



# LURBINECTEDIN INVESTOR UPDATE

JANUARY 10, 2020



Jazz Pharmaceuticals®

# Forward-Looking Statements

## "Safe Harbor" Statement Under the Private Securities Litigation Reform Act of 1995

This presentation contains forward-looking statements, including, but not limited to, statements related to the potential benefits to Jazz Pharmaceuticals plc from the exclusive license agreement with PharmaMar for lurbinectedin in the U.S., including potential meaningful near-term revenue opportunity; potential accelerated FDA approval and launch of lurbinectedin in the U.S. in 2020; potential regulatory, sales and development milestones under the licensing agreement between Jazz Pharmaceuticals and PharmaMar and related potential future payments by Jazz Pharmaceuticals to PharmaMar; and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: the closing of the licensing agreement between Jazz Pharmaceuticals and PharmaMar upon expiration or termination of HSR waiting period; Jazz Pharmaceuticals' ability to achieve the expected benefits (commercial or otherwise) from the license agreement; pharmaceutical product development and clinical success thereof; the regulatory approval process; effectively commercializing any product candidates; and other risks and uncertainties affecting Jazz Pharmaceuticals, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including the company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 and future filings and reports by the company. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect the company's forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

# Agenda

---

---

**Bruce Cozadd**

Chief Executive Officer

Background & Transaction Overview

---

**Dan Swisher**

President and Chief Operating Officer

Disease Overview

---

**Rob Iannone, MD, MSCE**

Executive Vice President, Research and Development

MOA & Clinical Data Overview

---

**Mike Miller**

Executive Vice President, U.S. Commercial

Commercial Initiatives

---





## BACKGROUND & TRANSACTION OVERVIEW

BRUCE COZADD  
CHIEF EXECUTIVE OFFICER

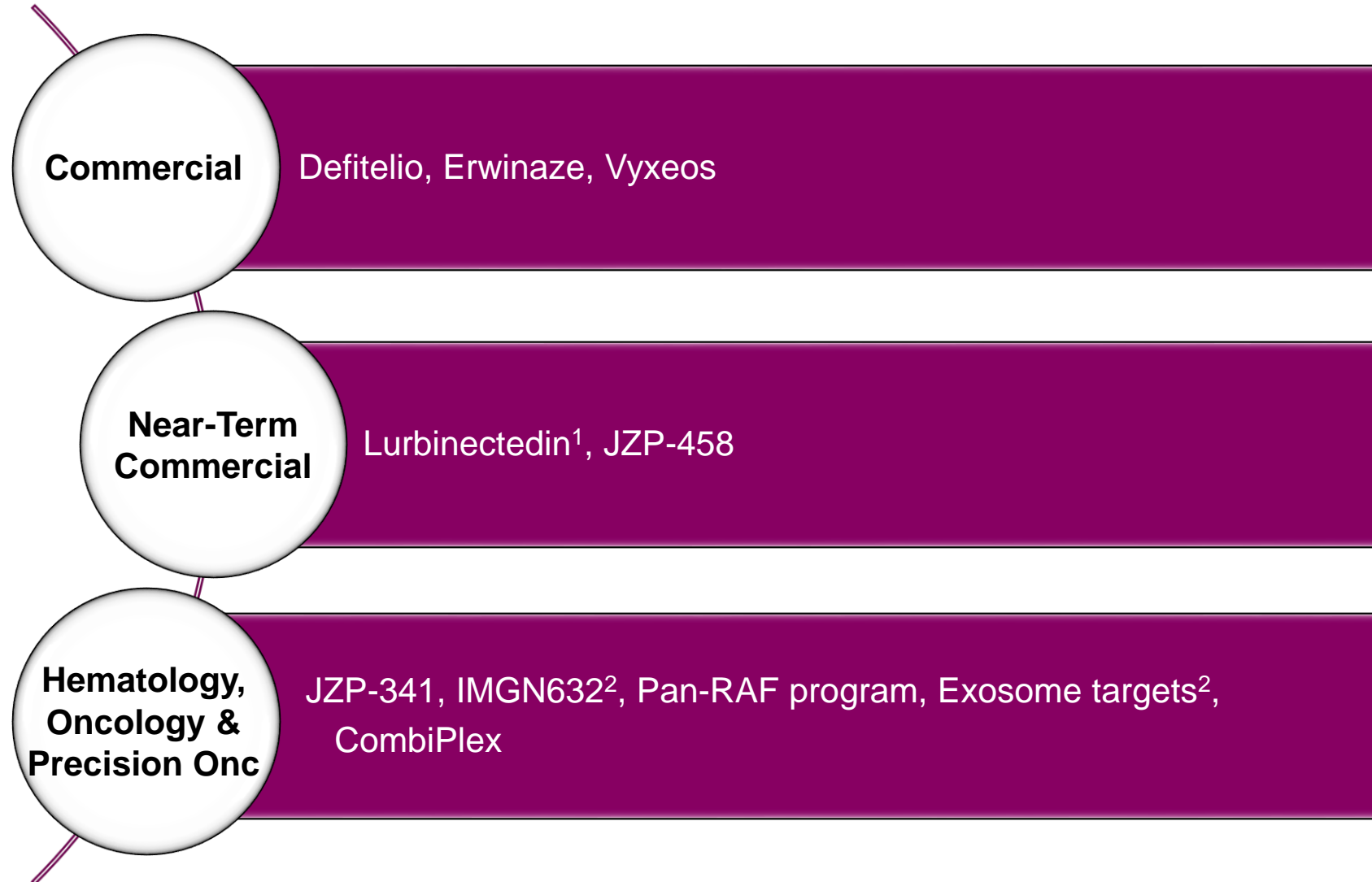


Jazz Pharmaceuticals®



# Lurbinectedin Expands Our Oncology Therapeutic Area into Solid Tumors

## Potential Meaningful Near-term Revenue Opportunity



<sup>1</sup> Subject to the closing of the license transaction with PharmaMar for lurbinectedin upon HSR clearance; NDA submission December 2019. <sup>2</sup> Partnered

# Lurbinectedin Represents Attractive Late-Stage Opportunity for Jazz

<b>Differentiated Molecule</b>	<ul style="list-style-type: none"> <li>Lurbinectedin clinical data has shown significant response rate improvement over SOC in relapsed SCLC, along with improved safety, tolerability and administration profile</li> </ul>
<b>Development Status</b>	<ul style="list-style-type: none"> <li>Phase 2 monotherapy basket trial results presented at ASCO 2019 and World Lung 2019</li> <li>Lurbinectedin achieved its primary endpoint and demonstrated an ORR of 35.2%, which compares favorably to topotecan's historical ORR of 16.9% by investigator assessment.</li> <li>Post pre-NDA meeting, PharmaMar submitted an NDA in December 2019 under accelerated approval regulations</li> <li>Priority review requested with potential for approval and launch in 2020</li> </ul>
<b>Unmet Medical Need</b>	<ul style="list-style-type: none"> <li>Limited treatment options for relapsed SCLC</li> <li>~30,000 new cases of SCLC each year in the U.S.<sup>1</sup></li> </ul>
<b>Exclusivity</b>	<ul style="list-style-type: none"> <li>Granted Orphan Drug Designation by FDA in August 2018</li> <li>IP includes composition of matter patent expiring in 2024 (with patent term extension 2029); formulation patent expiry 2028</li> <li>Patent applications for combo therapy are pending and, if issued, could extend to 2031</li> </ul>

