



ZEPZELCA INVESTOR UPDATE

JUNE 17, 2020



Jazz Pharmaceuticals®

Forward-Looking Statements

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

This slide deck and the accompanying oral presentation contain forward-looking statements, including, but not limited to, statements related to the Jazz Pharmaceuticals' expectations relating to the execution of a successful launch of Zepzelca, product availability and the timing thereof; the company's expectations relating to market opportunity, payor landscape, potential near-term revenues and growth prospects, and pricing and cost of treatment for Zepzelca; sales and development milestones under the licensing agreement between the company and PharmaMar and related potential future payments by the company to PharmaMar; and other statements that are not historical facts. These forward-looking statements are based on the company's 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: effectively launching and commercializing new products; obtaining and maintaining adequate coverage and reimbursement for the company's products; the scale, duration and evolving effects of the COVID-19 pandemic and resulting global economic, financial and healthcare system disruptions that could have an effect on the successful commercialization of new products; 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 March 31, 2020 and future filings and reports by the company. Other risks and uncertainties of which the company 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 made in this slide deck and the accompanying oral presentation 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 the company on its website or otherwise. The company 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

Kathee Littrell

VP, Investor Relations

Welcome/Opening comments

Bruce Cozadd

Chairman and Chief Executive Officer

Introduction

Jacob Sands, M.D.

Dana Farber Cancer Institute & Instructor of Medicine, Harvard Medical School

SCLC Disease Overview / Lurbinectedin Clinical Data

Anne Borgman, M.D.

VP, Therapeutic Area Head, Hematology/Oncology

Label Overview and MOA

Robert Iannone, M.D., M.S.C.E

EVP, Research & Development

Development Overview

Dan Swisher

President and Chief Operating Officer

Launch and Commercial Landscape

Renée Galá

EVP and Chief Financial Officer

Financial Overview

All

Q&A



INTRODUCTION

BRUCE COZADD
Chairman and
Chief Executive Officer

 **ZEPZELCA**[™]
(lurbinectedin) for injection 4 mg



Jazz Pharmaceuticals[®]

2020-2021: Multiple Value Drivers and Catalysts

Diversification, Expansion and Development Pipeline Advances

PRODUCT APPROVALS

Sunosi

- ✓ EDS in OSA & Narcolepsy (Europe)—Jan 2020

Zepzelca

- ✓ Relapsed SCLC (U.S.)¹—Jun 2020

JZP-258

- EDS & Cataplexy for Narcolepsy (U.S.); PDUFA July 21, 2020
- Expect to launch as early as 4Q20

