BerGenBio ASA (OSE: BGBIO)

H.C. Wainwright Global Life Sciences Conference

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Richard Godfrey, CEO

BerGenBio

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BGBIO – Investment Highlights

World leaders in understanding AXL biology

AXL is a novel oncology target to overcome immune evasion, therapy resistance & spread

AXL upregulates PDL1 on dendritic cells and blocks T-cell immunity

AXL inhibitors – potential cornerstone of cancer therapy

Pipeline opportunities in multiple cancers and fibrosis

3 selective AXL inhibitors in clinical development

Bemcentinib (Ph2), AXL-antibody BGB149 (Ph1), AXL ADCT601* (Ph1)

Monotherapy and combinations with immune-, targeted and chemotherapies

Biomarker correlation across programme, parallel CDx development

Phase II Proof of Concept

43% ORR in R/R AML/MDS (monotherapy)

40% ORR in 2L NSCLC (KEYTRUDA combo)

Resourced to deliver significant milestones

Clinical trial collaborations with Merck and leading academic centres

*AXL antibody out licensed to ADC Therapeutics SA

38 staff at two locations:
HQ & R&D in Bergen, Norway;
Clinical Development in Oxford, UK

Cash NOK 360m/USD 41m

Increasing profile and recognition of bemcentinib at international clinical congresses in 2018

January	February	March	April	May	June	July	August	September	October	November	December

ASCO-SITC
Lung cancer, TNBC and AML trial update

- ✓ KEYTRUDA combo well tolerated
- ✓ Bemcentinib induces diversification of T-cell receptor repertoire (AML)

AACR
Preclinical Update

Bemcentinib increases efficacy of checkpoint inhibitors

ASCO
NSCLC, AML, Melanoma and biomarker update

Bemcentinib enhances responses to
- ✓ IO,
- ✓ chemo,
- ✓ targeted therapies
- ✓ and has monotherapy efficacy

EHA
AML trial update

Responses to bemcentinib monotherapy correlated with AXL biomarker

WCLC
Lung cancer trials update

- ✓ 40% ORR in AXL+ pts in combo w/ KEYTRUDA
- ✓ Improved PFS in combo with erlotinib and chemo

ESMO
Biomarker update

- ✓ AXL biomarkers identified
- ✓ Melanoma clinical update
- ✓ AXL's role in low-risk MDS (pre-clinical)

SITC
NSCLC data late breaking

Late-breaking abstract: 5.9m PFS in AXL+ previously treated NSCL in combo w/ KEYTRUDA (c80% improvement in AXL+ pts vs AXL-)

ASH
AML trial data update

43% CR/Cri/CRp rate in AXL biomarker positive pts

Key data presented in Q4 supports future strategy for late-stage clinical development of bemcentinib in AML/MDS and NSCLC

ASCO-SITC: Clinical Immuno-Oncology symposium, San Francisco
ASCO: American Society of Clinical Oncology, Chicago
WCLC: World Conference of Lung Cancer, Toronto
ESMO: European Society of Medical Oncology, Munich
AACR: American Association for Cancer Research, Chicago
EHA: European Hematology Association, Stockholm
SITC: Society for Immunotherapy of Cancer, DC
ASH: American Society for Hematology, San Diego

Two significant late stage development opportunities

2L AML
monotherapy

NSCLC
Combo with **Checkpoint inhibitor**

Defined patient population, potential first & accelerated path to registration

Potential to significantly increase addressable patient population

Bemcentinib

First-in-class oral, selective AXL inhibitor

2019
launch trial

2020
interim

2022
registration

CPI effective

CPI not effective

PDL1 high

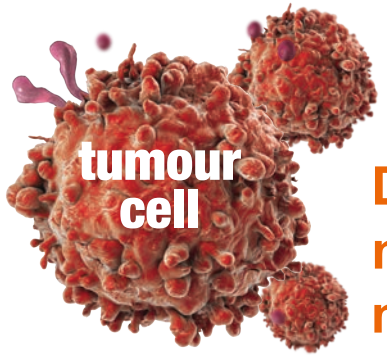
PDL1 neg/low

Effective and well tolerated monotherapy treatment option for frail patient population

Effective and well tolerated combination for 1L or 2L NSCLC patients

AXL drives aggressive cancer

AXL receptor tyrosine kinase drives aggressive disease including therapy resistant, immune-evasive tumours

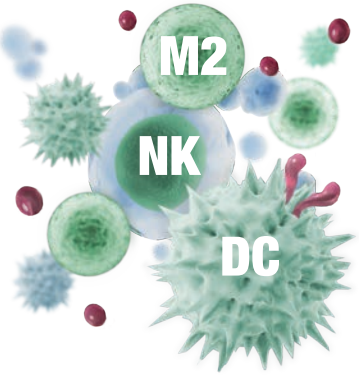


Drives tumour cell plasticity: non-genetic resistance mechanism

AXL drives features of aggressive cancer:

- Acquired therapy resistance
- Immune escape
- Metastasis

Key suppressor of innate immune response



AXL is an innate immune checkpoint:

- M1 to M2 macrophage polarisation
- Decreased antigen presentation by DCs
- Immunosuppressive cytokine profile

very **low** expression under healthy **physiological conditions** (ko mouse phenotypically normal)

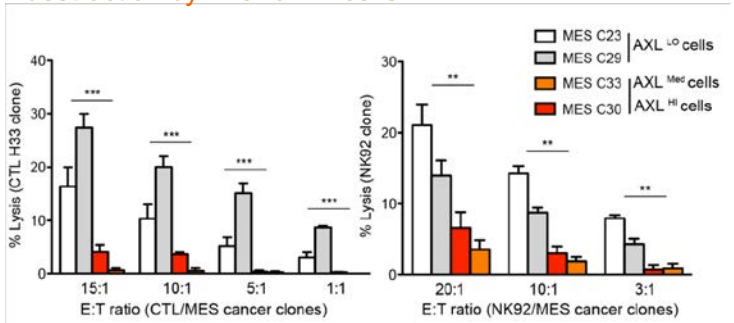
overexpressed in response to **hypoxia, immune reaction, cellular stress** / therapy

overexpression correlates with **worse prognosis in most cancers**

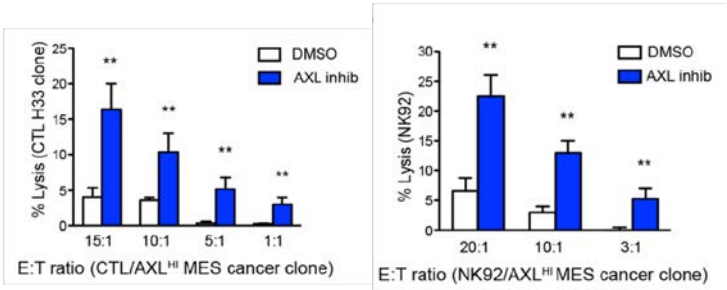
Preclinical data at AACR reinforces bemcentinib's potential to reverse tumour immunosuppression and therapy resistance

Chouaib *et al*

NSCLC cells high in AXL are less susceptible to destruction by T- and NK cells



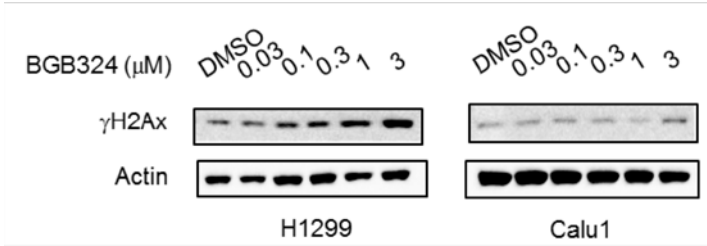
Bemcentinib treatment of the tumour cells with high AXL expression reverses this effect



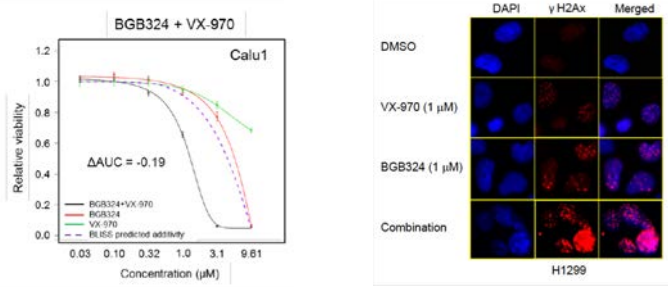
Pre-clinical data supporting the rationale of combining bemcentinib with IO / bemcentinib's IO MoA

Ramkumar, Byers *et al*

Bemcentinib dose-dependently induces DNA damage in NSCLC cells (γH2Ax is a marker of DNA damage



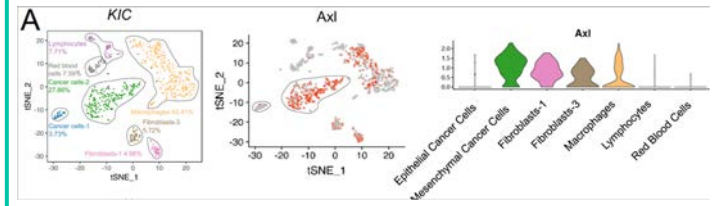
Bemcentinib has synergistic effect when given in combination with DNA damage targeting agents (VX-970)



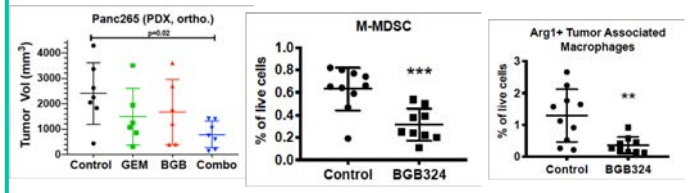
Supports the rationale of combining bemcentinib with chemo and DNA damaging agents

Du, Brekken *et al*

AXL highly expressed in pacreatic tumour models, particularly in cancer cells, fibroblasts & macrophages



Bemcentinib has synergistic effect when given in combination with chemo, reverses immunosuppression



Supports the rationale of combining bemcentinib with chemotherapy & bemcentinib's IO MoA

BerGenBio provided drug and in some instances part funding for the work

Two AXL-targeting drug candidates in clinical development

Block AXL signalling, reverse aggressive tumour traits & counteract immune escape

Bemcentinib – Phase 2, late stage in H2 ‘19

- Oral small molecule TKI, highly selective for AXL
- Clinical PoC in NSCLC & AML, broad ILS support
- Excellent safety and biomarker correlation reported

NSCLC:

40% ORR | **6m PFS**

in AXL+ve, predominantly PDL1 -ve/low
2L NSCLC in combination w/ KEYTRUDA

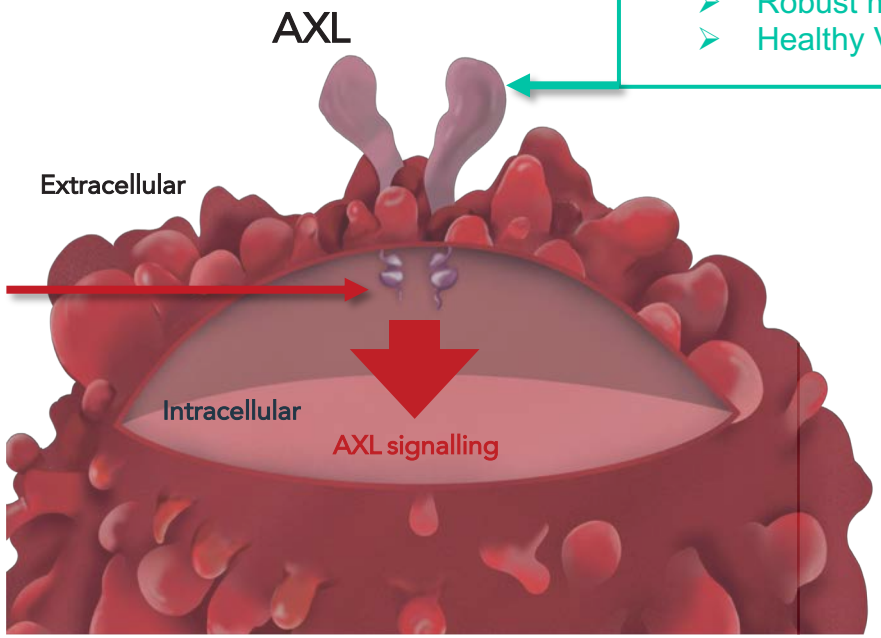
AML:

43% CR/Cri/CRp

in AXL+ve
relapsed/refractory AML/MDS as a monotherapy

BGB149 – Phase 1

- AXL function blocking antibody
- Highly selective to human AXL
- Robust manufacturing process
- Healthy Volunteer Ph1 ongoing