<sup>1</sup> Sources: SEER Cancer Stat Facts <https://seer.cancer.gov/statfacts/html/lungb.html>, accessed April 19, 2019; American Cancer Society, <https://www.cancer.org/cancer/small-cell-lung-cancer/about/what-is-small-cell-lung-cancer.html>, accessed April 12, 2019

# Background/Transaction Overview

- On December 19, 2019, Jazz and PharmaMar announced the signing of an exclusive license agreement for U.S. rights to lurbinectedin across all indications, including SCLC
- PharmaMar to receive \$200M upfront payment and up to \$800M in potential milestone payments, in addition to incremental tiered royalties on future net sales of lurbinectedin ranging from the high teens up to 30 percent. Potential milestone payments include:
  - up to \$250M upon the achievement of accelerated and/or full regulatory approval of lurbinectedin by FDA within certain timelines, and
  - up to \$550M in potential commercial milestone payments
- PharmaMar may receive additional payments on approval of other indications, with any such payments creditable against commercial milestone payment obligations
- PharmaMar will supply Jazz with launch quantities of lurbinectedin and on an ongoing basis will supply API
- Closing of the agreement is subject to expiration or termination of the HSR waiting period
  - Expect to record \$200M upfront payment as acquired IPR&D expense on close
  - Approval and post-approval milestone payments to be capitalized as intangible assets





A microscopic image showing two cells. The cell on the left is purple and covered in numerous small, round, pinkish-purple granules. The cell on the right is yellow and has a more textured, bumpy surface. The background is a dark blue, slightly out-of-focus field of similar purple granules.

## DISEASE OVERVIEW

DAN SWISHER  
PRESIDENT AND CHIEF OPERATING OFFICER



Jazz Pharmaceuticals®



# Relapsed SCLC: Low Survival Rates & Limited Treatment Options

## Increased Need for Effective Therapies

### Disease

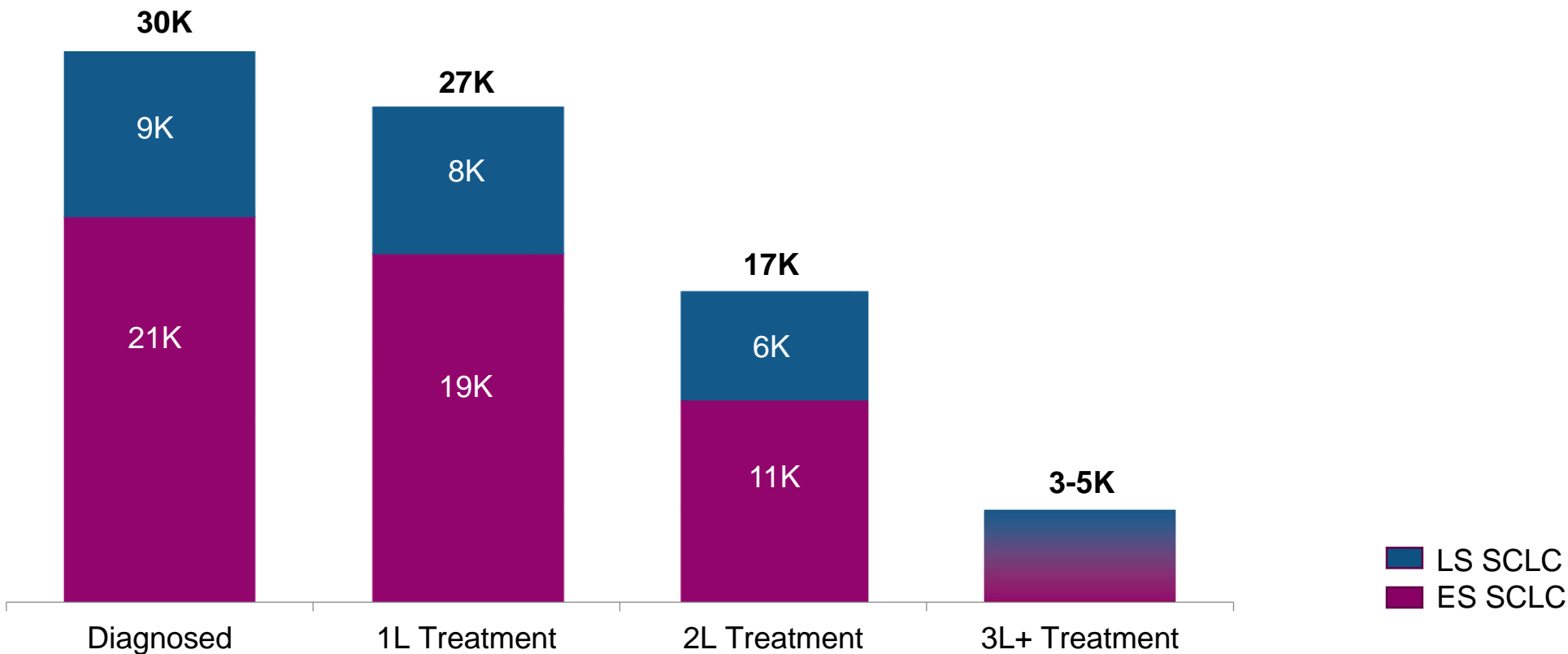
- SCLC is a very aggressive cancer that usually is diagnosed with advanced stages<sup>1</sup>
  - LS SCLC 5-year survival ranges from 20–40%<sup>2</sup>
  - ES SCLC 5-year survival <5%<sup>2</sup>
- SCLC is distinct from NSCLC
  - rapid doubling time
  - high growth fraction
  - early development of widespread metastases
  - dramatic initial responses to chemotherapy and radiation
- Despite multiple 1L therapies and high initial responses to therapy, most patients relapse

### Limited Treatment Options

- The addition of a PD-L1 antagonist to up-front extensive stage SCLC represents a major advance and is now standard of care
- Despite the inclusion of PD-L1 antagonists in 1L, the great majority of patients will progress.
  - The last FDA approved NCE in 2L SCLC was topotecan, in 1996 and is commonly used in 2L but with a relatively low objective response rate of 16.9%<sup>3</sup>
- Use of I/O in 1L SCLC increases the need for safe and effective therapies in the relapsed setting
- Pending the results of the Adriatic study, PD-L1 antagonists may also be used as initial therapy in limited stage SCLC, leaving a similar unmet need for patients who relapse after initial therapy.