JZP-458

- ALL (U.S.); Expect BLA submission as early as 4Q20

CORPORATE DEVELOPMENT

- **Expand portfolio** through multiple acquisitions or partnerships

DEVELOPMENT PIPELINE

Sleep/Neuroscience

JZP-258 for IH

- ✓ Completed Phase 3 enrollment 1Q20
- Top-line data

JZP-385

- Initiate Phase 2b 1H21

Hematology/Oncology

JZP-458 for ALL pivotal Phase 2/3

- Conduct IA at ~50 patients

Defitelio for prevention of acute GvHD

- Phase 2 top-line data 2H20

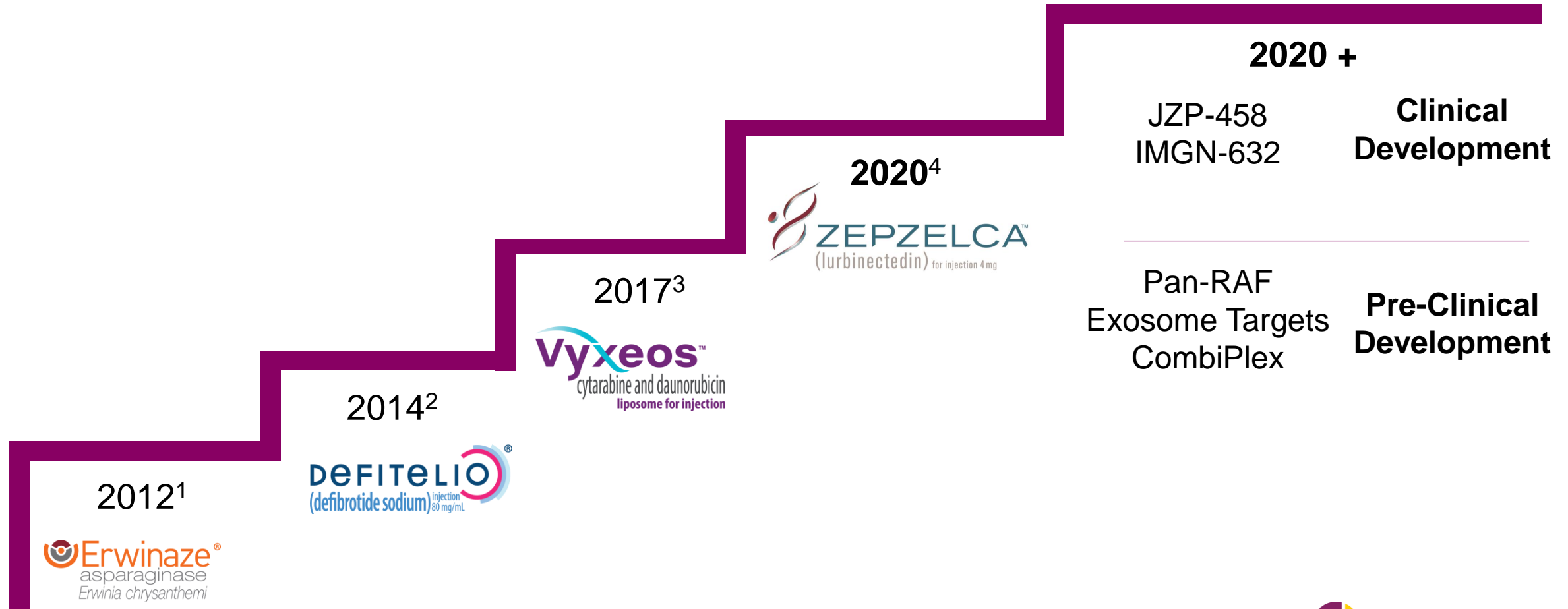
Zepzelca

- ATLANTIS Phase 3 top-line 2H20

¹ Exclusive U.S. license

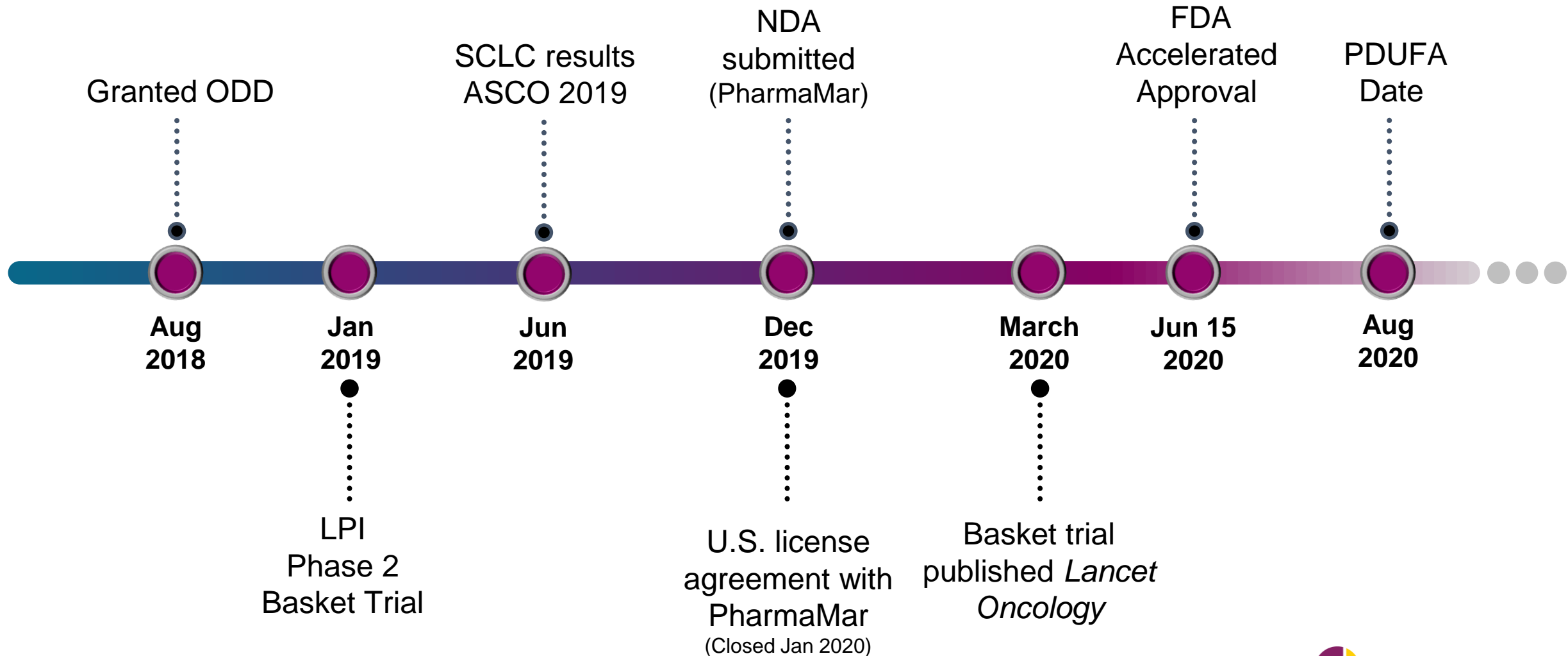
Strategic Evolution in Oncology to Improve Outcomes in Cancer

Focused Expansion Into Solid Tumors with Innovative Approaches



¹ Acquired in 2012 through acquisition of EUSA Pharma; ² EU approval 2014, U.S. approval 2016; ³ U.S. approval 2017, EU approval 2018; ⁴ U.S. accelerated approval, exclusive U.S. license

Rapid Path to FDA Approval



Zepzelca: Further Diversification of Our Commercial Portfolio

DIVERSIFY

- Expansion into solid tumors
- Meaningful revenue opportunity
- Synergistic with existing portfolio



COMMERCIAL EXECUTION

- Prioritized and expedited launch plan
- Expanded customer facing sales and medical teams
- Strong focus on patient access, GPO contracting and reimbursement

PARTNER OF CHOICE

- Strong collaboration with PharmaMar
- Prioritization of program
- Maximizing joint value generation

R&D CAPABILITIES

- Comprehensive development plan underway
- Leveraging broad oncology expertise



SCLC DISEASE LANDSCAPE

JACOB SANDS, M.D.

