Cotellic, Zelboraf
   - OC: Tecentriq, Avastin
   - HCC: Tecentriq, Avastin

6. **Hemophilia A**
   - Hemlibra

7. **Neuroscience** (9, 10, 11, 12, 13, 14)
   - MS: Ocrevus update
   - SMA: risdiplam
   - NMOSD: satralizumab
   - Huntington's disease: HTT-ASO
   - Autism: balovaptan
   - Parkinson`s disease: prasinezumab

9. **Immunology** (15, 16, 17, 18)
   - Lupus nephritis: Gazyva
   - Ulcerative colitis: etrolizumab
   - Crohn`s disease: etrolizumab
   - Food allergy: Xolair
   - Nasal polyps: Xolair

8. **Infectious diseases** (19)
   - Influenza A/B: baloxavir marboxil

6. **Ophthalmology** (20, 21, 22, 23)
   - DME, nAMD: faricimab
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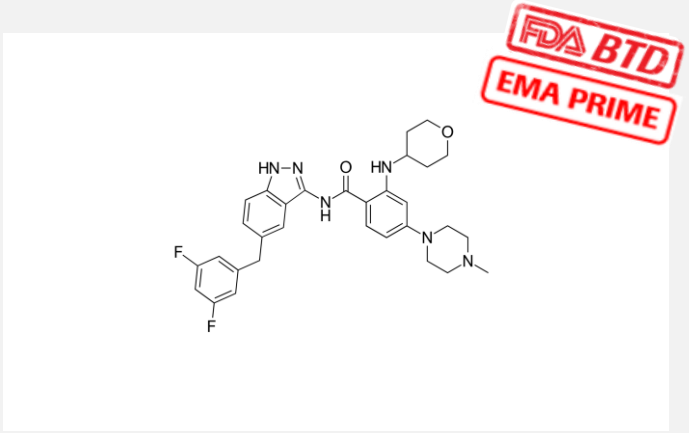
Pan tumor franchise

First pan tumor approval for NTRK+ solid tumors with CNS disease

Selective NTRK/ROS1 inhbitor



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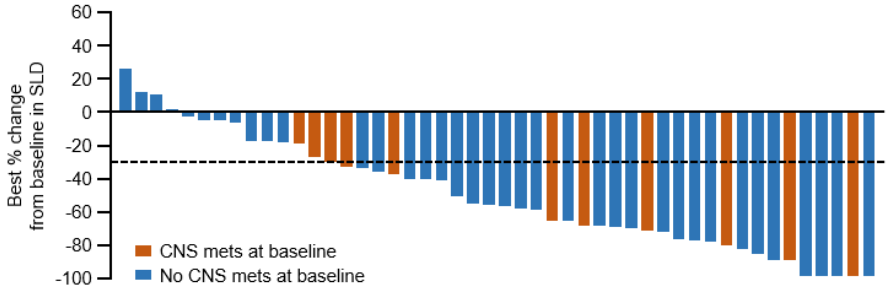
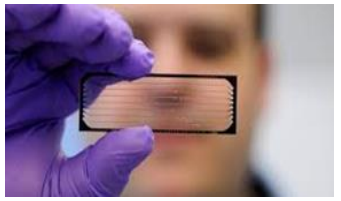
Phase II (ALKA; STARTRK-1/2):

Change in tumor size (NTRK+ solid tumors)



FMI NGS assay:

FOUNDATIONONE CDx™



- ***detects all classes of genetic alterations in 324 oncogenes + CIT biomarkers MSI and TMB***
- ***18 therapies currently approved for inclusion in the report***

- ORR of 57% in NTRK+ solid tumors observed across 10 tumor types; ORR was similar in patients with and without baseline CNS disease
- Rozlytrek has systemic and intracranial efficacy and is a potential treatment option for patients with NTRK+ solid tumors with primary and metastatic CNS disease (high unmet need)

Siena S. et al., XXX; HR=hazard ratio; mOS=median overall survival; mPFS=median progression free survival

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   - Influenza A/B: baloxavir marboxil

6. **Ophthalmology**
   - DME, nAMD: faricimab
   - AMD: Port Delivery System
   - GA: ASO factor B
   - Choroideremia: Gene therapy