<sup>1</sup> American Cancer Society, <https://www.cancer.org/cancer/small-cell-lung-cancer/about/what-is-small-cell-lung-cancer.html>, accessed January 2, 2020; <sup>2</sup> Nat Rev Clin Oncol. 2017 Sep 14(9) 549–561 <sup>3</sup> von Pawel et al. J Clin Oncol 32:4012-4019

# SCLC U.S. Market Opportunity



Sources: SEER Cancer Stat Facts <https://seer.cancer.gov/statfacts/html/lungb.html>, accessed April 19, 2019; American Cancer Society, <https://www.cancer.org/cancer/small-cell-lung-cancer/about/what-is-small-cell-lung-cancer.html>, accessed April 12, 2019; Kantar Health Treatment Architecture SCLC July 2018; Jazz primary market research May 2019



# U.S. SCLC Treatment Paradigm

	Extensive Stage, 1L	Limited Stage, 1L	2L
FDA Approved	<ul style="list-style-type: none"> <li>Platinum + etoposide + atezolizumab</li> </ul>		<ul style="list-style-type: none"> <li>Topotecan</li> </ul>
NCCN Guidelines <sup>1</sup> - Preferred regimens	<ul style="list-style-type: none"> <li>Carboplatin + etoposide + atezolizumab</li> <li>Carboplatin + etoposide + durvalumab</li> </ul>	<ul style="list-style-type: none"> <li>Cisplatin + etoposide +/- radiation</li> </ul>	<ul style="list-style-type: none"> <li>Relapse <math>\leq</math> 6 months: topotecan or clinical trial</li> <li>Relapse <math>&gt;</math> 6 months: original regimen (without I/O)<sup>2</sup></li> </ul>
NCCN Guidelines <sup>1</sup> - Other recommended regimens	<ul style="list-style-type: none"> <li>Carboplatin + etoposide</li> <li>Cisplatin + etoposide</li> <li>Useful under certain circumstances: cisplatin + irinotecan</li> </ul>		<ul style="list-style-type: none"> <li>Relapse <math>\leq</math> 6 months: multiple other chemos (gemcitabine, docetaxel, paclitaxel, irinotecan, CAV, vinorelbine, bendamustine or pembrolizumab)</li> </ul>

<sup>1</sup> NCCN v 2.2019

<sup>2</sup> For patients who relapse after  $>$  6 months of atezolizumab or durvalumab maintenance therapy, recommend re-treatment with carboplatin + etoposide alone or cisplatin + etoposide alone





## MOA & CLINICAL DATA OVERVIEW

ROB IANNONE, MD, MSCE  
EXECUTIVE VICE PRESIDENT, RESEARCH AND DEVELOPMENT



Jazz Pharmaceuticals®

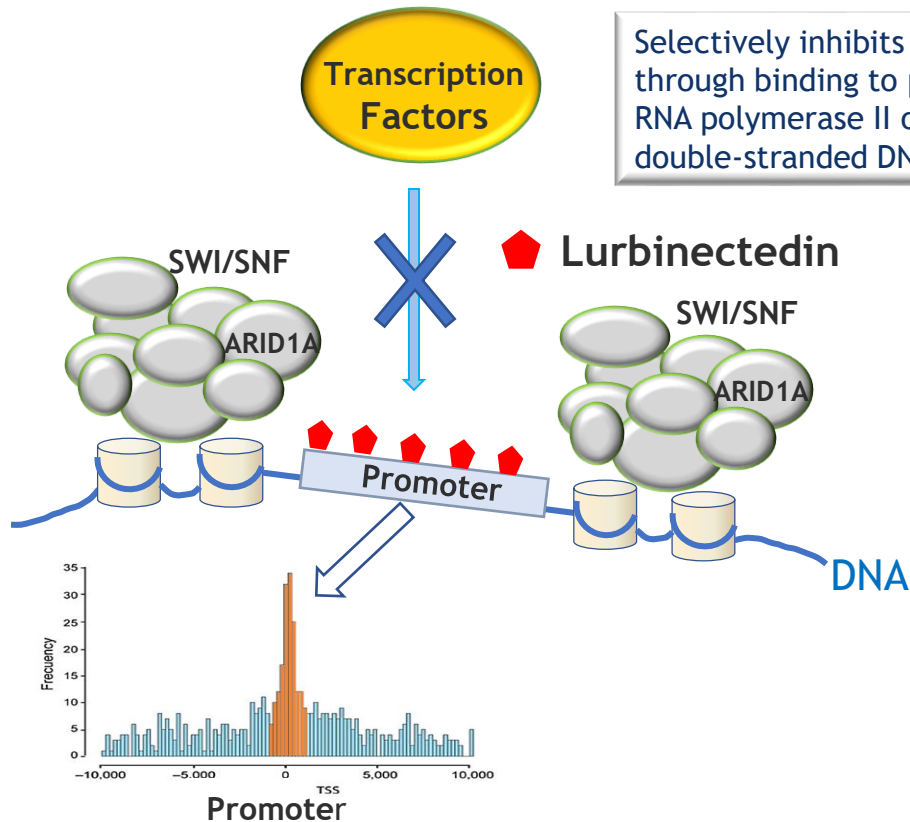


# Lurbinectedin MOA

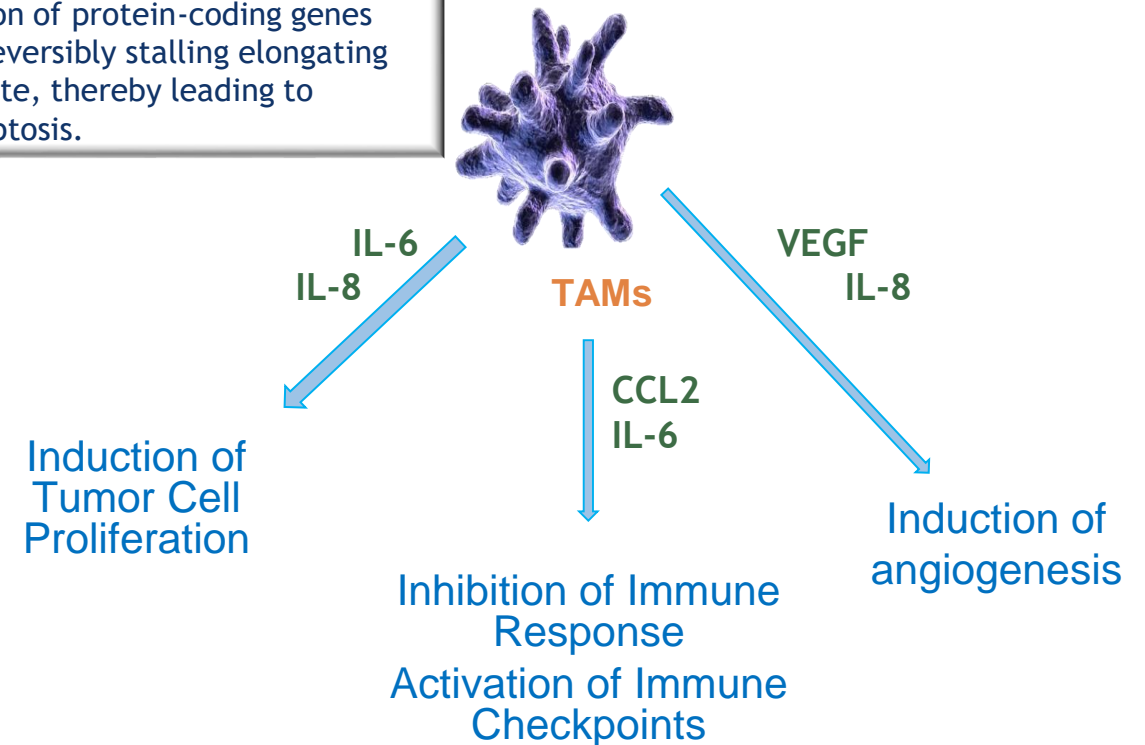
## A Selective Inhibitor of Oncogenic Transcription

Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors

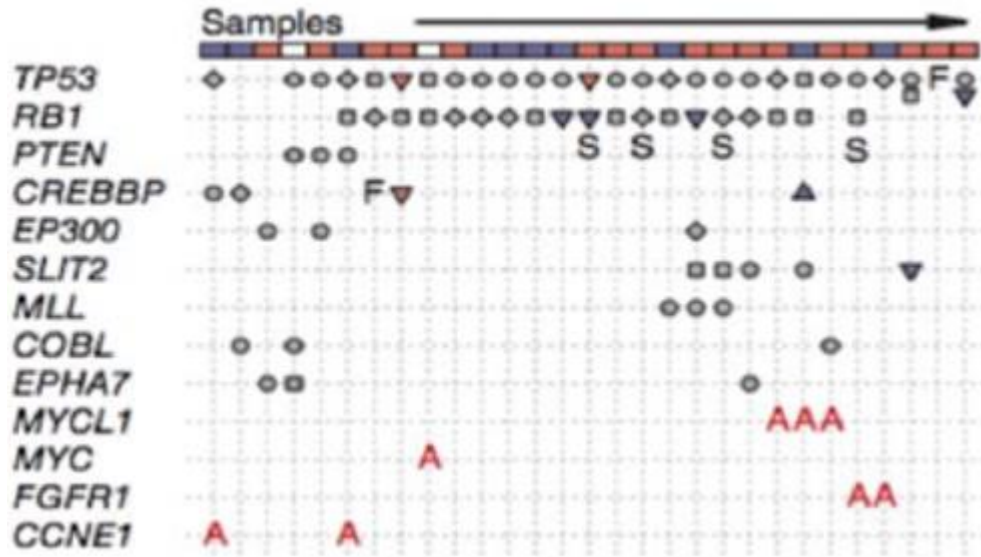
By inhibiting active transcription in Tumor Associated Macrophages (TAMs), lurbinectedin downregulates IL-6, IL-8, CCL2 and VEGF



Selectively inhibits active transcription of protein-coding genes through binding to promoters and irreversibly stalling elongating RNA polymerase II on the DNA template, thereby leading to double-stranded DNA breaks and apoptosis.



# Why is SCLC So Hard to Target?



Source: Peifer et al Nature Genetics 2012

- Most common genomic alterations are in tumor suppressor genes
  - Turning off an “off switch” is a real challenge

## Drug class failures 2L SCLC:

- Aurora Kinase
- BCL2
- C-Kit
- DLL-3
- EGFR
- FLT3
- HDAC
- IGF
- mTOR
- PD1
- Proteasome inhibitor
- VEGF

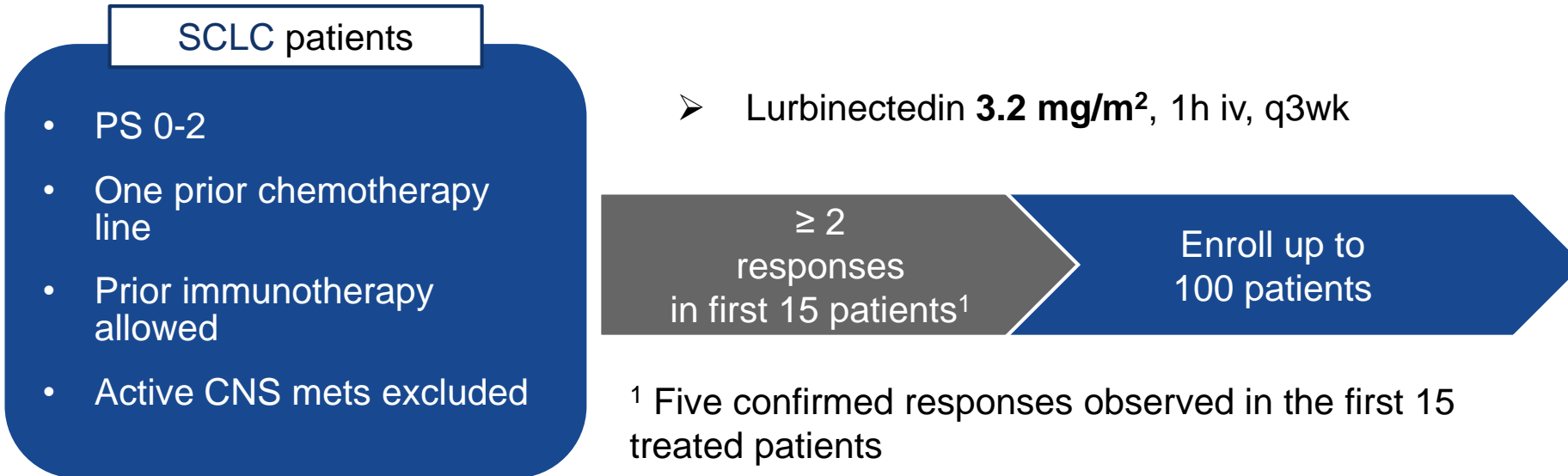
***“SCLC is difficult to treat in part because you can’t target an absent protein the way you can target a mutant protein—there’s nothing against which a drug can be directed”***

Source: Rudin C. Looking Ahead to New Therapies in Small Cell Lung Cancer. Clinical Advances to Hematology & Oncology 2018;16 (4): 269-272



# Lurbinectedin Monotherapy in 2L SCLC: Phase 2 Basket Trial Design

- Primary endpoint: ORR
- Secondary objectives: Duration of response; clinical benefit: response or stable disease (SD)  $\geq 4$  months; PFS; OS; safety