DANA-FARBER CANCER INSTITUTE

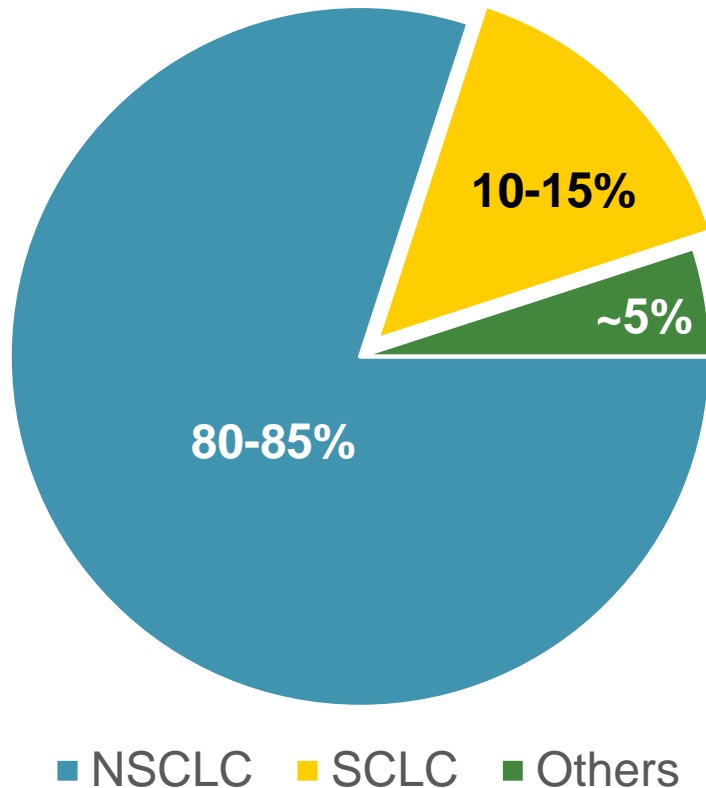
INSTRUCTOR OF MEDICINE, HARVARD MEDICAL SCHOOL



What is Small-Cell Lung Cancer (SCLC)

SCLC is Clinically and Pathologically Distinct from Other Types of Lung Cancer¹

Types of lung cancer¹



Characteristics of SCLC²

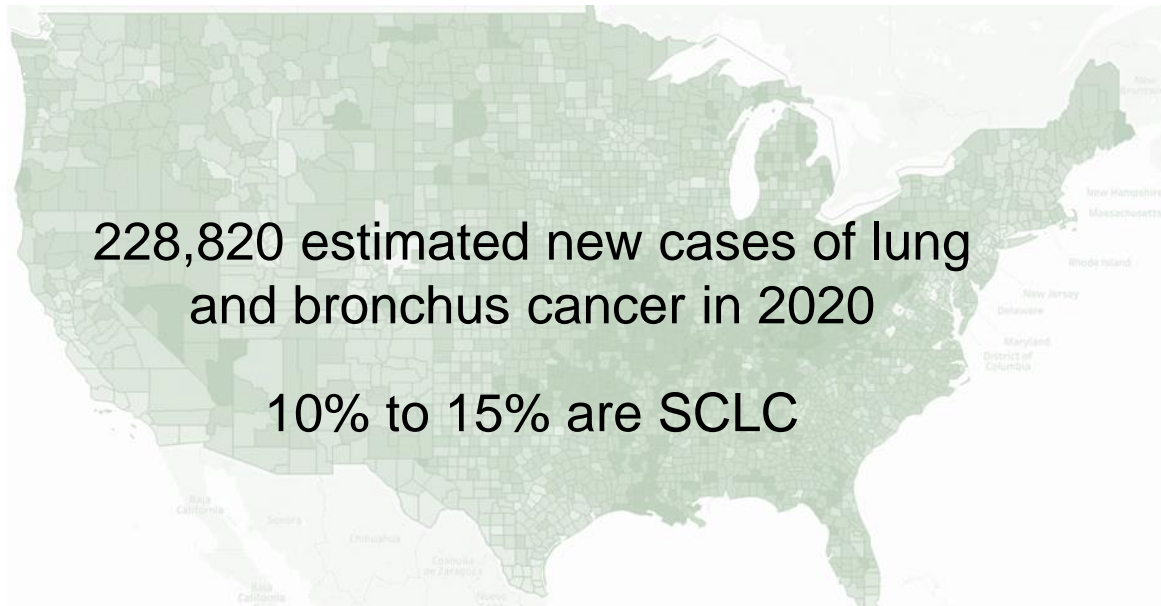
- Rapid doubling time
 - High growth fraction
 - Paraneoplastic syndromes
 - Early development of widespread metastases
-
- SCLC is a very aggressive cancer that is usually diagnosed at the extensive stage³
 - 5 year survival
 - Limited stage ranges from 20–40%⁴
 - Extensive stage <5%⁴
 - Extent of disease at diagnosis is indicative of prognosis⁵

¹ American Cancer Society. What is Lung Cancer? <https://www.cancer.org/cancer/lung-cancer/about/what-is.html>, ² Dowell JE, et al. In: Grippi MA, et al. eds. *Fishman's Pulmonary Diseases and Disorders*, Fifth Edition. New York, NY: McGraw-Hill; 2015, ³ American Cancer Society, <https://www.cancer.org/cancer/small-cell-lung-cancer/about/what-is-small-cell-lung-cancer.html>, ⁴ Nat Rev Clin Oncol. 2017 Sep 14(9) 549–561 ³ von Pawel et al. J Clin Oncol 32:4012-4019, ⁵ National Cancer Institute. Small cell lung cancer treatment (PDQ®) – health professional version. <https://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq>