Oncology / Hematology
Neuroscience
Ophthalmology
Infectious diseases
Immunology

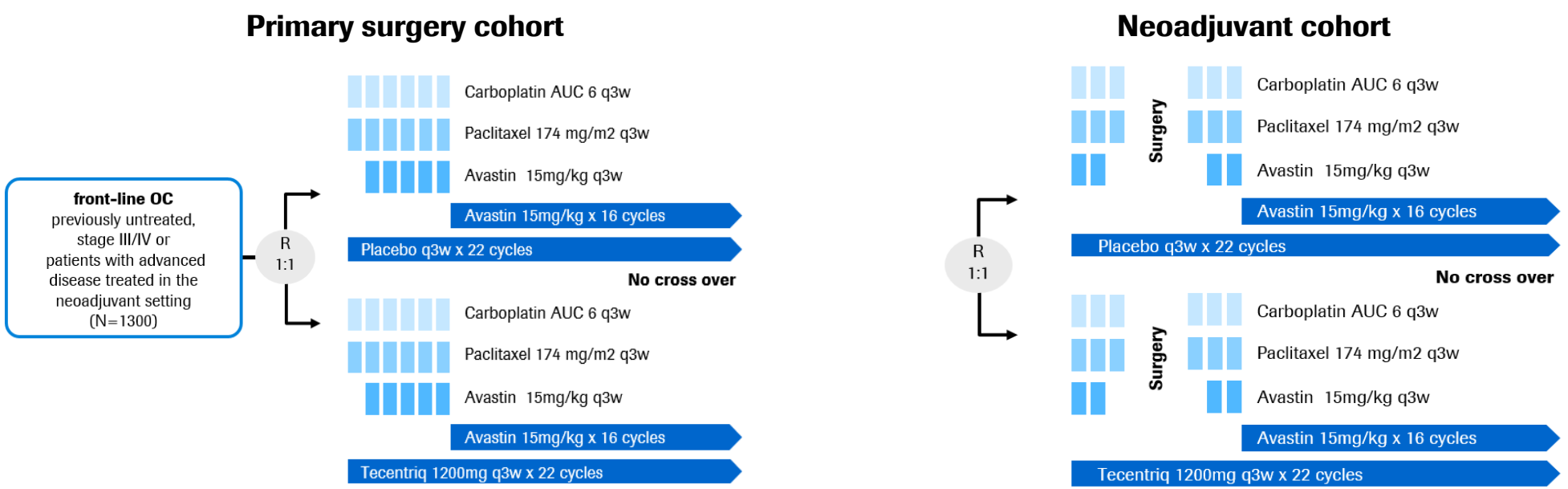
1 Topics main presentations
1 Topics break-out sessions

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 18 results presentation appendix or visit the IR homepage

Ovarian cancer: Tecentriq + Avastin in front line OC

Ph III first in class results expected in 2020

Ph III (IMaGYN050) trial design:



- Ph III (PAOLA-1) results for olaparib + Avastin in 1L OC to be presented at ESMO
- Ph III (IMaGYN050) results for all comers and PDL1+ patients expected in 2020

Kathleen N Moore, and Sandro Pignata Int J Gynecol Cancer 2019;29:430-433

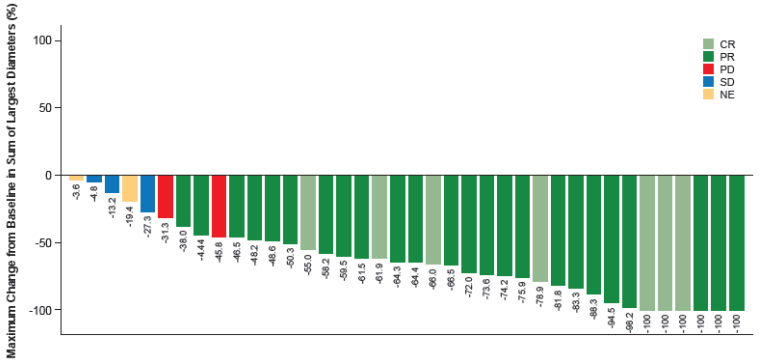
Melanoma: Tecentriq + Zelboraf + Cotellic in 1L BRAF+ mM

ORR of 82% and good durability; Ph III results expected in 2019

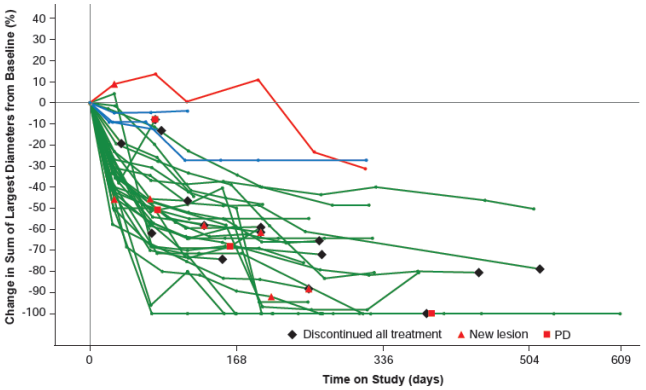
Ph I (NCT01656642) results:

Best objective response, RECIST v1.1	T + Z + C (N=38), n (%)
ORR	**31 (82%)**
CR	7 (18%)
PR	24 (63%)
SD	3 (8%)
PD	2 (5%)
Non-evaluable	2 (7%)