Bemcentinib is formerly known as BGB324

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Bemcentinib: once-a-day pill

Highly selective, orally bioavailable small molecule, administered once a day, in phase II clinical trials

Blocks AXL signalling, reverses aggressive tumour traits & counteracts immune escape

Clinical PoC in AML and NSCLC as a monotherapy and in combination

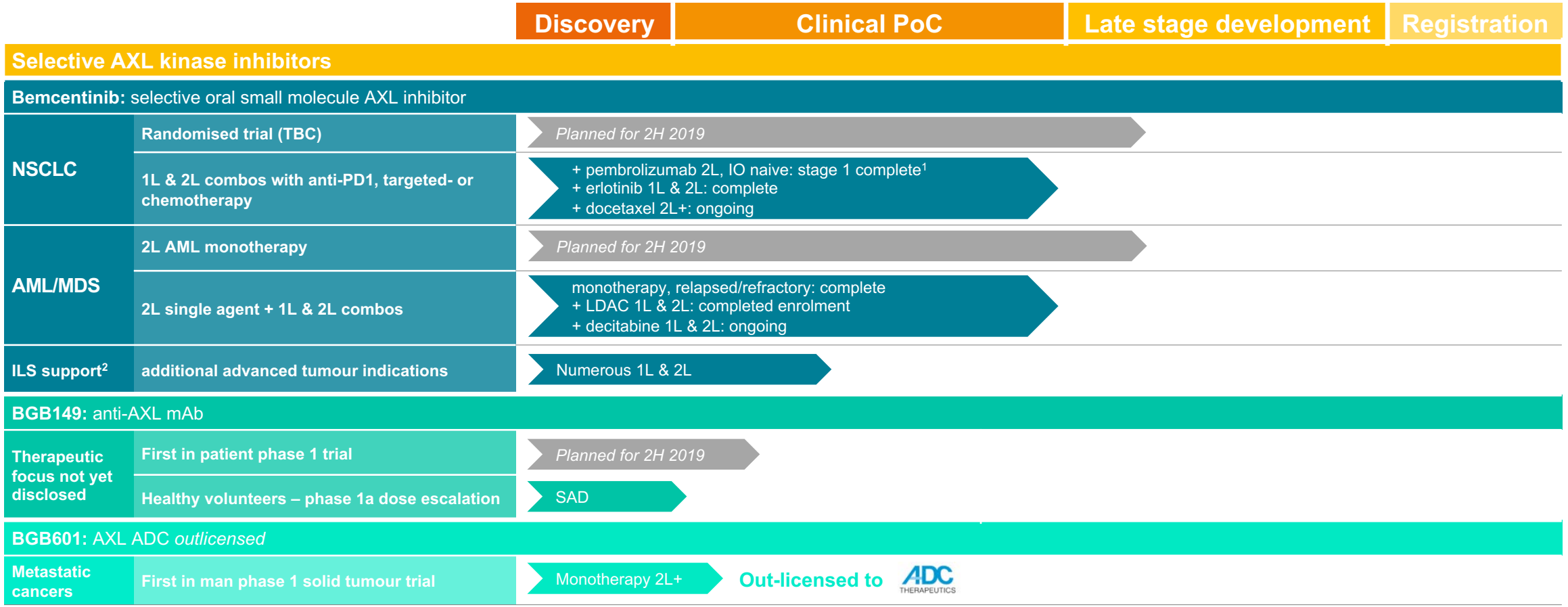
Correlation of clinical efficacy with AXL biomarkers observed

Excellent clinical safety profile: >250 subjects dosed

Randomised, late stage clinical trials planned to start in H2 2019

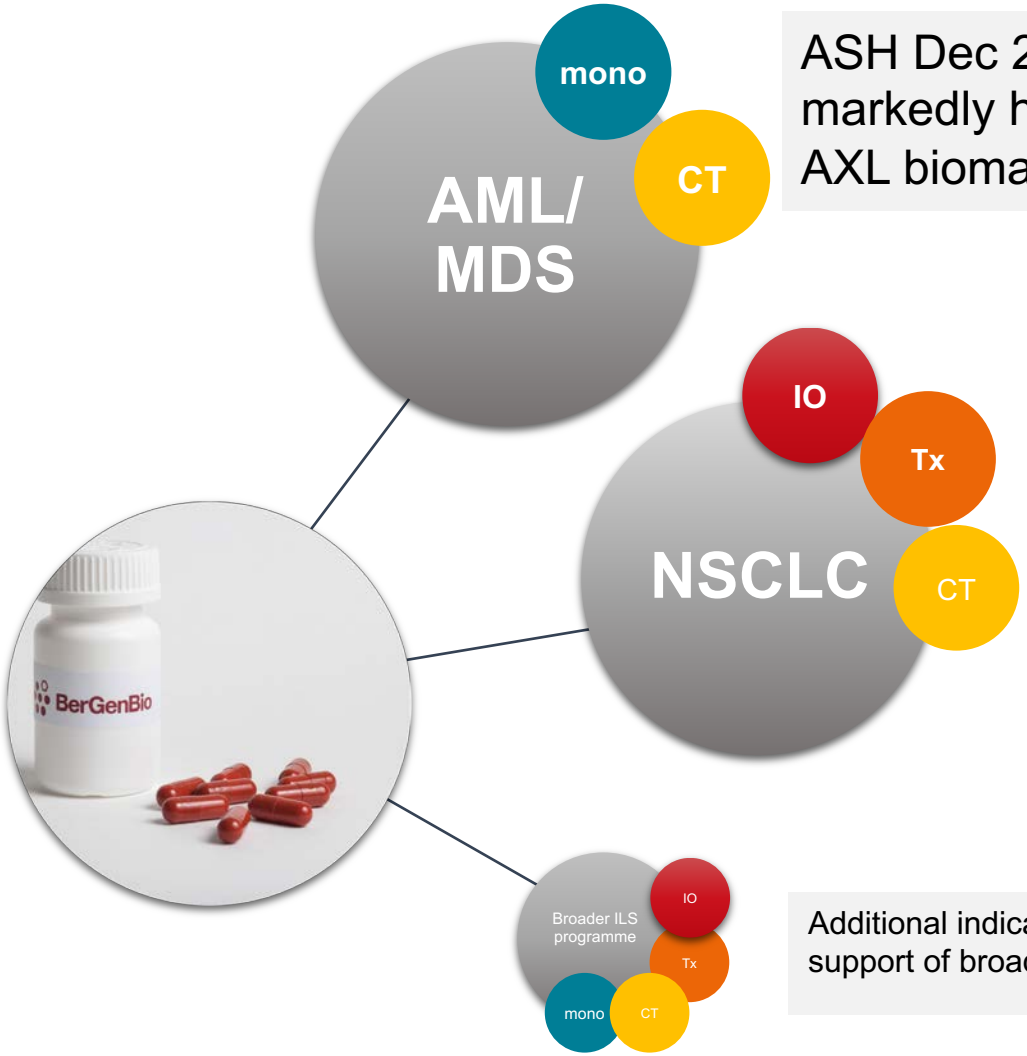
Portfolio of selective AXL inhibitors

Late stage programme in NSCLC and AML planned for H2 2019



(1): Clinical trial collaboration with Merck & Co, no preferential rights (2) Investigator initiated trial programme, BerGenBio does not act a regulatory sponsor

Clinical development focus: Leukaemia & Lung Cancer



ASH Dec 2018, **bemcentinib monotherapy in R/R AML/MDS:** markedly higher response rate in patients identified by the AXL biomarker: ORR of 43%

SITC Nov 2018, **combination with KEYTRUDA in 2L NSCLC:** Superior response rate and PFS in AXL positive patients – ORR of 40% and ca. 6 months PFS

Additional indications with strong rationale and KOL endorsement are being pursued through active support of broad ILS programme

PFS = Progression Free Survival ORR= Overall Response rate

Clinical Development opportunities for bemcentinib

	Clinical Proof-of-concept	Late stage clinical trials 2019
Monotherapy opportunities Selected, biomarker directed, indications	**AML / MDS (complete)** **Glioblastoma (ongoing, IIT)** **EMT signature selected (potential)**	→
Chemotherapy combos Improve responses in hard to treat settings	**AML / MDS + LDCT** **Pancreatic, (IIT in set-up)** **NSCLC (ongoing, IIT)**	⇢
Immunotherapy combos Target resistance, enlarge addressable pt population	**NSCLC (PD-L1 all comers)** • **IO naïve (ongoing, stage 1 complete)** **Melanoma, (ongoing, IIT)** **Mesothelioma (IIT in set-up)** **Bladder ++, CAR-T combos (under consideration)**	→
Targeted therapy combos Target resistance, enlarge addressable pt population	**NSCLC + EGFRi (complete)** **Melanoma, (ongoing, IIT)** **PARPi combos ++ (under consideration)**	⇢
Earlier line opportunities Radiotherapy and maintenance opportunities	**Multitude of maintenance opportunities given very favourable safety profile**	

Companion Diagnostics Programme

- ✓ Selects AXL positive patients
- ✓ Enriched clinical trials
- ✓ Improved chances of regulatory success
- ✓ Precision medicine approach to reimbursement

Biomarkers and Assays

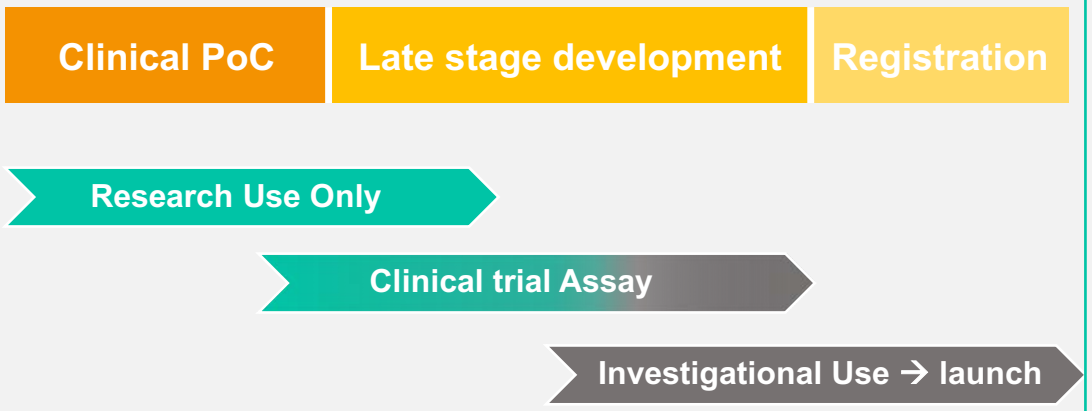
AXL IHC

✓ Improved ORR and PFS in AXL +ve NSCLC pts treated with bemcentinib + KEYTRUDA*

AXL liquid biopsy

✓ Improved response in relapsed/refractory AML/MDS with lower plasma amounts of inactive AXL (soluble AXL)

Contemporaneous regulatory approval strategy



* independent of PDL1, BGBC008 trial in 2L, IO naive NSCLC, all comers

Ref. BGBC003 / NCT02488408

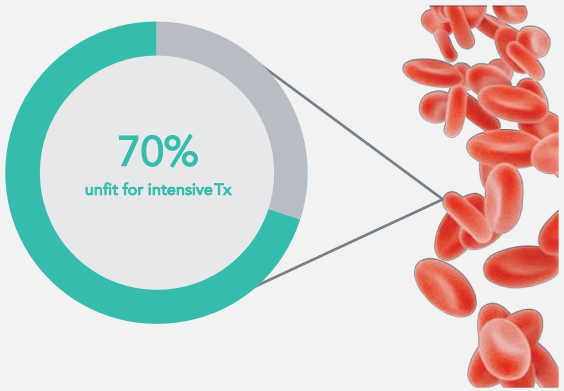
Bemcentinib in myeloid malignancies: monotherapy & combos

PoC clinical data from monotherapy, combination data in H1 2019

- ***43% ORR in AXL +ve R/R AML and MDS patients***
- ***chemo combos in 1L ongoing***

Bemcentinib: Favourable safety profile offers treatment opportunity for a large group of AML & MDS

AML evolving standard of care (SoC)



AML & MDS – difficult to treat malignancies, predominantly elderly frail patient population

~ 20,000 new cases diagnosed and >10,000 deaths (2018, U.S.)