Data cutoff: January 15, 2019

## Statistical assumptions for SCLC cohort

- Null hypothesis:  $\leq 15\%$  response rate ( $p \leq 0.15$ )
- Alternative hypothesis:  $\geq 30\%$  response rate ( $p \geq 0.30$ )
- Statistical power 95%
- $\geq 23\%$  of confirmed responses required to reject the null hypothesis

# Lurbinectedin Phase 2 Study Patient Characteristics

		n=105
Age (years)	Median (range)	60 (40-83)
	≥ 65 years / ≥ 75 years	35.2% / 6.7%
Gender	Male / Female	60% / 40%
ECOG PS	0	36.2%
	1	56.2%
	2	7.6%
CNS metastases	History	3.8%
Liver metastases		41%
Prior lines of therapy	Median (range)	1 (1-2)
Prior immunotherapy	Single agent or in combination	7.6%
Response to prior platinum-based therapy	CR	8.6%
	PR	66.7%
	SD	18.1%
	PD/UNK	3.8% / 2.9%
Chemotherapy	Median, months (range)	3.5 (0-16.1)
CTFI	< 30 days (resistant)	20%
	30-89 days (resistant)	23%
	≥ 90 days (sensitive)	57%

# Lurbinectedin Demonstrates Evidence of Single Agent Anti-Tumor Activity

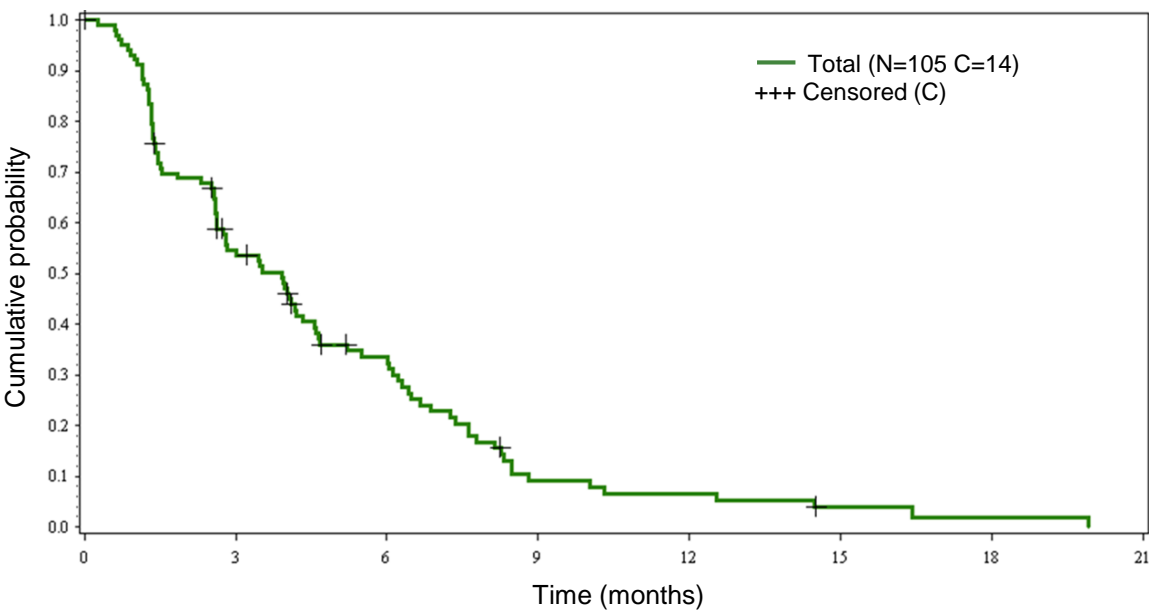
	Phase 2 Efficacy Results ASCO 2019 <sup>1</sup>		Phase 2 Efficacy Results by CTFI ≥ 30 days World Lung <sup>2</sup>		
	Overall (n=105)	Resistant CTFI < 90 days (n=45)	Overall (n=84)	CTFI 30-89 days (n=24)	CTFI ≥ 90 days (n=60)
ORR, % (95% CI)	35.2 <sup>3,4</sup> (26.2-45.2)	22.2 <sup>3</sup> (11.2-37.1)	40.5 (29.9-51.7)	29.2 (12.6-51.1)	45.0 (32.1-58.4)
PR, n (%)	37 (35.2)	10 (22.2)	34 (40.5)	7 (29.2)	27 (45.0)
SD	35 (33.3)	13 (28.9)	-	-	-
SD ≥ 4 months, n (%)	-	-	10 (11.9)	2 (8.3)	8 (13.3)
SD < 4 months, n (%)	-	-	15 (17.9)	1 (4.2)	14 (23.3)
PD, n (%)	28 (26.7)	18 (40.0)	22 (26.2)	12 (50.0)	10 (16.7)
Clinical benefit <sup>5</sup> (95% CI)	-	-	52.4 (41.2-63.4)	37.5 (18.8-59.4)	58.3 (44.9-70.9)
Disease Control Rate <sup>6</sup> , % (95% CI)	68.6 (58.8-77.3)	51.1 (35.8-66.3)	70.2 (59.3-79.7)	41.7 (22.1-63.4)	81.7 (69.6-90.5)
Duration of response (months), median (95% CI)	5.3 (4.1-6.4)	4.7 (2.6-5.6)	5.3 (3.5-6.4)	4.1 (2.6-5.3)	6.2 (3.5-7.3)
PFS months, median (95% CI)	3.9 (2.6-4.6)	2.6 (1.3-3.9)	-	-	4.6 (3.0-6.5)
OS months, median (95% CI)	9.3 (6.3-11.8)	5.0 (4.1-6.3)	-	-	11.9 (9.7-16.2)

<sup>1</sup> Source: Presented by Dr. Luis Paz Ares at the 2019 ASCO Annual Meeting; <sup>2</sup> Source: Poster P1.12-03. Presented at World Lung 2019. Lead author: J.M. Trigo Perez Hospital Universitario Virgen de la Victoria, Málaga, Spain; <sup>3</sup> 5 of 8 patients who failed prior immunotherapy had confirmed response; 3 of 5 patients with resistant disease and 2 of 3 patients with sensitive disease; <sup>4</sup> Tumor assessments performed every 2 cycles until cycle 6 and every 3 cycles thereafter; <sup>5</sup> Clinical benefit (%): ORR + SD ≥ 4 months; <sup>6</sup> Disease control rate: Response or SD