Reduction in tumor burden by best overall response (unconfirmed)



Change in tumor burden over time by unconfirmed best response



- Triplet has a manageable safety profile
- Estimated median duration of response 10.6m and mPFS 12.9m (data immature)
- Triplet may differentiate on durability
- Ph III (IMspire150/TRILOGY) results expected in 2019

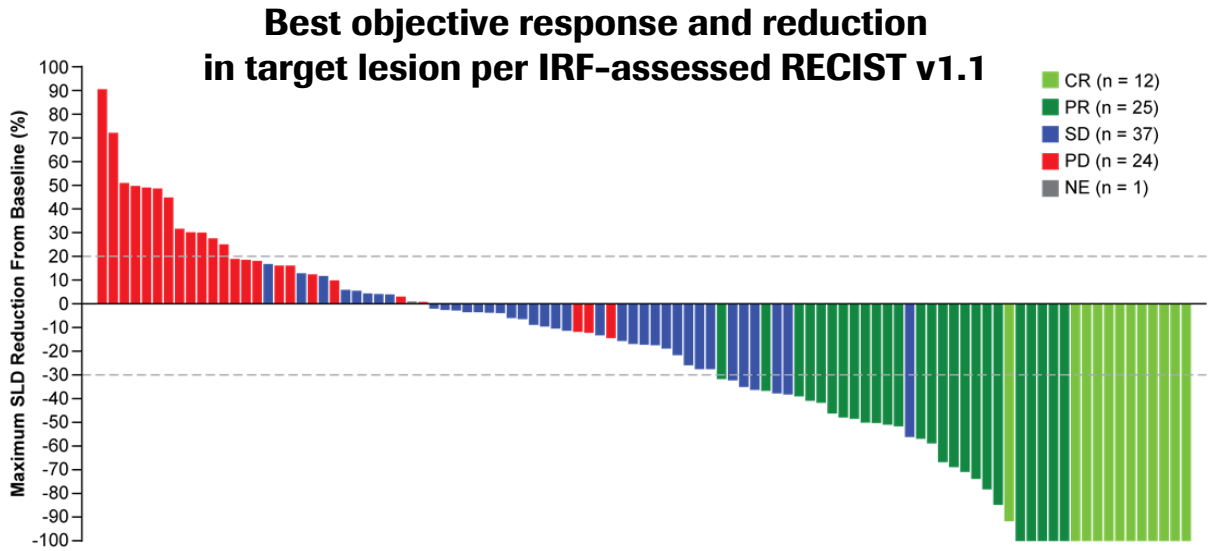
Sullivan R. *et al,* ASCO 2017; mM=metastatic melanoma; ORR=overall response rate; CR=complete response; PR=partial response; SD=stable disease; PD=progressive disease; Cotellic in collaboration with Exelixis; Zelboraf in collaboration with Plexxikon

Liver cancer: Tecentriq + Avastin in 1L HCC

Strong ORR, long durability and high number of CRs observed

Ph Ib (NCT02715531) results Arm A (Tecentriq+Avastin):

	Arm A: Tecentriq + Avastin N = 104		
	IRF RECIST 1.1	IRF HCC mRECIST	INV RECIST 1.1
Confirmed ORR, n (%) (95% CI), %	**37 (36) (26 – 46)**	**41 (39) (30 – 50)**	**34 (33) (24 – 43)**
CR, n (%)	12 (12)	16 (15)	3 (3)
PR , n (%)	25 (24)	25 (24)	31 (30)
DCR, n (%)	74 (71)	74 (71)	78 (75)
On-going response, n (%)	28 (76)	28 (68)	24 (71)
Median DOR (mo) (95% CI)	**NE (11.8 – NE)**	**NE (11.8 – NE)**	**NE (11.7– NE)**
DOR range (mo)	1.6+ – 31.0+	1.6+ – 31.0+	3.5+ – 31.0+
≥ 9 mo, n (%)	20 (54)	25 (61)	21 (62)
≥ 12 mo, n (%)	11 (30)	11 (27)	12 (35)

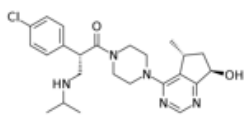
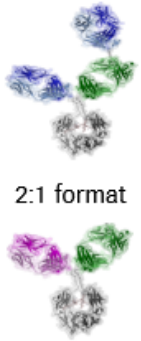
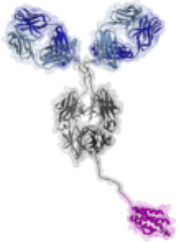
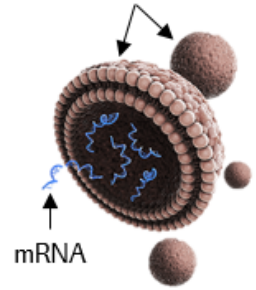
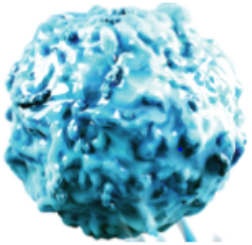