Younger fit patients	>75 yo / unfit for intensive therapy
Induction chemotherapy +/- FLT3 inhibitor	low dose chemo / hypomethylating agents / best supportive care

New therapies needed in 1L & 2L for less fit patients w/o actionable mutations

Treatment options beyond chemotherapy still limited

Urgent need particularly in older and R/R patients

Treatment Opportunity

1L: low intensity therapy +/- venetoclax

bemcentinib combo opportunity

2L: targeted therapy* or best supportive care

IDH1/2 FLT3

bemcentinib monotherapy opportunity

* In R/R AML, targeted inhibitors are approved for patients harbouring IDH1, IDH2 or FLT3 mutations

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Ref. BGBC003 / NCT02488408

Phase II PoC in AML/high risk MDS:
Monotherapy and combination with LDCT*

Relapsed/refractory AML & high-risk MDS

up to 75 pts

Monotherapy (completed)

R/R AML & MDS
N = 36 pts

43%* CR/Cri/CRp

* Ca. half of patients found to be AXL positive

Immune activation and clonal stabilisation observed

Combinations

Decitabine combo
1L AML, N = 14 pts

Low-dose cytarabine (LDAC) combo
1L AML, N = 14 pts

Ongoing

- **Efficacy endpoint met in LDAC group:**
  - ✓ **3 CR/CRis among first 10 pts evalued for response**
- **Data further maturing**

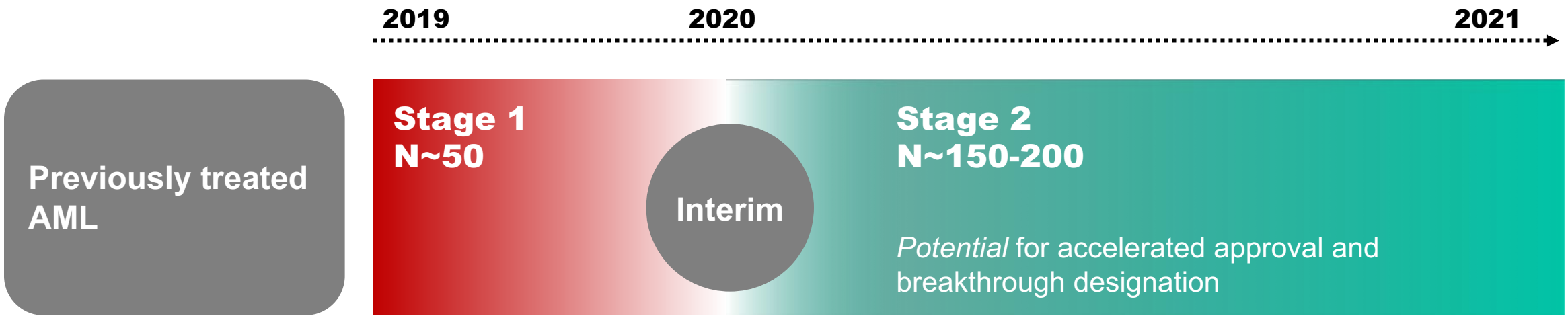
Endpoints

Primary
safety / ORR
Secondary
RFS
OS
biomarkers

*LDCT: approved low dose chemotherapy regimens

Late stage development in AML:

Monotherapy activity is registerable endpoint in previously treated AML



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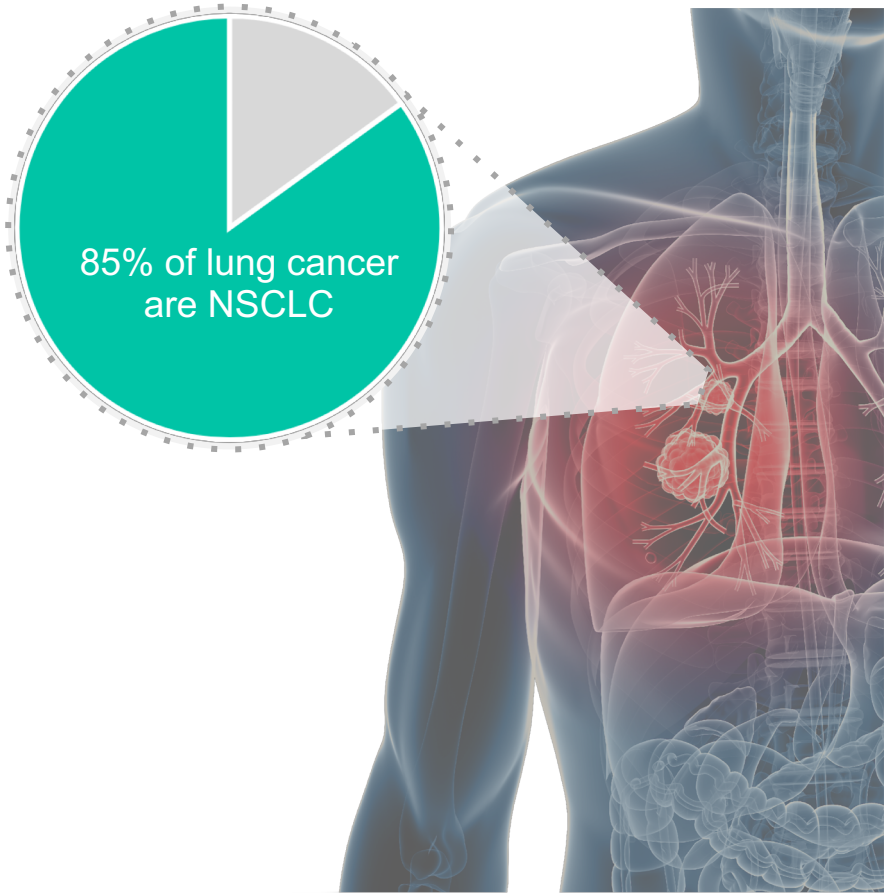
Ref. BGBC008 / NCT03184571

Bemcentinib in NSCLC: Combination with anti-PD(L)1

PoC data in combo with KEYTRUDA, previously treated, IO naïve NSCLC*:*

- ***27% ORR in PD-L1 –ve patients***
- ***40% ORR in AXL+ve patients***

NSCLC causes more cancer related deaths than breast, colon, pancreas and prostate combined



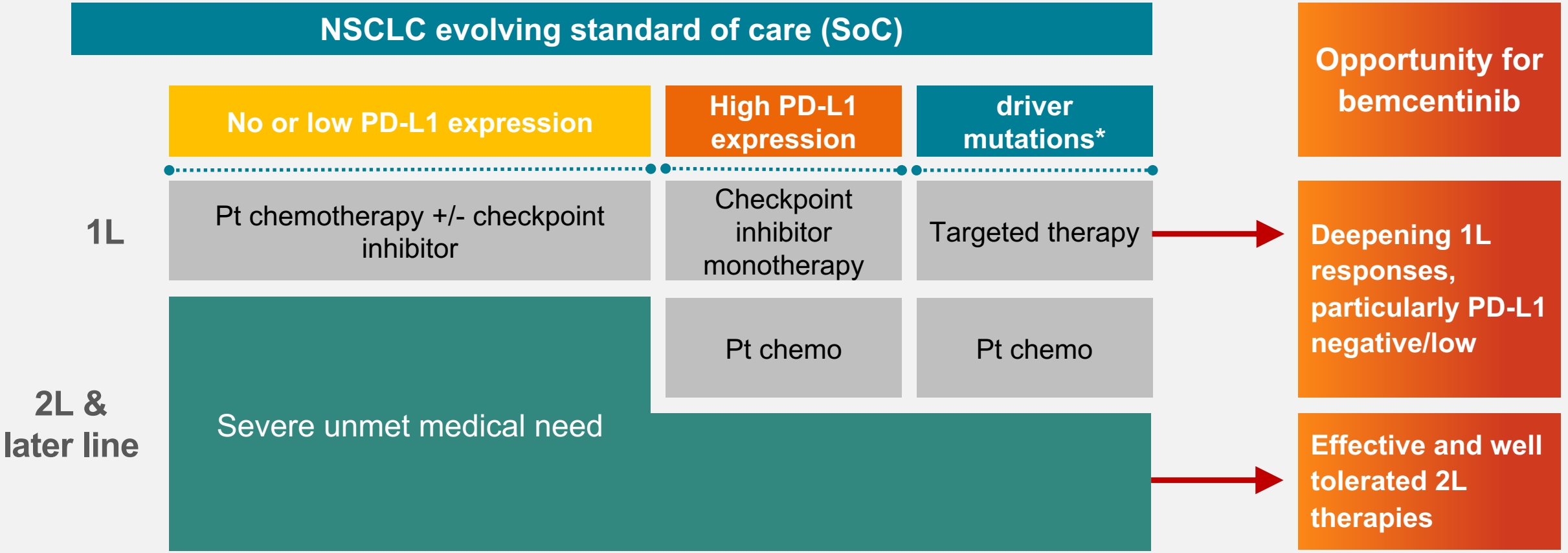
The largest cancer killer, most patients depend on drug therapy

- 2.09 million new cases of lung cancer diagnosed/yr worldwide, making up 11.6% of all cancer cases[1]
- 1.76 million lung cancer deaths/yr worldwide[1]
- In the U.S, 5-year survival rate is approximately 18.6%, and **4.7%** in patients with distant metastases[2]

Non-small cell lung cancer is the most common type of lung cancer, making up 80-85% of lung cancers

(1) Globocan 2018 (2) SEER

Rapidly emerging SoC creates opportunities for novel effective, chemo free regimens



* Mutations / rearrangements with available targeted therapies such as EGFR and ALK

Ref. BGBC008 / NCT03184571 – clinical trial collaboration with Merck & Co.

Phase II 2L NSCLC study of bemcentinib with KEYTRUDA

Cohort A

Previously treated, unresectable adenocarcinoma of the lung

PD-L1 / AXL all-comers

IO naive

Stage 1 (complete)	Stage 2 (recruiting)	Endpoints
N = 24 pts	If ≥ 4 PRs → N = 24 pts	**Primary** ORR **Secondary** ORR according to biomarker PFS OS safety
	Update Data in Q2 2019	

Cohort B

IO REFRACTORY

PD-L1 / AXL all-comers

Stage 1 (ongoing)	Stage 2	Endpoints
N = 13 pts	If ≥ 1 PRs → N = 16 pts	As in cohort A