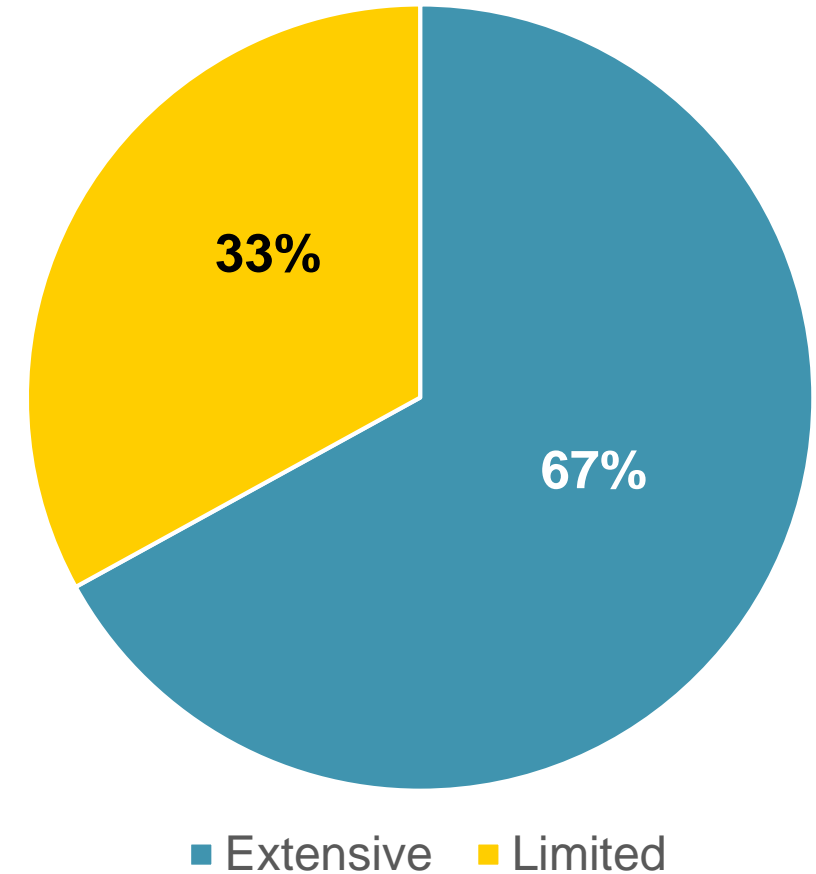
Majority of SCLC Patients Present with Extensive Stage at Diagnosis

~30,000 New SCLC Cases Annually in U.S.

U.S. 2020 Estimated Prevalence¹



SCLC Stage at Diagnosis¹



¹ American Cancer Society. What is Lung Cancer? <https://www.cancer.org/cancer/lung-cancer/about/what-is.html>,

SCLC Risk Factors

Smoking and Age are the Most Common Risk Factors

Tobacco exposure

- ~98% of SCLC patients are current or former smokers (vs 85% with NSCLC)¹
- SCLC is the type of lung cancer most strongly associated with smoking²

Older age³

- Incidence rate peaks between ages 70 and 84 years
- Very low incidence before age 50 years



Other risk factors⁴

- Family history of lung cancer
- Environmental air pollution
- Radiation exposure from therapy, medical imaging tests, or workplace
- Occupational exposure to asbestos, arsenic, chromium, beryllium, nickel, and other agents
- HIV infection
- Exposure to second-hand smoke
- Beta carotene supplements in heavy smokers

¹ Pelosof L, et al. *J Natl Cancer Inst.* 2017;109(7). doi: 10.1093/jnci/djw295, ² Kahnert K, et al. *Clin Lung Cancer.* 2016;17;325-333, ³ National Cancer Institute. SEER Cancer Statistics Review (CSR) 1975-2016. https://seer.cancer.gov/csr/1975_2016/, ⁴ National Cancer Institute. Small cell lung cancer treatment (PDQ®) – health professional version. <https://www.cancer.gov/types/lung/hp/small-cell-lung-treatment-pdq>,

Clinical Presentation of SCLC

Similar to That of Other Lung Cancers¹

Key Signs and Symptoms Due to Primary Tumor or Regional Lymphatic Metastases²

Worsening cough

Dyspnea

Pericardial effusion and tamponade

Hemidiaphragm elevation

Dysphagia

Hoarseness

Superior vena cava syndrome

Lymph node enlargement (Cervical or supraclavicular)