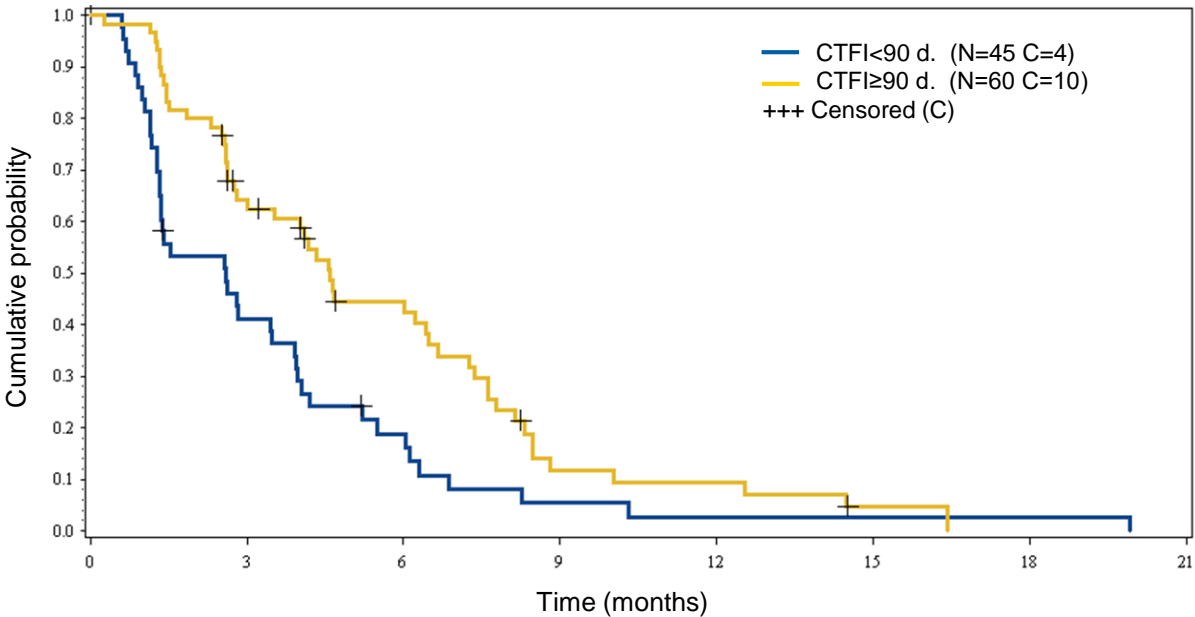


# Progression Free Survival Phase 2 Results

Overall Progression Free Survival



Progression Free Survival: Sensitive and resistant SCLC populations



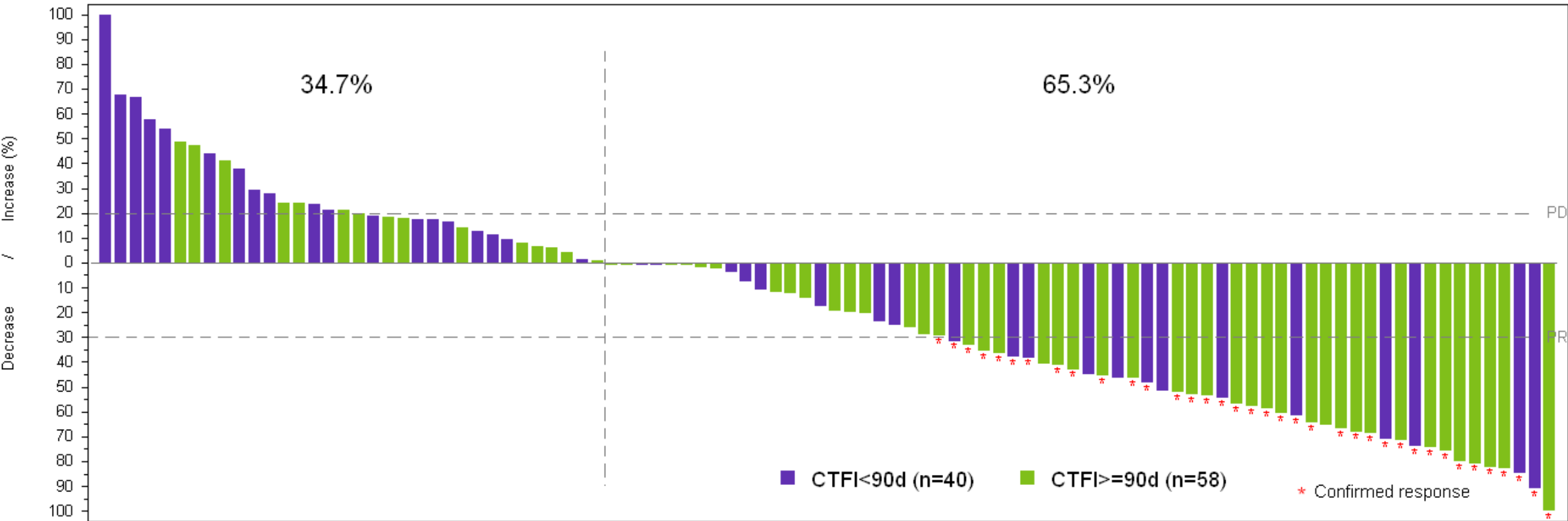
	Overall (n=105)	Resistant, CTFI < 90 days (n=45)	Sensitive, CTFI ≥ 90 days (n=60)
PFS months, median, (95% CI)	3.9 (2.6-4.6)	2.6 (1.3-3.9)	4.6 (3.0-6.5)
PFS at 6 months, %, (95% CI)	33.6 (24.0-43.1)	18.8 (6.8-30.9)	44.6 (31.2-57.9)

Source: Presented by Dr. Luis Paz Ares at the 2019 ASCO Annual Meeting

# Lurbinectedin for Relapsed Small Cell Lung Cancer

## Data from Phase 2 Monotherapy Basket Trial

Decrease in Tumor Size in 65% of Patients



# Lurbinectedin Phase 2 Monotherapy Safety Data – ASCO 2019

## Well-Tolerated AE Profile

### Safety: Related or Unknown Events

n=105	n (%)
AEs	89 (84.8)
- Gr ≥ 3	36 (34.3)
SAEs	11 (10.5)
AEs leading to death	0 (0.0)
AEs leading to treatment discontinuation	2 (1.9)
Dose delays treatment related	21 (22.1) <sup>1</sup>
Dose reductions <sup>2</sup>	25 (26.3) <sup>1</sup>
G-CSF	23 (21.9)
Transfusions (red blood cells and/or platelets)	10 (9.5)

### Treatment Related (or Unknown) Adverse Events (AEs) (>5% or Gr 3-4)

	n=105	GR 1-2	GR 3-4
		n (%)	n (%)
<b>Hematological AEs<sup>3</sup></b>	Neutropenia	6 (5.7)	24 (22.9)
	Anemia	2 (1.9)	7 (6.7)
	Thrombocytopenia	2 (1.9)	5 (4.8)
<b>Non-Hematological AEs</b>	Febrile neutropenia	-	5 (4.8)
	Fatigue	54 (51.4)	7 (6.7)
	Nausea	34 (32.4)	-
	Decreased appetite	22 (21.0)	-
	Vomiting	19 (18.1)	-
	Diarrhea	13 (12.4)	1 (1.0)
	Constipation	10 (9.5)	-
	Pneumonia	-	2 (1.9)
	Alanine aminotransferase increased <sup>3</sup>	-	2 (1.9)
	Skin ulcer	-	1 (1.0)