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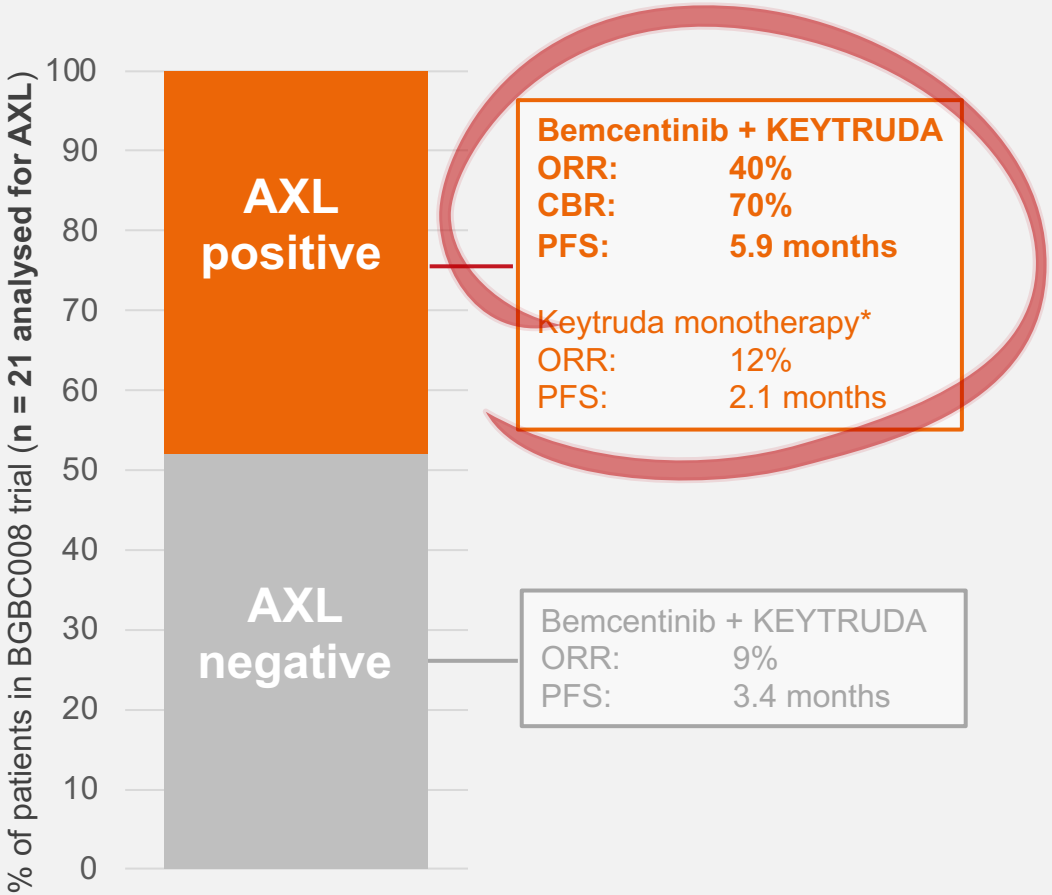
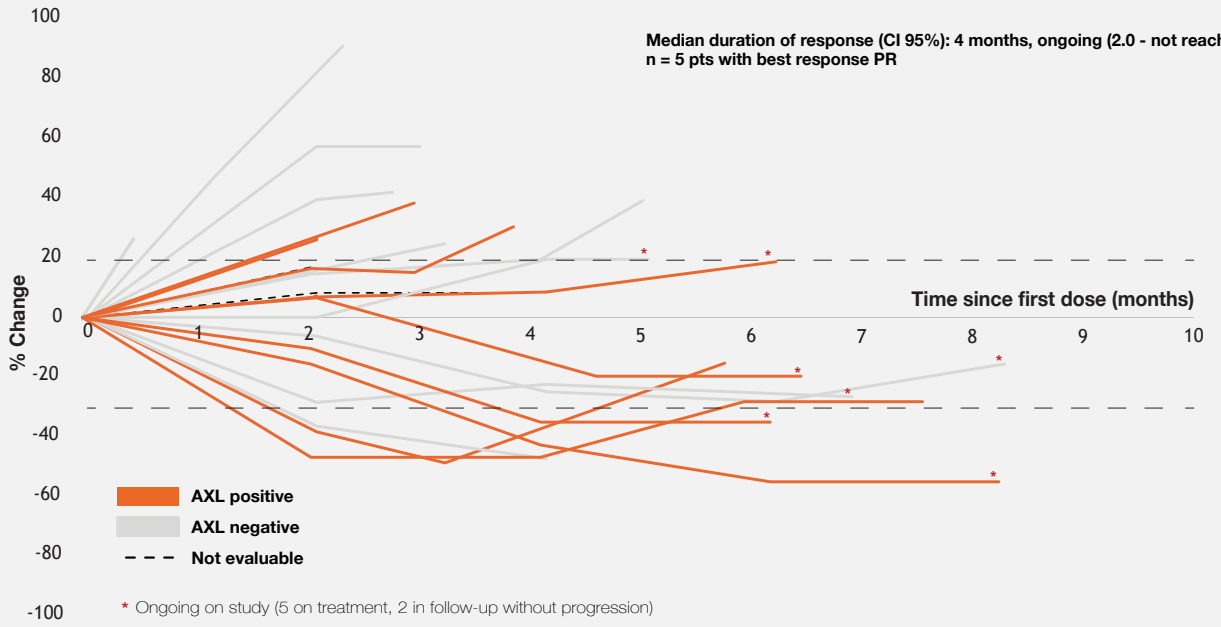
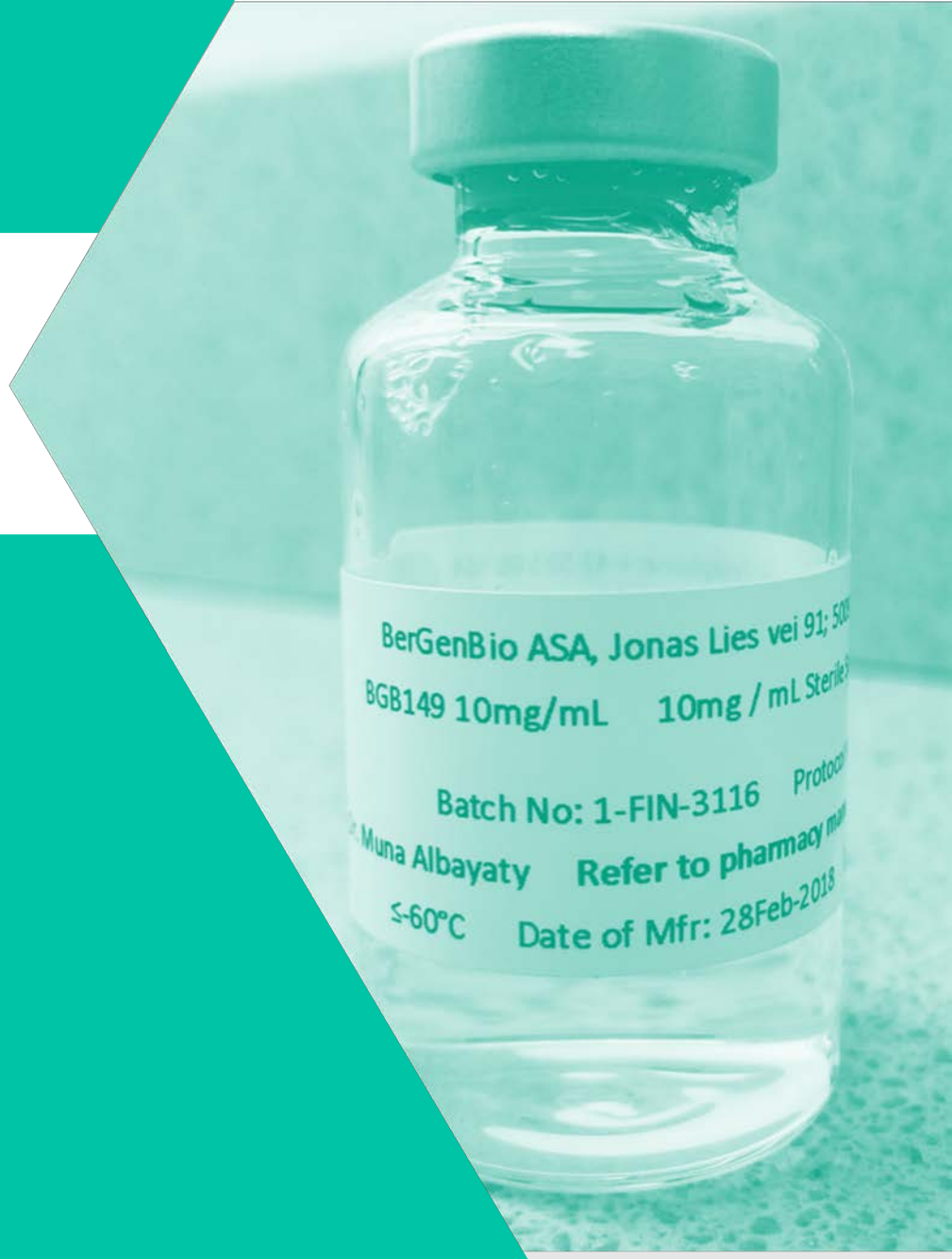
Ref. BGBC008 / NCT03184571

Cohort A PoC data bemcentinib + KEYTRUDA: Superior efficacy in AXL +ve pts.





BGB149 – a monoclonal anti-AXL antibody



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Ref. BGB149-101 / NCT03795142

BGB149: Anti-AXL monoclonal antibody

Phase I clinical trial ongoing

Functionally blocking humanised monoclonal antibody

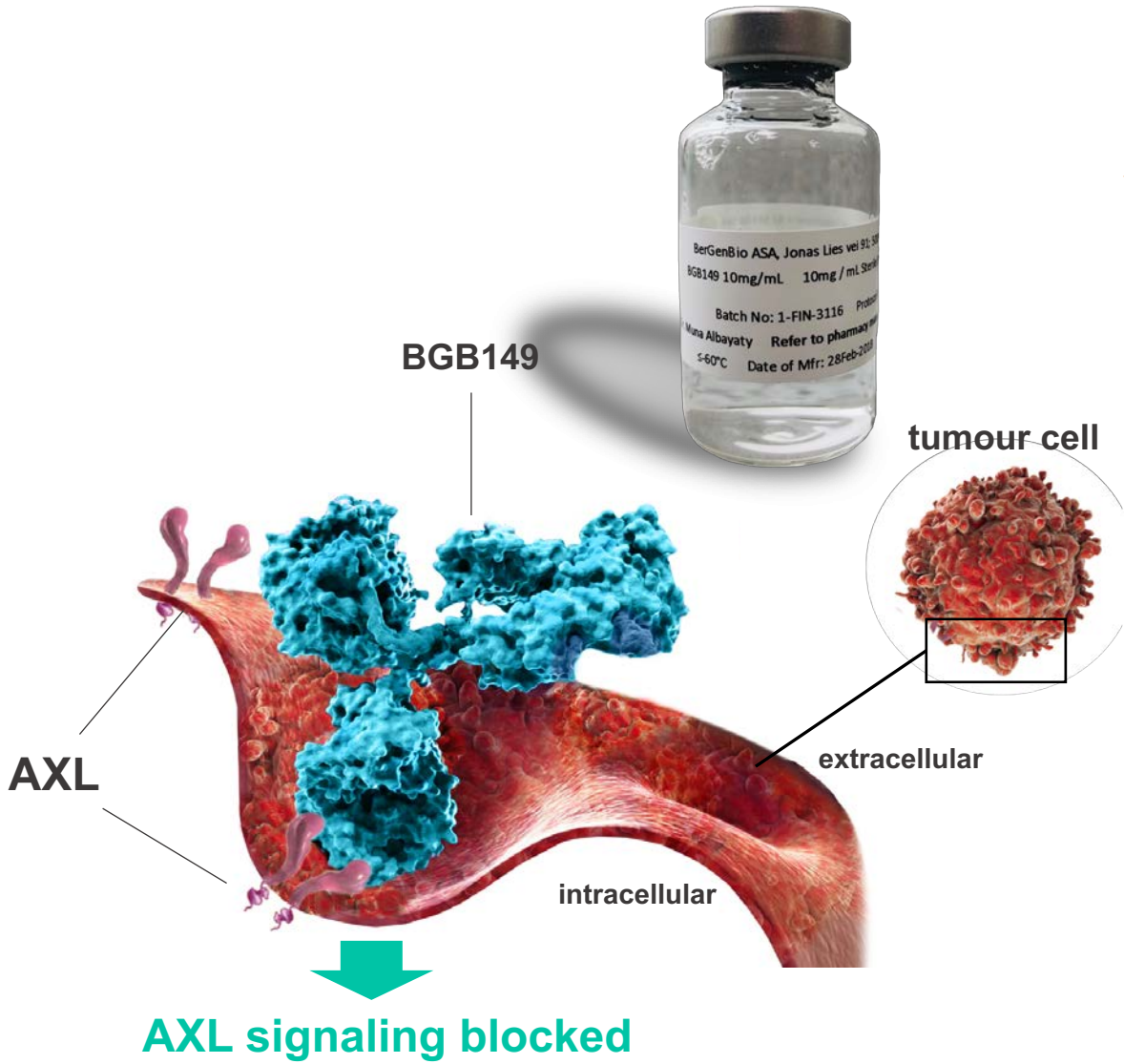
Binds human AXL, blocks AXL signalling

High affinity (KD: 500pM), Anti-tumour efficacy demonstrated *in vivo*

Robust manufacturing process established, 18 months stability

First-in-human healthy volunteer Phase I study initiated
- Up to 36 subjects
- Safety, PK/PD

First-in-patient trial expected in H2 2019



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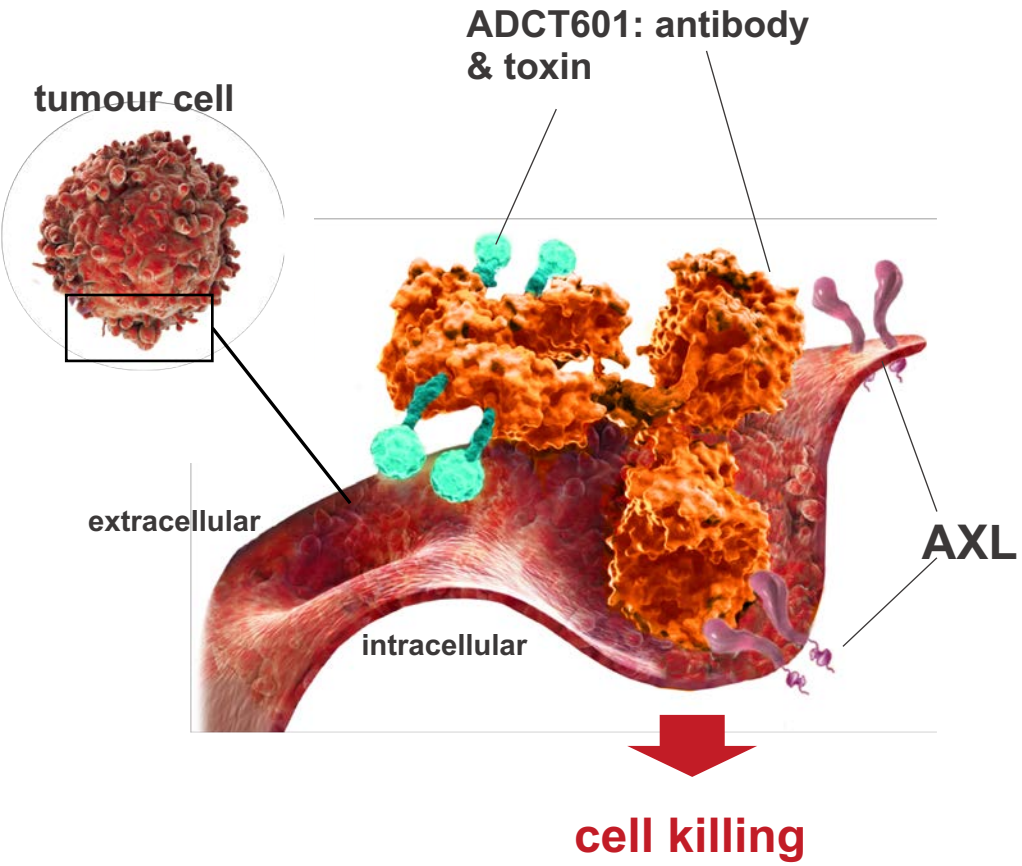
ADCT-601 – AXL ADC