Chest pain

Key Signs and Symptoms Due to Extrathoracic Metastases²

Weight loss, fatigue

Bone pain, back pain

Muscle weakness, numbness

Loss of bowel / bladder control

Leptomeningeal carcinomatosis

Right upper quadrant pain, jaundice, fever

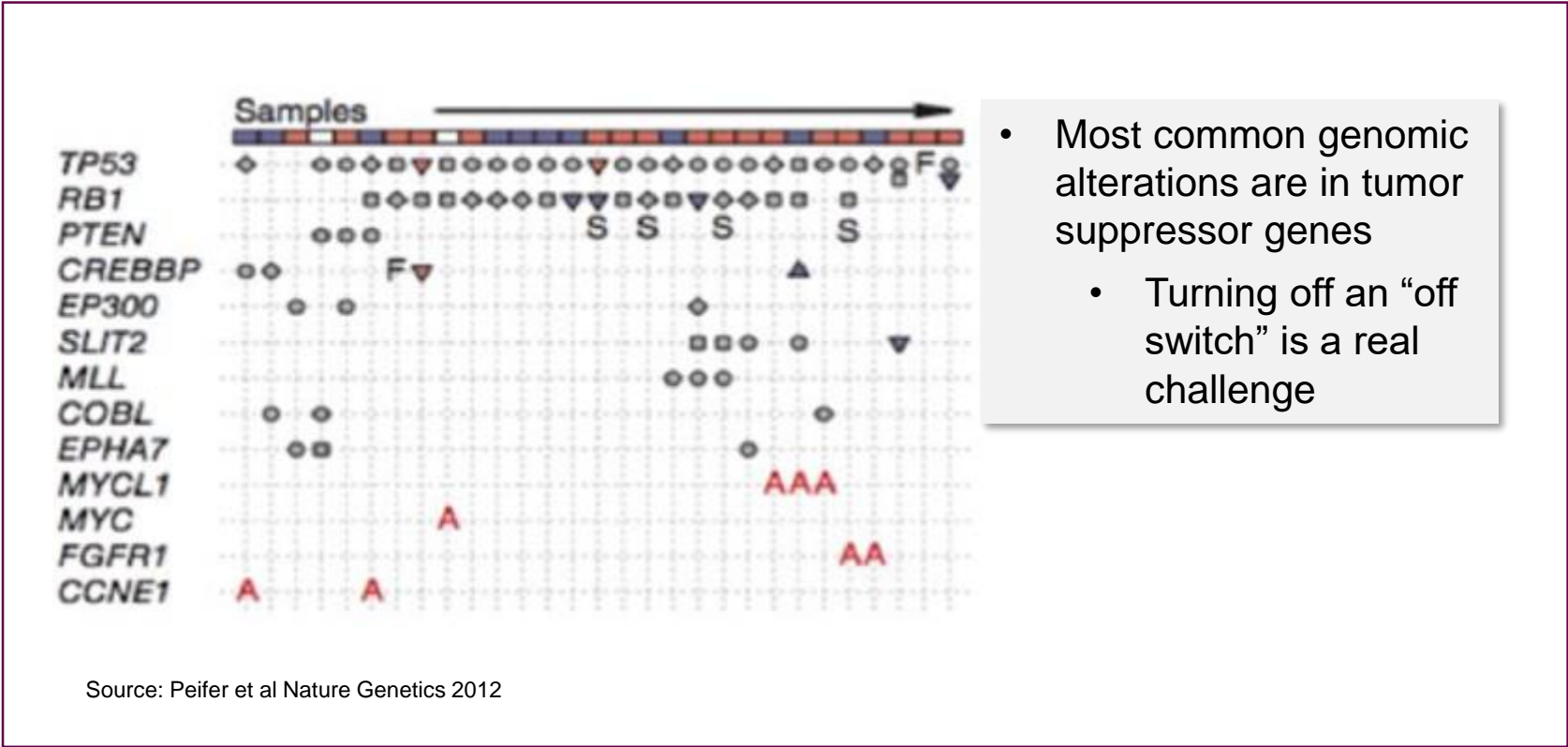
Headache

Confusion / slurred speech

Instability, lack of coordination

¹ Dowell JE, et al. In: Grippi MA, et al. eds. *Fishman's Pulmonary Diseases and Disorders*, Fifth Edition. New York, NY: McGraw-Hill; 2015, ² Kalemkerian GP, et al. *J Natl Compr Canc Netw*. 2018;16:1171–1182.

Why is SCLC So Hard to Target?



Source: Peifer et al Nature Genetics 2012

- Drug class failures 2L SCLC:**
- Aurora Kinase
 - BCL2
 - C-Kit
 - DLL-3
 - EGFR
 - FLT3
 - HDAC
 - IGF
 - mTOR
 - PD1
 - Proteosome 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

U.S. SCLC Treatment Paradigm

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

¹ NCCN v 2.2020

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



CLINICAL EVIDENCE FOR LURBINECTEDIN

JACOB SANDS, M.D.

DANA-FARBER CANCER INSTITUTE

INSTRUCTOR OF MEDICINE, HARVARD MEDICAL SCHOOL



Lurbinectedin Monotherapy in Metastatic SCLC

Trial Design

Multicenter study of single-agent lurbinectedin in patients with 9 different tumor types, including second-line SCLC (NCT02454972).

Patient eligibility (SCLC):

- ECOG PS 0-2
- One prior chemotherapy line
- Prior immunotherapy was allowed
- CNS metastases excluded

≥2 responses in
first
25 patients

Enroll up to
100 patients

Primary objective:
ORR by
investigator
assessment
(RECIST v.1.1)

Lurbinectedin 3.2 mg/m², 1 hour IV, q3wk

Prophylactic use of G-CSF was not permitted

¹ Trigo J, et al. *Lancet Oncol.* 2020

Lurbinectedin Phase 2 SCLC Study

Patient Baseline Characteristics

Characteristic	All patients (n = 105)
Age, median (range), years	60 (40-83)
Male sex, n (%)	63 (60)
ECOG PS, n (%)	
0-1	97 (92)
2	8 (8)
Abnormal LDH (>ULN), n/N (%)	47/104 (45)
Former/current smoker, n (%)	97 (92)
Disease stage at diagnosis	
Limited	32 (30)
Extensive	73 (70)
Number of sites at baseline, median (range)	3 (1-6)
Most common sites other than lung, n (%)	
Lymph nodes	86 (82)
Liver	43 (41)
CNS involvement, n (%) ^a	4 (4)

Characteristic	All patients (n = 105)
Number of prior lines, median (range)	1 (1-2)
1 line, n (%)	98 (93)
Prior agents, n (%)	
Platinum compounds	105 (100)
Immunotherapy	8 (8)
Prior radiotherapy	75 (71)
Best response to prior platinum, n (%)	
Complete response	9 (9)
Partial response	70 (67)
Stable disease	19 (18)
Progressive disease	4 (4)
CTFI, median (range), months	3.5 (0-16.1)
<90 days, n (%)	45 (43)
≥90 days, n (%)	60 (57)

¹ Trigo J, et al. *Lancet Oncol.* 2020 ^a Three patients had a history of CNS involvement; 1 patient had CNS metastases at baseline (protocol deviation).