<sup>1</sup> Based on 95 patients who received ≥ 2 cycles of treatment

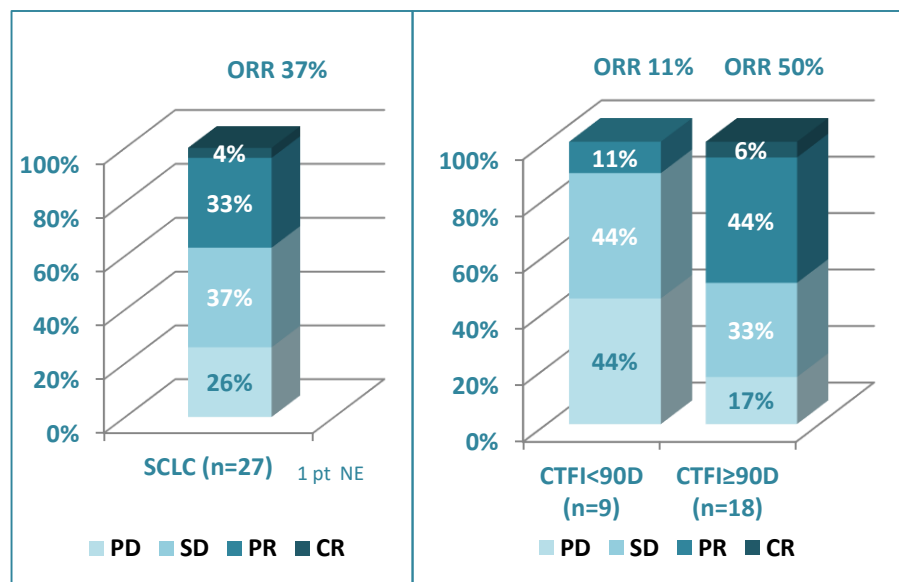
<sup>2</sup> Per protocol: dose had to be reduced in case of grade 4 neutropenia

<sup>3</sup> Lab abnormalities associated with a specific treatment, were considered a SAE, or were reasons for dose reduction or treatment delay

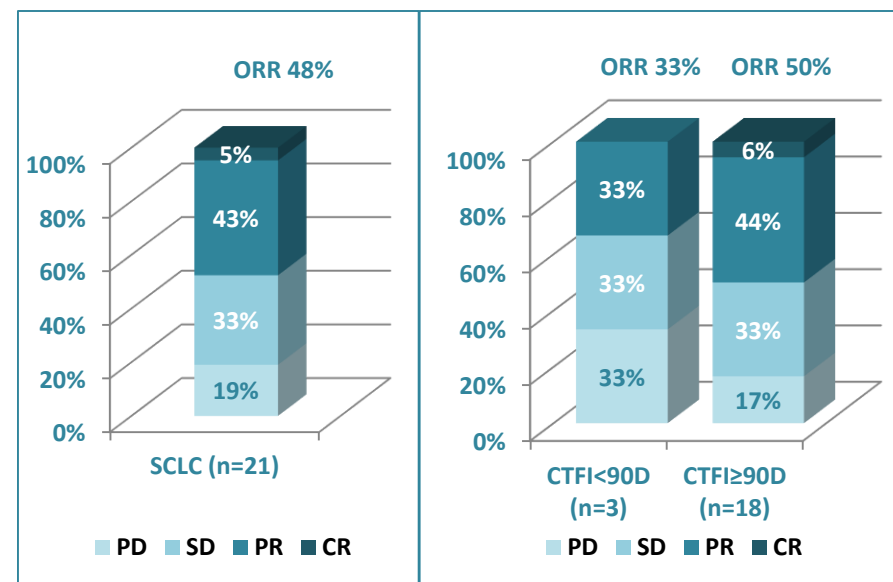


# Lurbinectedin + Doxorubicin in Relapsed SCLC Phase 1b Data

**Cohort B: Objective responses in SCLC and according to Chemotherapy-free interval (CTFI) (sensitive vs resistant)**



**Cohort B: Objective responses in SCLC excluding pts with CTFI < 30 days and according to Chemotherapy-free interval (CTFI) (sensitive vs resistant)**

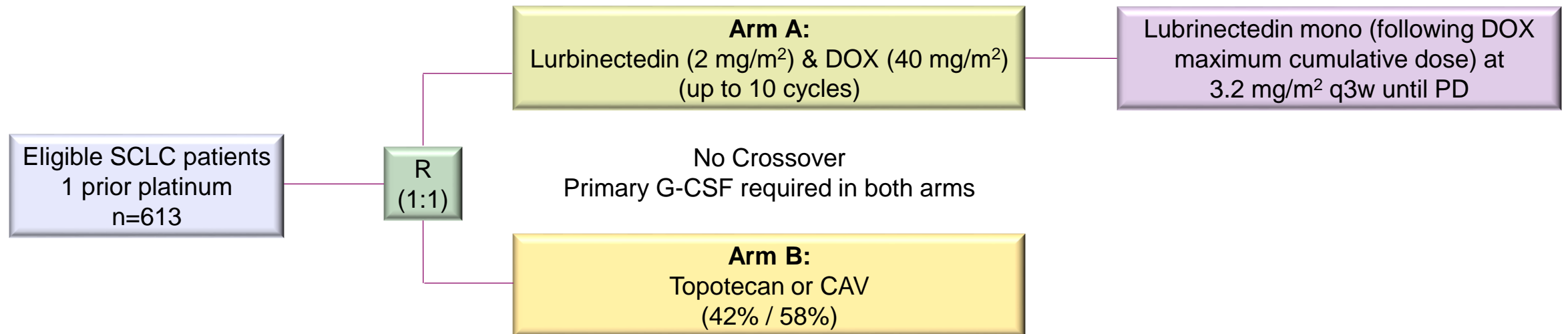


- Main hematological toxicity was myelosuppression; well-managed with G-CSF and dose reductions
- Hematological adverse events included: GR3/4 neutropenia, thrombocytopenia and febrile neutropenia were 25%/68%, 7%/11% and 7%/7%, respectively, and GR3 anemia was 21%

# ATLANTIS Phase 3 Combination Study in Relapsed SCLC

## Unique Study Design with Monotherapy Maintenance Arm Following Combination Therapy

- Randomized clinical trial of lurbinectedin + doxorubicin vs topotecan or CAV in relapsed SCLC
- Primary endpoint: median OS HR  $\leq 0.75$  with 90% power at ~510 events (control arm modeled for ~7.5 months)
- Secondary endpoint: PFS by an Independent Review Committee