Ref. NCT03700294

BGB601/ADCT-601: Anti-AXL ADC Phase 1 in solid tumours ongoing

Out-licensed to ADC Therapeutics (ADCT)



Antibody Drug Conjugate (ADC)

Targets human tumour AXL, induces cell death when internalised

Potent and specific anti-tumour activity demonstrated preclinically[1]

First-in-human Phase I study initiated in Jan 2019

- Solid tumours
- Up to 75 patients
- Safety, PK/PD, preliminary efficacy

Based on anti-AXL antibody BGB601 licensed from BerGenBio

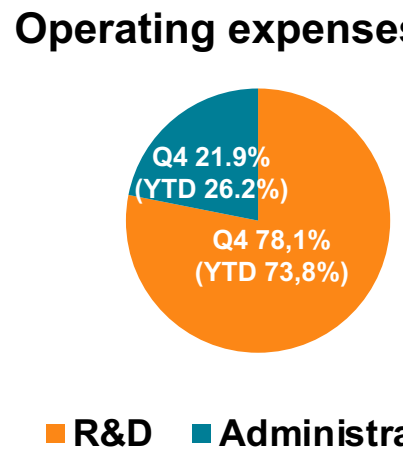
(1) AACR 2018

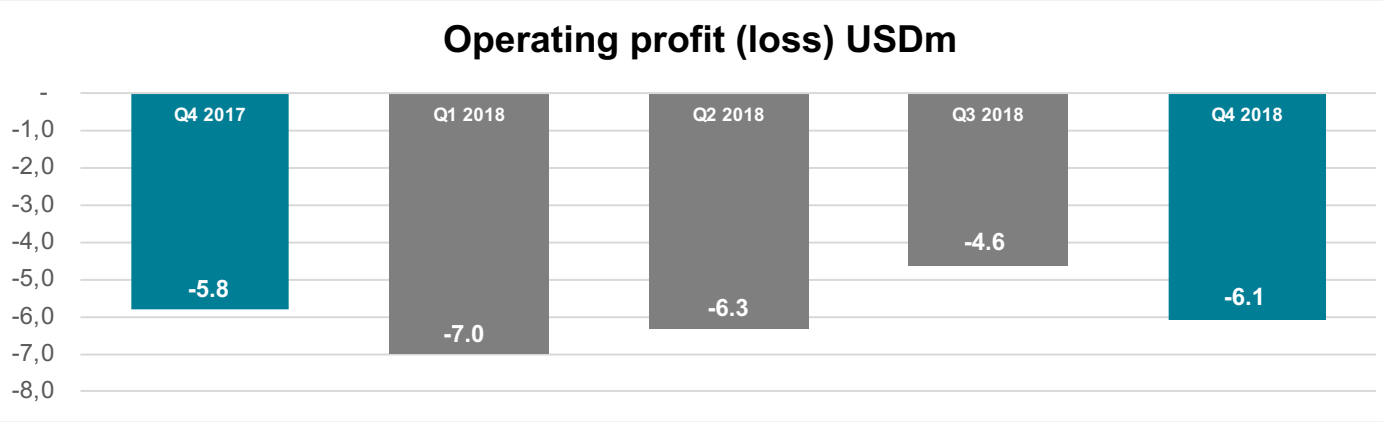
Finance

BerGenBio

Key financial figures

(USD million)	Q4 2018	Q4 2017	FY 2018	FY 2017
Operating revenues	**0.3**	0	**0.3**	0
Operating expenses	**6.3**	5.8	**24.2**	22.2
Operating profit (loss)	**-6.1**	-5.8	**-23.9**	-22.2
Profit (loss) after tax	**-6.1**	-5.8	**-23.6**	-22.0
Basic and diluted earnings (loss) per share (USD)	**-0.11**	-0.12	**-0.44**	-0.48
Net cash flow in the period	**-4.5**	-3.5	**-1.0**	25.2
Cash position end of period	**41.5**	45.1	**41.5**	45.1



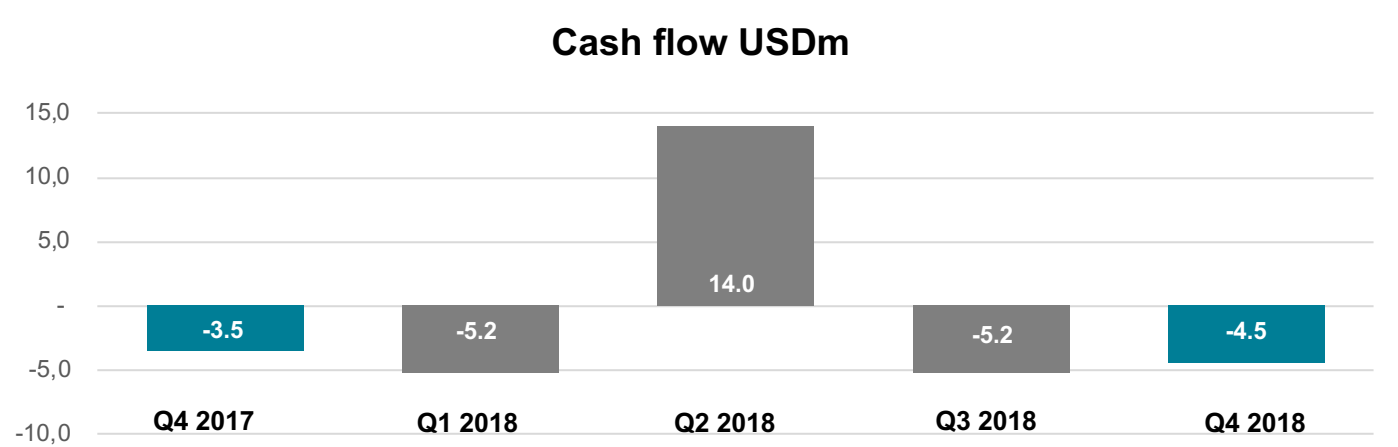


- Effective organisation
- 78.1% (YTD 73.8%) of operating expenses in Q4 2018 attributable to Research & Development activities

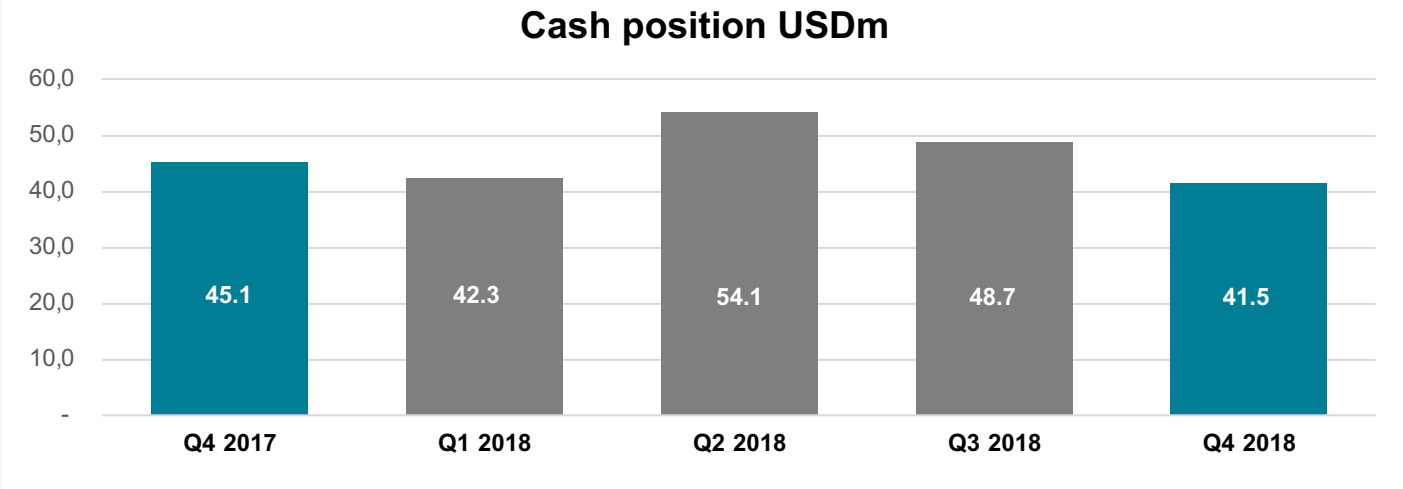
- Q4 18 operating loss reflecting level of research and development activities in the quarter
  - Revenue USD 0.3 million, licence revenue triggered by pre-clinical milestone (ADCT-601)
  - Stage 2 of NSCLC combination with Keytruda re-opened in Q4 18 and ongoing (mandatory safety review in Q3 18)

http://www.bergenbio.com/investors/reports/quarterly-reports/

Cash flow and cash position



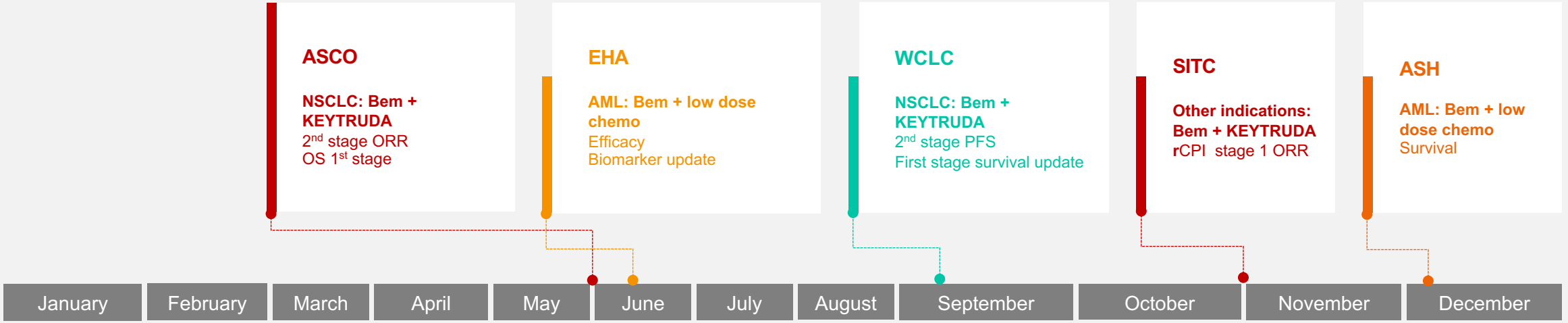
- Private placement Q2,18 strengthened cash position - gross funds raised USD 24m
- Quarterly cash burn average 2018 at USD 5.7 million



- Cash position gives runway to deliver key clinical read outs from ongoing clinical studies
- Cash runway into 2020 based on current burn rate

2019 news flow

Expected clinical updates in 2019



ASCO-SITC: Clinical Immuno-Oncology symposium, San Francisco
ASCO: American Society of Clinical Oncology, Chicago
WCLC: World Conference of Lung Cancer, Toronto
ESMO: European Society of Medical Oncology, Munich

AACR: American Association for Cancer Research, Chicago
EHA: European Hematology Association, Stockholm
SITC: Society for Immunotherapy of Cancer, DC
ASH: American Society for Hematology, San Diego