Lurbinectedin Demonstrates Single Agent Anti-Tumor Activity

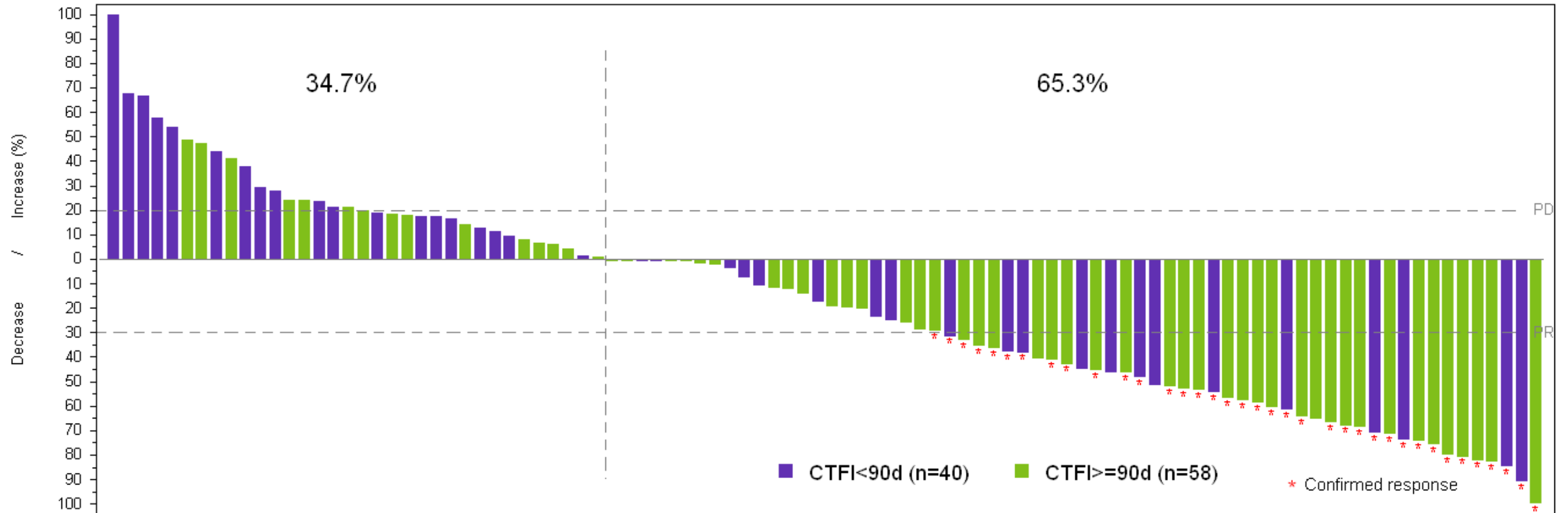
		Lurbinectedin SCLC Cohort ¹		
Patient population		All CTFI (n = 105)	CTFI < 90 days (n = 45)	CTFI ≥ 90 days (n = 60)
Investigator Assessed Response	Response rate (95% CI)	35% (26% - 45%)	22% (11% - 37%)	45% (32% - 58%)
	Median DoR (months) (95% CI)	5.3 (4.1 - 6.4)	4.7 (2.6 - 5.6)	6.2 (3.5 - 7.3)
IRC Assessed Response	Response rate (95% CI)	30% (22% - 40%)	13% (5% - 27%)	43% (31% - 57%)
	Median DoR (months) (95% CI)	5.1 (4.9 - 6.4)	4.8 (2.4 - 5.3)	5.3 (4.9 - 7.0)