- Confirmed ORR is 36% per IRF-assessed RECIST 1.1 with 12% achieving a complete response; mDOR has not been reached with 76% of responses ongoing per IRF-assessed RECIST 1.1
- Ph I update Arm F (Tecentriq+Avastin vs Tecentriq) to be presented as late breaker at ESMO
- Ph III (IMbrave150) results (Tecentriq+Avastin vs sorafenib) expected in Q4 2019

Lee M.S. et al. APPLE 2019 (Data cutoff: 14 June 2019; median follow-up: 12.4 months); ORR=objective response rate; DOR=duration of response; CR=complete response; PR=partial response; PD=progressive disease; SD=stable disease; DCR=CR+PR+SD; SLD=sum of largest diameters. NE=not evaluable or missing; INV=investigator; IRF=independent review facility

Our technology platforms in cancer

Roche pipeline includes differentiated therapeutic platforms

Small molecules	Bi-specifics	Fusion protein	mAb	ADC	Personalized mRNA vaccine	Personalized T cells
						
• **ipatasertib** • **idasanutlin** • **PI3Kα inhibitor** • **SERD**	• **mosunetuzumab** • **CD20 x CD3** • **CEA x CD3** • **Her2 x CD3** • **glypican-3 x CD3**	• **FAP x IL2v**	• **aTIGIT (tiragolumab)**	• **Polivy** • **Kadcyla**	• **iNeST**	• **programmed T cells**
Target oncogenes, induce apoptosis, supress tumor growth, etc.	*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*

ADC=antibody–drug conjugate; iNeST=Individualized Neoantigen-Specific Therapy

CIT evolution

Investing in new technologies

Cure Rate

Time

First wave 1

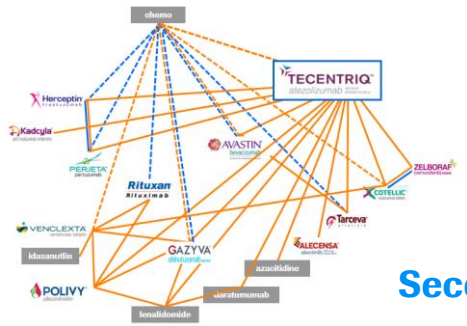
Checkpoint inhibitors monotherapy & PD-L1 IHC ✓

- *Tecentriq (2016)* ✓

Second wave 2

Combine with existing medicines & TMB, MSI, blood based NGS, pan tumor ✓

- *Tecentriq + chemo* ✓
- *Tecentriq + Avastin, Cotellic, Zelboraf, Tarceva, Alecensa, Gazyva, Herceptin, Perjeta, Kadcyla* ✓



Third wave 3

Expand to novel CITs including novel Ab formats & advanced diagnostics

- *Immune doublets: Tecentriq + CIT 1, CIT 2…*
- *Immune doublets: CIT 1 + CIT 2*
- *e.g. CD20 x CD3; aFAP-IL2v FP; aTIGIT etc.*

Fourth wave 4

Truly personalized CIT & neoantigen sequencing, RNAseq

- *Combos/NMEs/"programmed" immune cells targeted at individual immune profiles e.g. iNEST; Adaptive Biotechnologies etc.*

✓ = approved

Upcoming conferences in 2019*

Hematology franchise:

- **mosunetuzumab:** Ph I (*GO29781*) safety/efficacy update in R/R NHL
- **CD20 x CD3:** Ph I results for various combinations
- **Polivy + Gazyva + lenalidomide:** Ph I (*GO29834; inHarmony)* in R/R FL

Lung franchise:

- **Tecentriq:** Ph III (*IMpower110*): 1L PDL1+ non-sq and sq NSCLC

Breast franchise:

- **Perjeta + Herceptin:** Ph III *(APHINITY)* 2nd OS 5-year update in eBC

Tumor agnostic franchise:

- **Rozlytrek:** Ph I/Ib efficacy update in NTRK1/2/3+ tumors and ROS1+ NSCLC

GU/GI franchise:

- **Tecentriq + chemo:** Ph III (*IMvigor130*) in 1L mUC
- **Tecentriq + Avastin:** Ph III (*IMbrave150*) in 1L HCC
- **Tecentriq + Avastin:** Ph I (GO30140) Arm F update in 1L HCC

Immunology franchise:

- **Gazyva + SOC:** Ph II (*NOBILITY*) in lupus nephritis

* Planned submissions (to be confirmed); Outcome studies are event driven, timelines may change

Doing now what patients need next