BGBIO – Summary

World leaders in understanding AXL biology

Pipeline opportunities in multiple cancers and fibrosis

3 selective AXL inhibitors in clinical development

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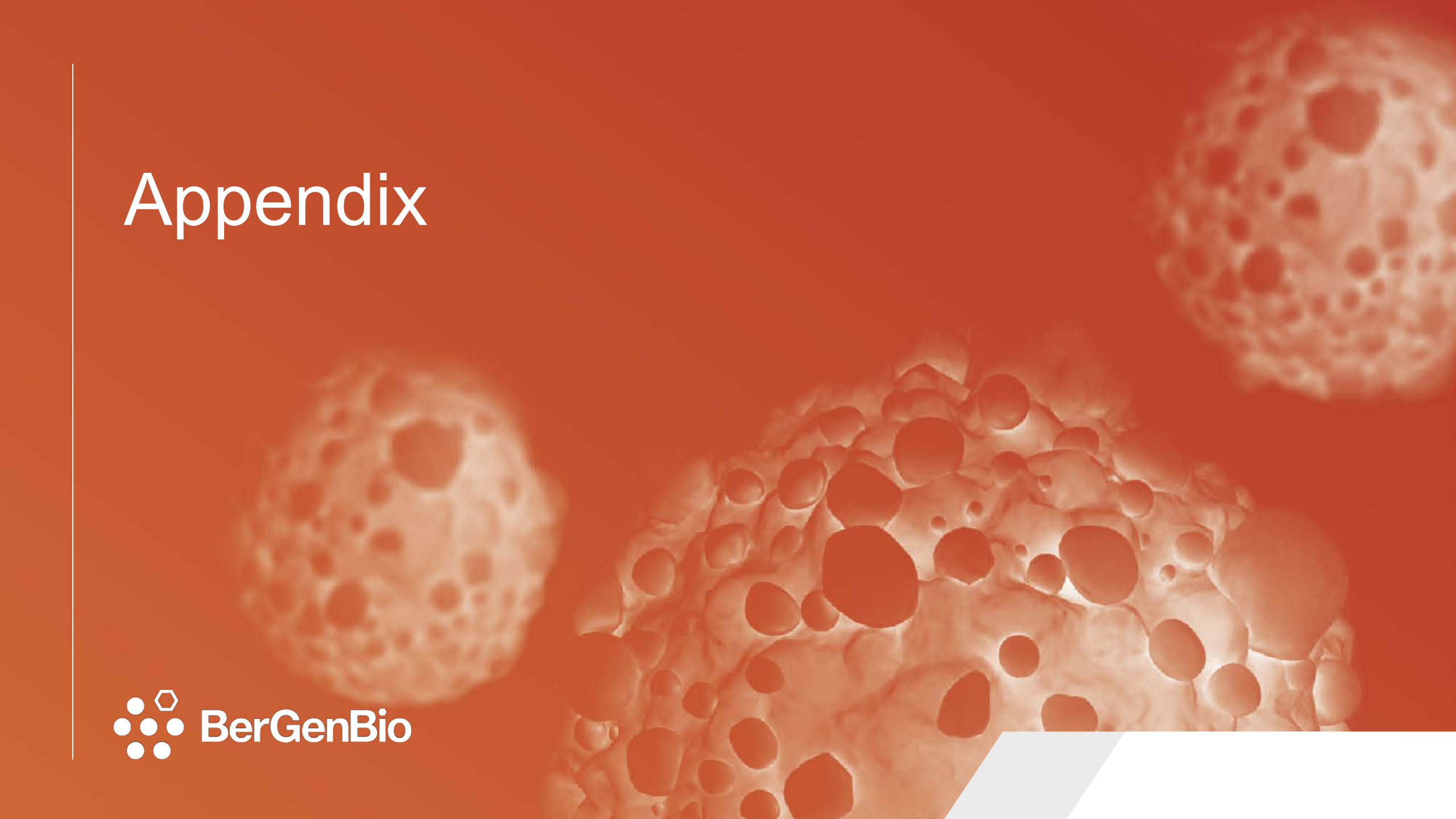
(monotherapy)

40% ORR in 2L NSCLC
(KEYTRUDA combo)

Resourced to deliver significant milestones

YE 2018
Cash NOK 360m/USD 41m

Appendix



BerGenBio

References

Bemcentinib:

Ludwig, K.F.,*et al.,*(2017) Small molecule Axl inhibition targets tumor immune suppression andenhances chemotherapy in pancreatic cancer,' Epub ahead of print.

- Axl associated with poor outcomes in pancreatic cancer uniquely links drug resistance andimmune evasion.
- Bemcentinib blocks aggressive traits of pancreatic cancer&enhances activity of gemcitabine.
- Bemcentinib drives tumour cell differentiation and provokes an immune stimulatory microenvironment. Treatment reduces expression of Arginase-1 a key player in immune-suppression.

Guo et al (2017) Axl inhibition induces the antitumor immune response which canbe further potentiated by PD-1 blockade in the mouse cancer models, Oncotarget

- Axl inhibition via bemcentinib reprograms immunological microenvironmentoIncreased proliferation and activation of CD4 and CD8
- Bemcentinib and PD-1 blockade act synergistiaclly

Mode of Action & Biomarkers

Haaland, G.S.,*et al.,*(2017) 'Association of warfarin use with Lower overall cancer incidenceamong patients older than 50 years,'*JAMA Intern Med.*, Nov 6.

- Warfarin inhibits Axl signalling and Axl-mediated biological response at doses lower than thosewhich mediate anti-coagulation effects.
- Retrospective analysis of a large population cohort demonstrates that patients on low doseWarfarin had a significantly lower incidence of cancer.

Aguilera, T.A.&Giaccia, A.J. (2017) 'Molecular Pathways: Oncologic Pathways and Their Role inT-cell Exclusion and Immune Evasion-A New Role for the AXL Receptor Tyrosine Kinase,'*Clin.Cancer Res.,*June 15th.

- Immune checkpoint inhibitors are most effective against T-cell inflamed tumours. Non-T-cell or T-cell excluded tumours remain a significant barrier to treatment.
- Axl identified as a key mediator of immune evasion and experimental evidence demonstrates Axltargeting leads to greater anti-tumour immune response post radiotherapy.

Miller, M.A.,*et al.,*(2017) 'Molecular Pathways: Receptor Ectodomain Shedding in Treatment,Resistance, and Monitoring of Cancer,' Cl*in. Cancer Res.,*Feb 1.

- Proteases known as sheddases cleave the extracellular domain of several receptor tyrosinekinases such as Axl generating soluble Axl (sAxl).
- Plasma levels of sAxl are predictive of patient response to standard of care BRAF&MEKinhibitor therapy and could be used for patient stratification strategies.

Antony et al (2017) The GAS6-AXL signaling network is a mesenchymal (Mes) molecular subtype–specific therapeutic target for ovarian cancer.*Science Signalling*

- Axl particularly abundant in ovarian cancer subtype designated as mesenchymal (Mes)
- Axl co-clustered cMET, EGFR, and HER2, producing sustained extracellular signal–regulated kinase (ERK) activation in Mes cells
- Bemcentinib reduced tumor growth in chick chorioallantoic membrane model.

Kanzaki, R.,*et al.,*(2017) 'Gas6 derived from cancer-associated fibroblasts promotes migration ofAxl-expressing lung cancer cells during chemotherapy,'*Nature Scientific Reports,*Sept 6th.

- Tumor stroma microenvironment (TME) is comprised of cancer-associated fibroblasts (CAFs)which influence cancer cells such as non-small cell lung cancer (NSCLC).
- In a murine model, NSCLC treated with cisplatin induced an up-regulation of Gas6.
- NSCLC line H1299 migrated in response to Gas6.
- The CAF cell line LCAFhertexpresses GAS6 and can promote H1299 cell migration.
- Conclusion- CAF derived GAS6 promotes migration of Axl-expressing lung cancers.

Reviews

Levin et al (2016) Axl Receptor Axis: A New Therapeutic Target inLung Cancer.*J Thoracic Oncol*

Chouaib et al (2014) Tumor Plasticity Interferes with Anti-Tumor Immunity. *Critical RevImmunology*

Gay et al (2017) Giving AXL the axe: targeting AXL in human malignancy.*BJC*

Brown et al (2016) Gene of the month: Axl.*BMJ*

Halmos et al (2016) New twists in the AXL(e) of tumor progression. *Science Signalling*

Resistance

Zucca, L.E.,*et al.,*(2017) 'Expression of tyrosine kinase receptor AXL is associated with worseoutcome of metastatic renal cell carcinomas treated with sunitinib,'*Urol Oncol.,*Oct 3.

- Renal cell carcinoma (RCC) represents 2-3% of all cancers in the Western world.
- First line therapy is sunitinib (PDGF/VEGF TK inhibitor).
- 47% of RCC patients treated with sunitinib were +ve for Axl.
- Axl expression in sunitinib treated patients correlated with worse clinical outcome (13 months Vs 43 months survival).

Husain, H.,*et al.*, (2017) 'Strategies to Overcome Bypass Mechanisms Mediating ClinicalResistance to EGFR Tyrosine Kinase Inhibition in Lung Cancer,'*Mol. Cancer Ther.*, Feb 2017.

- Patient treated with EGFR based therapies develop resistance via multiple mechanisms.
- Resistant metastatic lung cancers exhibit increased AXL, EMT and PDL1 expression.

Elkabets et al (2015) AXL Mediates Resistance to PI3Ka Inhibition by Activating theEGFR/PKC/mTOR Axis in Head and Neck and Esophageal Squamous Cell Carcinomas.*CancerCell*

- Axl mediates persistent mTOR activation and upregulated in resistant tumors
- Combined treatment with PI3Ka and either EGFR, AXL, or PKC inhibitors reverts this resistance

Mak et al (2015) A patient-derived, pan-cancer EMT signature identifies global molecularalterations and immune target enrichment following epithelial to mesenchymal transition.*ClinCancer Res*

- EMT signature was developed based on 11 tumor types
- Axl frequently overexpressed in EMT tumors along with PD-L1, PD1, CTLA4, OX40L, and PDL2
- highlights the possibility of utilizing EMT status--independent of cancer type--as an additional selection tool to select patients who may benefit from immune checkpoint blockade

Zhang et al (2012) Activation of the AXL kinase causes resistance to EGFR targeted therapy in lung cancer. *Nature Genetics*

Mueller et al (2014) Low MITF/AXL ratio predicts early resistance to multiple targeted drugs inmelanoma

- high Axl in melanoma cells correlates with drug resistance
- BRAF and ERK inhibitors are more effective when using Axl inhibition

Fibrosis

Hogaboam, C.,*et al.,*(2017) 'Evaluation of TAM receptors inhibitors in IPF,' Keystone Symposium.

- IPF patients with high expression of Axl are rapid (declining lung function) progressors.
- Bemcentinib inhibited the fibrogenic phenotype of IPF patient derived fibroblasts.
- GAS6 knockout animals were protected from Bleomycin induced lung fibrosis (Gold standard model of pulmonary fibrosis).
- Bemcentinib inhibited the development of fibrosis in the IPF SCID mouse model (Human IPF fibroblasts induce pulmonary fibrosis in the SCID mouse).

Staufer K.,*et al.,*(2017) 'The non-invasive serum biomarker soluble Axl accurately detectsadvanced liver fibrosis and cirrhosis,'*Cell Death Dis*. Oct 26.

- sAxl confirmed to be accurate biomarker of liver fibrosis and cirrhosis.
- sAxl/albumin demonstrated to be further enhancing as a cheap and accurate biomarker.

Barcena et al (2015) Gas6/Axl pathway is activated in chronic liver disease and its targetingreduces fibrosis via hepatic stellate cell inactivation.*J Hepatology*

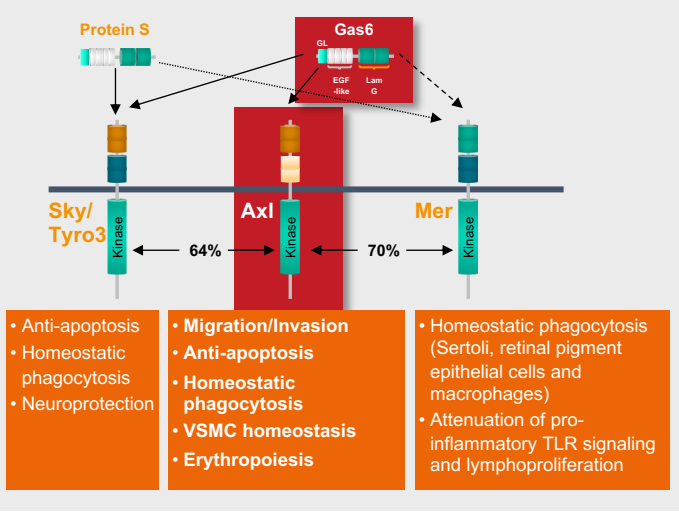
- Axl levels paralleled HSC activation
- Axl ko mice displayed decreased HSC activation in vitro and liver fibrogenesis after chronic damage by CCl4 administration
- Bemcentinib reduced collagen deposition and CCl4-induced liver fibrosis in mice.