¹ Lurbinectedin Prescribing Information

Change in Tumor Size in Patients With SCLC

Secondary Endpoint

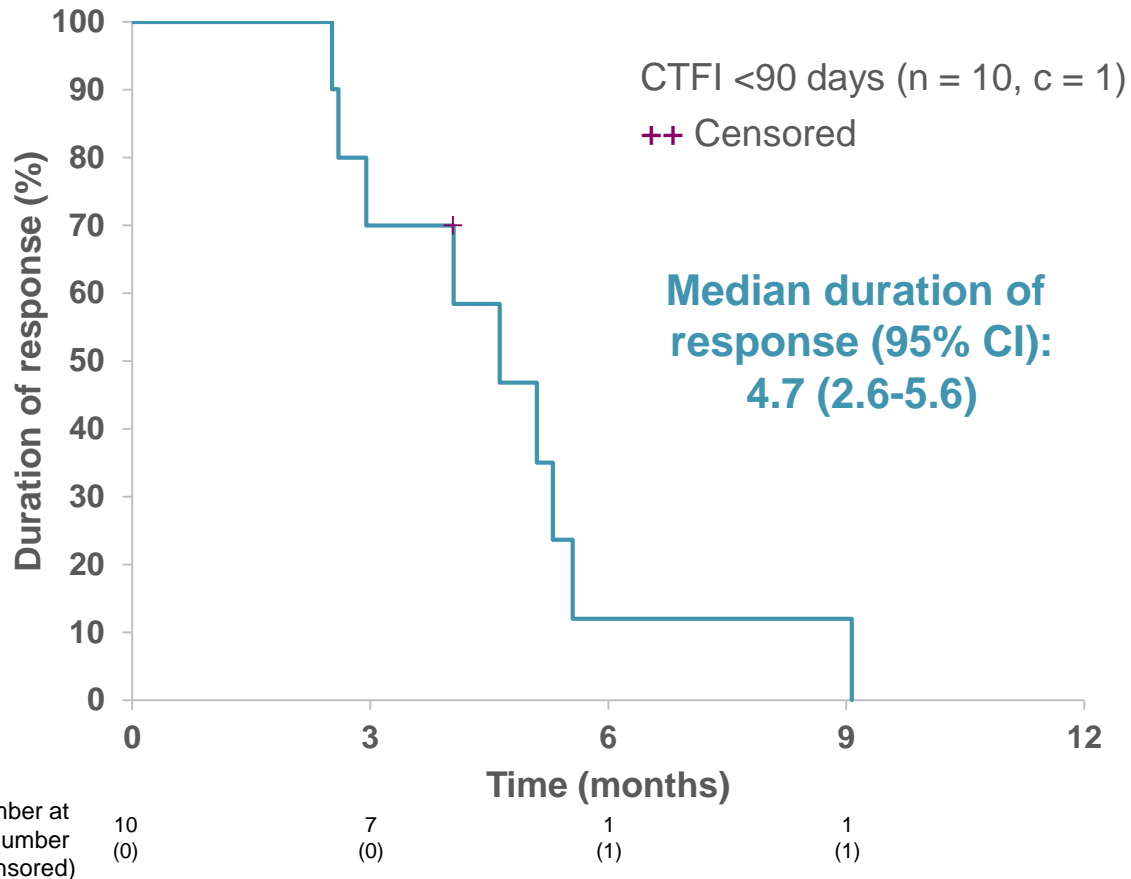
Decrease in Tumor Size in 65% of Patients



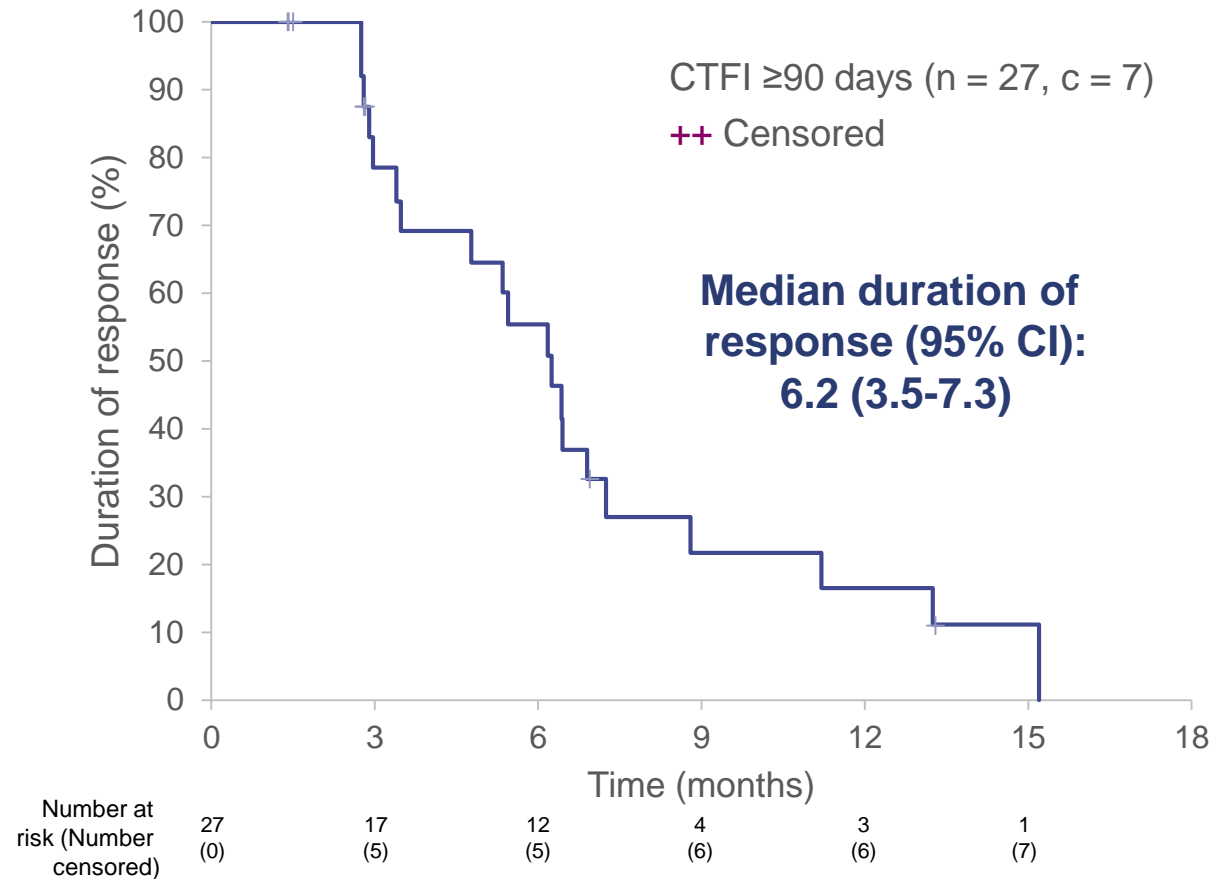
Duration of Response in Patients With SCLC