# Development/Regulatory Summary

---

## **Phase 2 basket study**

- NDA submitted December 2019 under accelerated approval regulations
- Priority review requested with submission
- FDA submission acceptance decision expected February 2020
- Potential for approval and launch in 2020

## **ATLANTIS current status:**

- Five safety analyses successfully completed (IDMC)
- Target enrollment reached July 2018
- 613 patients recruited in >150 centers; 20 countries; EU & North America accounts ~ 90%
- Data anticipated mid-2020





# COMMERCIAL INITIATIVES

MIKE MILLER  
EXECUTIVE VICE PRESIDENT, U.S. COMMERCIAL



Jazz Pharmaceuticals®

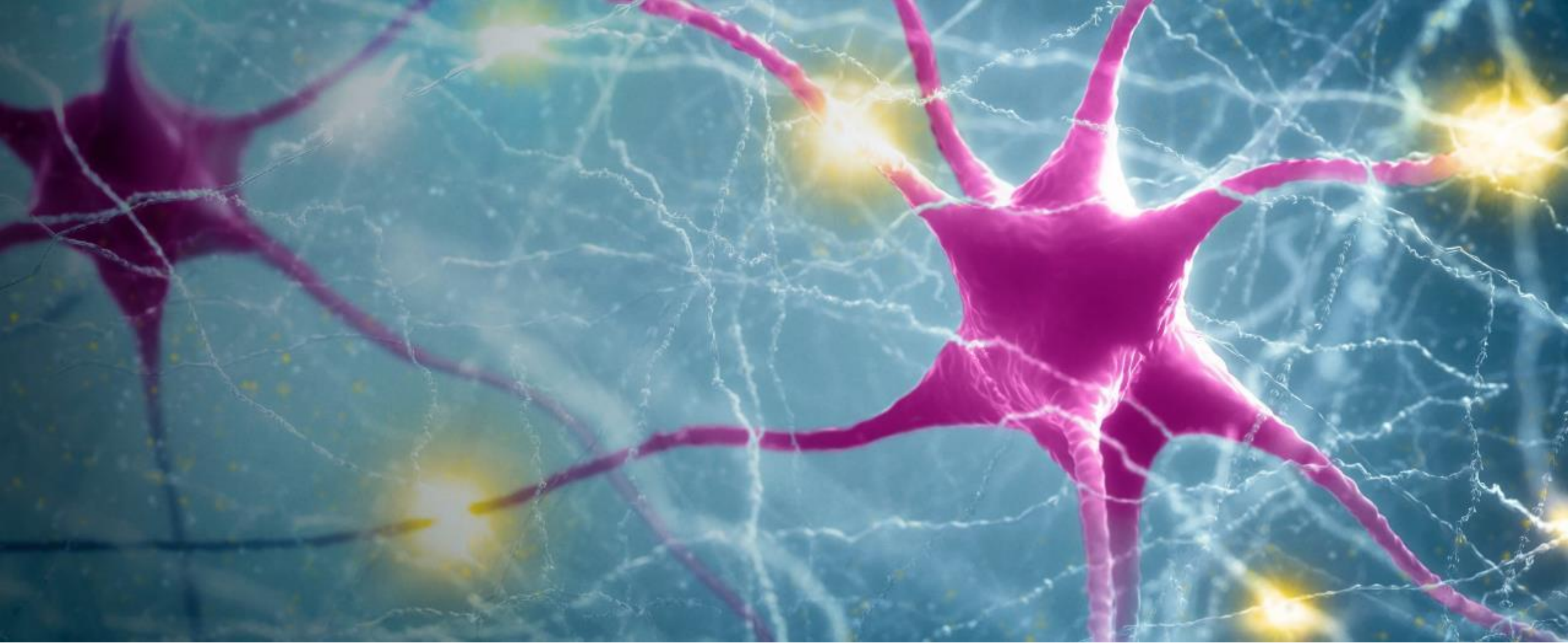


# Commercial Initiatives

Preparing for U.S. Approval and Launch in 2020

Highlight differentiated attributes of efficacy, tolerability and administration profile





## Appendix



# Glossary of Abbreviations

1L, 2L, 3L = First, Second, Third-Line Treatment  
AE = Adverse Event  
API = Active Pharmaceutical Ingredient  
ASCO = American Society of Clinical Oncology annual meeting  
CAV = Cyclophosphamide/Doxorubicin/Vincristine  
CI = Confidence Interval  
CNS = Central Nervous System  
CR = Complete Response  
CTFI = Chemotherapy Free Interval  
DNA = Deoxyribonucleic Acid  
DoR = Duration of Response  
DOX = Doxorubicin  
ECOG = Eastern Cooperative Oncology Group  
ES SCLC = Extensive-Stage Small-Cell Lung Cancer  
EU = European Union  
FDA = U.S. Food and Drug Administration  
GPO = Group Purchasing Organization  
GR = Grade  
G-CSF = Granulocyte Colony-Stimulating Factor  
HR = Hazard Ratio  
HSR = Hart-Scott-Rodino Act  
IDMC = Independent Data Monitoring Committee  
I/O = Immuno-Oncology

IP = Intellectual Property  
IPR&D = In-Process Research and Development  
LS SCLS = Limited-Stage Small-Cell Lung Cancer  
MOA = Mechanism of Action  
MSL = Medical Science Liaison  
NCCN = National Comprehensive Cancer Network  
NCE = New Chemical Entity  
NDA = New Drug Application  
NSCLC = Non-Small Cell Lung Cancer  
Onc = Oncology  
ORR = Overall Response Rate  
OS = Overall Survival  
PD = Progressive Disease  
PD-L1 = Programmed Death-Ligand 1  
PFS = Progression Free Survival  
PR = Partial Response  
PS = Performance Status  
RNA = Ribonucleic Acid  
SAE = Serious Adverse Event  
SCLC = Small-Cell Lung Cancer  
SD = Stable Disease  
SOC = Standard of Care  
UNK = Unknown

# Topotecan Efficacy & Safety in 2L SCLC

Select Efficacy Parameters

Efficacy	Overall (n=213)	Resistant CTFI < 90 days (n=93)	Sensitive CTFI ≥ 90 days (n=120)
ORR, %	16.9	9.4	23.1
OS months, median (95% CI)	7.8 (6.6-8.5)	5.7 (4.1-7.0)	9.9 (8.5-11.5)
PFS months, median (95% CI)	3.5 (2.9-4.2)	2.6 (1.8-3.3)	4.3 (3.8-5.4)

Select Hematological AEs

Safety	Overall (n=197)
Neutropenia, G3-4, %	53.8
Thrombocytopenia, G3-4, %	54.3
Anemia, G3-4, %	30.5

Source: von Pawel et al. J Clin Oncol 32:4012-4019