Bemcentinib PoC data

Bemcentinib: uniquely selective for AXL, excellent clinical safety profile

AXL is the only TAM member that drives aggressive cancer

- TAM family members Tyro and Mer have homeostatic roles[1]
- TAM kinase domains are highly homologous
- TAM ligands promiscuous

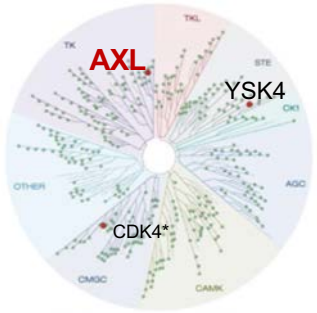


Bemcentinib was discovered by cell-based counterscreen and as a result is highly selective for AXL

- Bemcentinib is highly potent and selective, particularly over other TAM receptors
- Not spectrum-selective: no activity against Met, Flt3, Ron

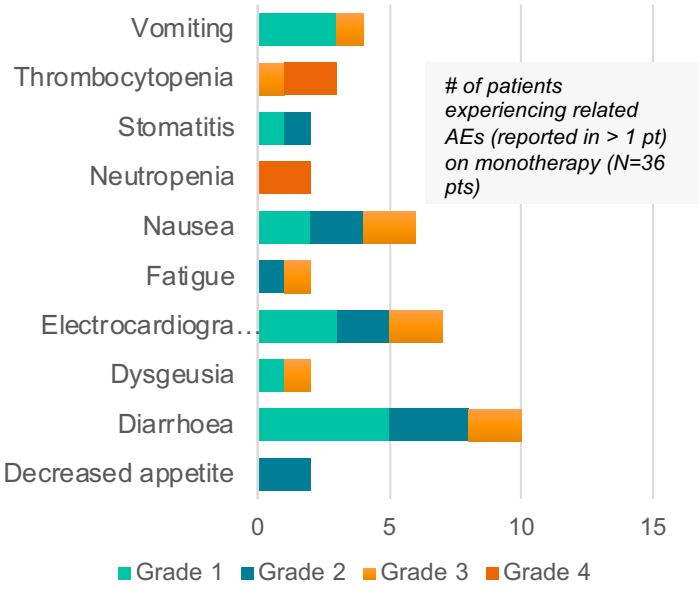
Cell based selectivity assay: EC50 (μM)[2]		
	AXL	0.014
	Mer	49.49
	Tyro	>160

KinomeScan at 4nM bemcentinib (biochemical selectivity assay)



Bemcentinib has excellent clinical safety profile

- Combo did not lead to new findings
- HV SAD study: 50mg – 1.5g, MTD not reached



(1) Mer -/-, Tyro -/- or TAM -/- mice exhibit broad spectrum autoimmune diseases, defective NK cell differentiation, impaired erythropoiesis, male sterility, blindness and seizures. AXL -/- mice are phenotypically normal. (2) Independently verified: Kimani, *Cell Communication and Signaling* 2016 *The observed CDK4 inhibition was not dose dependent and is thus not believed to be a real effect

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Source: Loges *et al* ASH 2018; Byers *et al* ENA 2016 and WCLC 2018

Monotherapy efficacy with biomarker correlation

Relapsed / refractory AML & MDS, unfit for intensive chemo (BGBC003)

All comers
Daily bemcentinib single agent

Dose escalation ASH 2018
N = 27*
(complete)

Expansion
N = up to 14 each
IIT
N = up to 43
(ongoing)

	Overall (n=27)		sAXL low (n=14)		sAXL high (n=11)	
	n	%	n	%	n	%
CR/CRi/CRp	6	22%	6	43%	0	0%
SD	8	30%	3	21%	5	45%
PD*	13	48%	5	36%	6	55%
ORR	**6**	**22%**	**6**	**43%**	**0**	**0%**

Median age of all patients: 74.5
Responses included poor risk and secondary disease
mDoR = 3.4 months

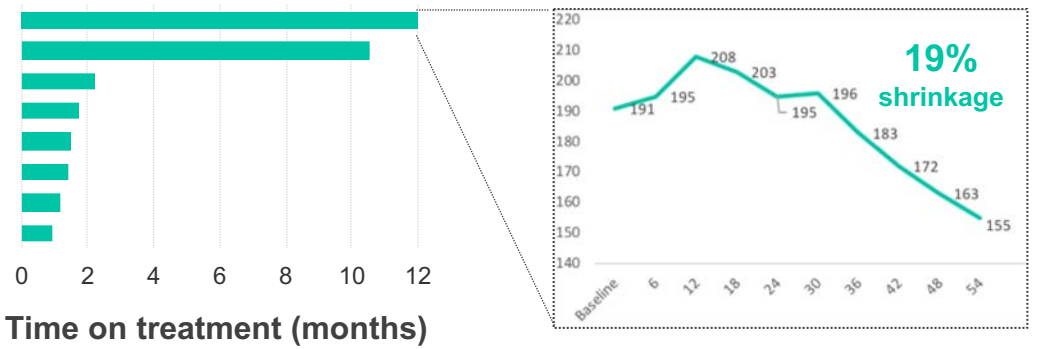
43% ORR in patients with +sAXL biomarker

Later line NSCLC, EGFR wt and mutant (BGBC004, trial complete)

All comers
Daily bemcentinib single agent

Phase I ENA 2016
N = 8
(complete)

RP2D confirmed for combination studies



25% DCR for ca 1 year, including 1 minor response

*27 evaluable pts: Patients who had completed at least one cycle of treatment and who had been relapsed or refractory to previous treatment. sAXL status was available for 25 of 27 evaluable patients.

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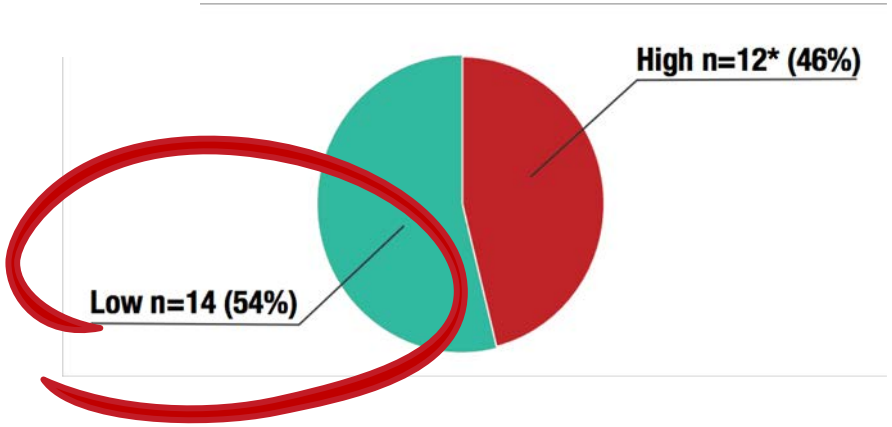
Bemcentinib monotherapy exhibits potent anti-leukaemic activity 2L R/R patients

Biomarker:
Soluble AXL (sAXL) at screen:
Inversely correlated with AXL receptor activity



Superior response rate in patients positive for AXL biomarker

	Overall (n=27)		sAXL low (n=14)		sAXL high (n=11)	
	n	%	n	%	n	%
CR/CRi/CRp	6	22%	6	43%	0	0%
SD	8	30%	3	21%	5	45%
PD*	13	48%	5	36%	6	55%
ORR	**6**	**22%**	**6**	**43%**	**0**	**0%**

- 2 evaluable patients were not evaluable for sAXL status
- Monotherapy responses. One additional response was reported in combination with decitabine for a total of 7 responses in phase I/II.
- 1 CR, 4 CRi, 1 CRp

* PD includes patients who progressed or came off study before having completed 3 cycles of treatment.

Median age of all patients: 74.5

Responses included poor risk and secondary disease

✓**Bemcentinib monotherapy is well tolerated: mild and manageable side effect profile with low incidence of Grade 3/4 events**

✓**Low incidence of hematological adverse effects**

Intention-to-treat population included 36 patients, 9 of whom were not evaluable for efficacy (8 were exposed to treatment for <21 days, 1 was a first line patient). sAXL levels were available for 25 evaluable patients.
Source: Loges, et al. ASH 2018.

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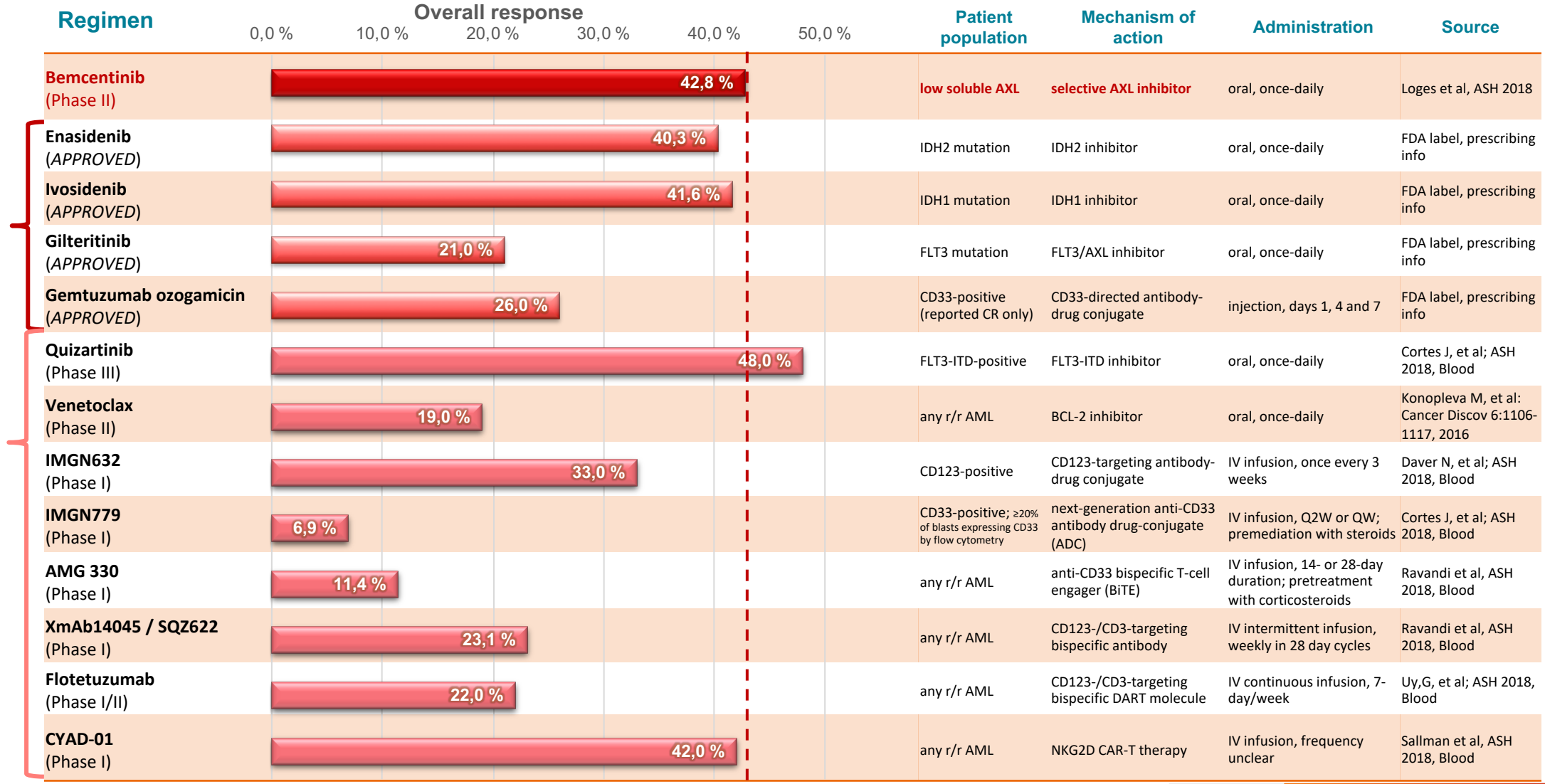
Monotherapy shows promising efficacy in comparison to approved & emerging regimens



	Regimen	Patient population	Mechanism of action	Administration	Source
	Bemcentinib (Phase II)	**low soluble AXL**	**selective AXL inhibitor**	oral, once-daily	Loges et al, ASH 2018
Approved, limited pt populations only	**Enasidenib** (*APPROVED*)	IDH2 mutation	IDH2 inhibitor	oral, once-daily	FDA label, prescribing info
	Ivosidenib (*APPROVED*)	IDH1 mutation	IDH1 inhibitor	oral, once-daily	FDA label, prescribing info
	Gilteritinib (*APPROVED*)	FLT3 mutation	FLT3/AXL inhibitor	oral, once-daily	FDA label, prescribing info
	Gemtuzumab ozogamicin (*APPROVED*)	CD33-positive (reported CR only)	CD33-directed antibody-drug conjugate	injection, days 1, 4 and 7	FDA label, prescribing info
Emerging therapies in R/R AML presented at ASH	**Quizartinib** (Phase III)	FLT3-ITD-positive	FLT3-ITD inhibitor	oral, once-daily	Cortes J, et al; ASH 2018, Blood
	Venetoclax (Phase II)	any r/r AML	BCL-2 inhibitor	oral, once-daily	Konopleva M, et al: Cancer Discov 6:1106-1117, 2016
	IMGN632 (Phase I)	CD123-positive	CD123-targeting antibody-drug conjugate	IV infusion, once every 3 weeks	Daver N, et al; ASH 2018, Blood
	IMGN779 (Phase I)	CD33-positive; ≥20% of blasts expressing CD33 by flow cytometry	next-generation anti-CD33 antibody drug-conjugate (ADC)	IV infusion, Q2W or QW; premediation with steroids	Cortes J, et al; ASH 2018, Blood
	AMG 330 (Phase I)	any r/r AML	anti-CD33 bispecific T-cell engager (BiTE)	IV infusion, 14- or 28-day duration; pretreatment with corticosteroids	Ravandi et al, ASH 2018, Blood
	XmAb14045 / SQZ622 (Phase I)	any r/r AML	CD123-/CD3-targeting bispecific antibody	IV intermittent infusion, weekly in 28 day cycles	Ravandi et al, ASH 2018, Blood
	Flotetuzumab (Phase I/II)	any r/r AML	CD123-/CD3-targeting bispecific DART molecule	IV continuous infusion, 7-day/week	Uy,G, et al; ASH 2018, Blood
	CYAD-01 (Phase I)	any r/r AML	NKG2D CAR-T therapy	IV infusion, frequency unclear	Sallman et al, ASH 2018, Blood

AXL+ve is 50% patient population (Loges *et al* ASH 2018), IDH2 is 10%, IDH1 is 9% (Aref *et al* 2015) & FLT3 is 20% (Cuervo-Sierra *et al* Blood 2013)

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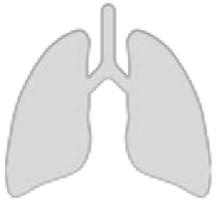
Source: Krebs *et al* SITC 2018; Schuster *et al* ESMO 2018

KEYTRUDA efficacy increased in combination and correlated with tumour AXL



Advanced NSCLC, 1 prior line of Pt, IO-naïve (BGBC008)

All comers

Bemcentinib 200 mg daily + 200 mg **KEYTRUDA** q3w

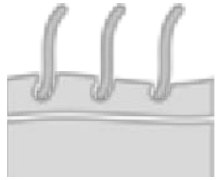
Stage 1
SITC 2018
N = 24*
(complete)

≥4 PR

Stage 2
ASCO 2019
N = 48 total
(ongoing)

Biomarker at screen	AXL pos	AXL neg
ORR	40%	9%
CBR	70%	45%
mPFS	5.9 months	3.3 months

40% ORR and 5.9 mth mPFS in AXL+ patients



Newly diagnosed advanced melanoma (BGBIL006)

BRAFwt / BRAFm w/ low tumour burden

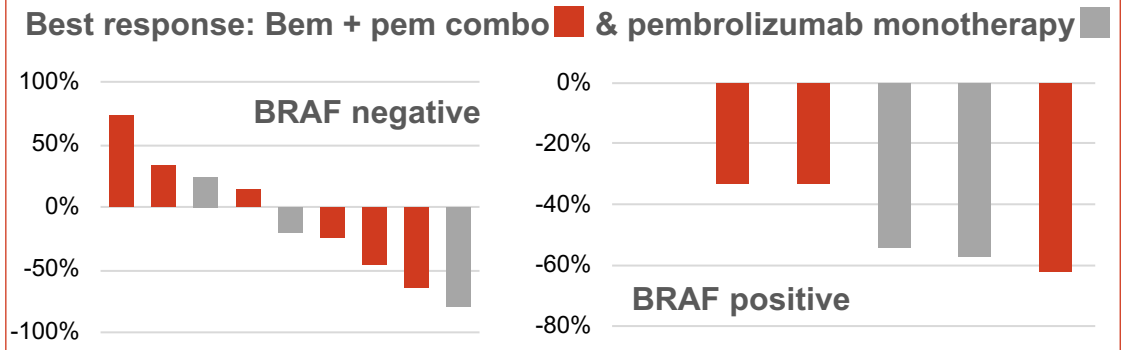
Bemcentinib 200 mg daily + 200 mg **KEYTRUDA** q3w

R

Bemcentinib + KEYTRUDA

KEYTRUDA

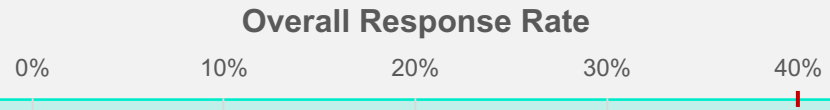
Phase II
ESMO 2018
N = ca 40
(ongoing)



Responses correlated w/ soluble biomarker

*Intention to treat analysis

Promising efficacy in comparison to approved monotherapy and emerging combinations*



Regimen	Overall Response Rate	PFS	Patient details / Biomarker	Mechanism of action	Administration	Source
Bemcentinib + pembrolizumab (Phase II)	n=10, 40%	5.9 mo	AXL positive, any PD-L1 (TPS 0-49% in 70%)	selective AXL inhibitor	oral, once daily	Krebs, M, et al; SITC 2018
Pembrolizumb (APPROVED)	n=344, 18%	3.9 mo	PD-L1 positive (TPS>1%)	PD-1 inhibitor	IV infusion, once every 3 weeks	FDA label, prescribing info
Atezolizumab (APPROVED)	n=425, 14%	2.8 mo	any PD-L1 (55% PD-L1 positive)	PD-L1 inhibitor	IV infusion, once every 3 weeks	FDA label, prescribing info
Nivolumab (APPROVED)	n=135, 20%	3.5 mo	any PD-L1 (53% PD-L1 positive), squamous	PD-1 inhibitor	IV infusion, once every 2 weeks	FDA label, prescribing info
Nivolumab (APPROVED)	n=292, 19%	2.3 mo	any PD-L1 (54% PD-L1 positive), non-squamous	PD-1 inhibitor	IV infusion, once every 2 weeks	FDA label, prescribing info
Epacadostat + pembrolizumab (Phase I/II)	n=70, 29%	4.0 mo	prior treatment w/ CT; IO-naive; responses regardless of PD-L1 (no details provided)	selective inhibitor of IDO1 enzyme	oral, twice daily	Villaruz, L, et al; WCLC 2018 abstract
HBI-8000 + nivolumab (Phase Ib/II)	n=8, 38%	not yet available	includes CPI-naïve and – experienced patients	HDAC class I & IIb inhibitor	oral, twice weekly	Khushalani, N, et al; SITC 2018
TSR-042 (Phase I)	n=32, 25%	not yet available	PD-L1 low (TPS 0-49%)	PD-1 inhibitor	IV infusion, once every 3 weeks	Perez, D, et al; SITC 2018
TSR-022 + TSR-042 (Phase I)	n=31, 13%	not yet available	patients include IO-naive and -experienced; all responses in PD-L1 positive (TPS>1%)	anti-TIM-3 antibody + anti-PD-1, respectively	IV infusion, once every 3 weeks	Davar, D, et al; SITC 2018
Ramucirumab + pembrolizumab (Phase Ia/b)	n=11, 18%	9.7 mo	PD-L1 negative (TPS<1%)	anti-VEGFR2	IV infusion, once every 3 weeks	Herbst, R, et al; ASCOPubs 2018, JCO

*emerging therapies presented at SITC, similar patient populations

Source: Byers *et al* WCLC 2018; Schuster *et al* ESMO 2018

Prevention and reversal of resistance to targeted therapy

Advanced NSCLC, first and second line (BGBC004, trial complete)

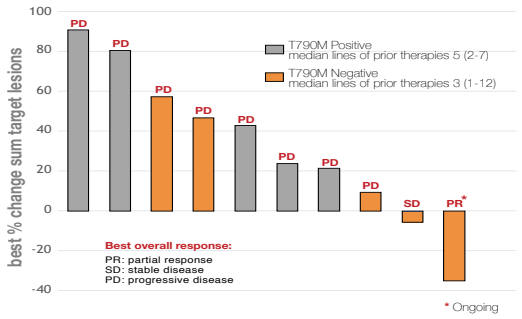
All comers

Bemcentinib 200 mg daily + 150 mg **TARCEVA** daily

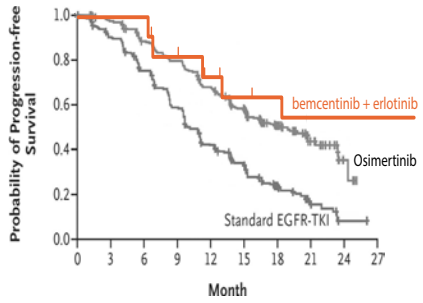
Arm B: reversal of resistance to TARCEVA
WCLC 2018
N = 14

Arm C: prevention of resistance to TARCEVA
N = 14

resistance reversal in T790 neg pts



1L combo, PFS extended



Extended PFS in 1L, 40% CBR in 2L, T790M neg pts

Newly diagnosed advanced melanoma (BGBIL006)

BRAFm w/ high tumour burden

Bemcentinib 200 mg daily + **BRAF/MEKi** daily

R

Bemcentinib + BRAF/MEKi

BRAF/MEKi

Phase II (ongoing) ESMO 2018

N = ca 40 total

Best response: Bem + BRAF/MEKi combo & BRAF/MEKi mono

Responses correlated w/ soluble biomarker

Soluble predictive markers identified

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Source: Gerber *et al* WCLC 2018

Prevention and reversal of resistance to chemotherapy

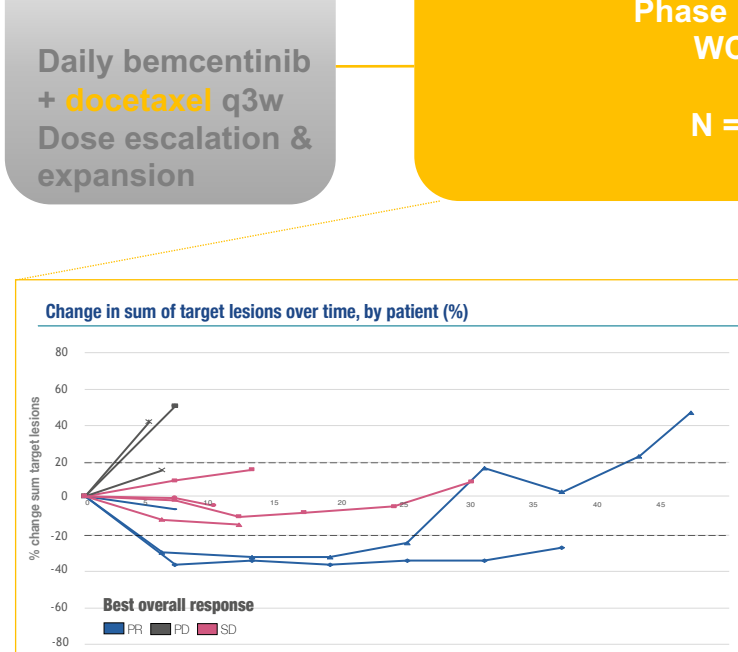
Later line NSCLC, includes CPI failures (BGBIL005)

All comers

Daily bemcentinib + docetaxel q3w
Dose escalation & expansion

Phase I/II (ongoing)
WCLC 2018

N = up to 30



PRs & SDs included patients who previously failed CPI

73% CBR (8 of 11 evaluable pts) incl. 2 PRs, PFS ca 7m

1L & 2L AML, combination with low-dose cytarabine (LDAC, BGBC003)

1L & 2L AML unfit for intensive therapy

Daily bemcentinib + LDAC

Phase II (ongoing)
Press release April 1

N = up to 14

30 % CR/CRi rate in first 10 evaluable patients

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Competitors

Axl inhibitors - competitive landscape