Secondary Endpoint

Patients with resistant disease (CTFI < 90 days)



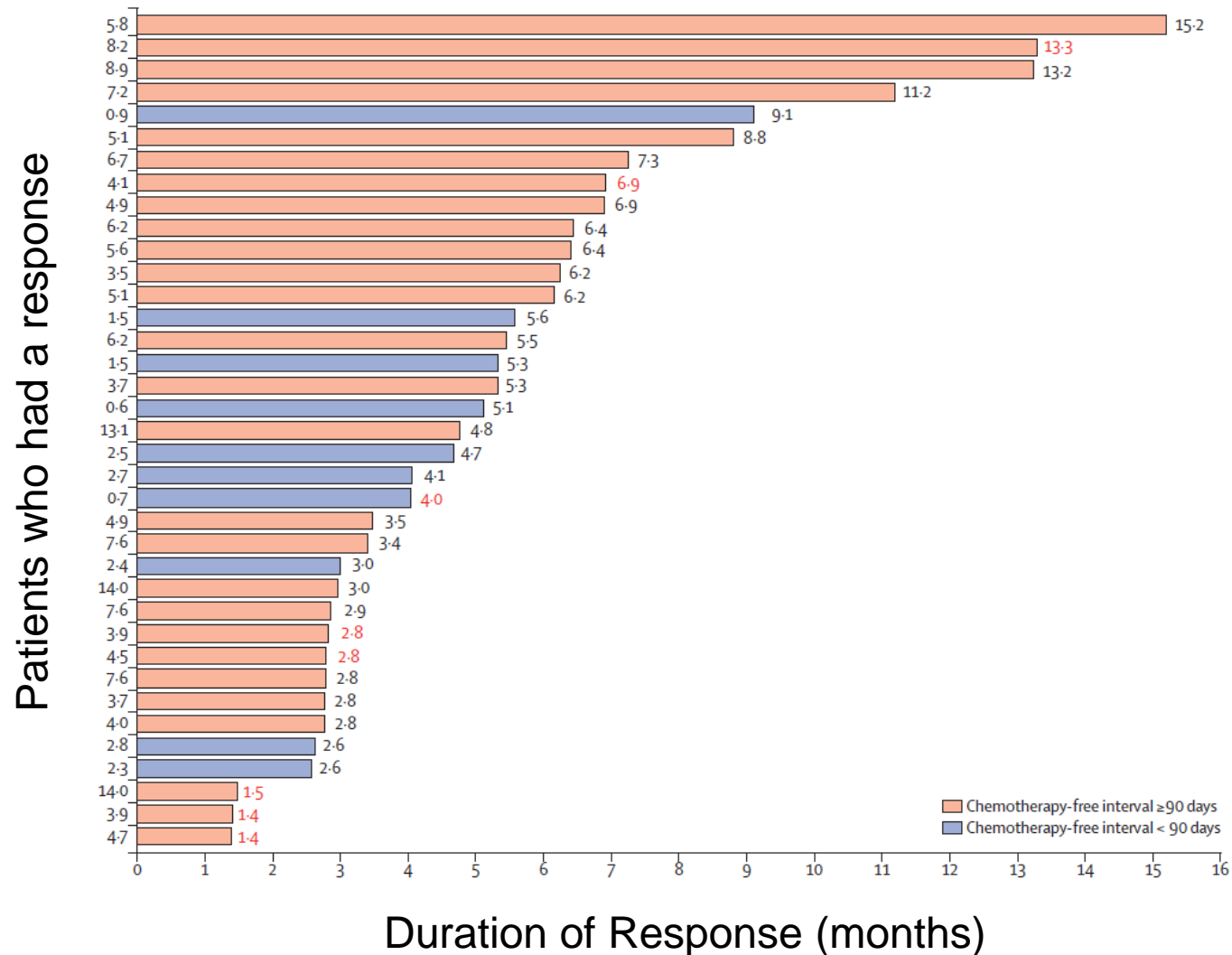
Patients with sensitive disease (CTFI ≥ 90 days)



¹ Trigo J, et al. *Lancet Oncol.* 2020
Based on Investigator Assessed Responses and using Kaplan Meier estimates

Duration of Response in Patients With SCLC

Of SCLC Patients Who Received Zepzelca, 29% Exposed for > 6 months and 6% Exposed > 1 Year



¹ Trigo J, et al. *Lancet Oncol.* 2020
 Based on Investigator Assessed Responses

Safety Profile in Patients With SCLC¹

No Grade 5 Adverse Reactions Reported

Adverse Reactions ≥ 10%		All Grades	Grade 3-4
General	Fatigue	77%	12%
	Pyrexia	13%	0
	Chest Pain	10%	0
Musculoskeletal ²	Musculoskeletal Pain	33%	4%
GI	Nausea	37%	0
	Constipation	31%	0
	Vomiting	22%	0
	Diarrhea	20%	4%
	Abdominal Pain	11%	1%
Metabolism and Nutrition Disorders	Decreased Appetite	33%	1%
Respiratory, Thoracic and Mediastinal Disorders	Dyspnea	31%	6%
	Cough	20%	0
Infections and Infestations	Respiratory tract infections	18%	5%
	Pneumonia	10%	7%
Nervous System Disorders	Peripheral Neuropathy	11%	1%
	Headache	10%	1%

¹ Lurbinectedin Prescribing Information, ² Musculoskeletal and Connective Tissue Disorders

Safety Profile in Patients With SCLC¹

Laboratory Abnormalities > 20% Worsening from Baseline		All Grades	Grade 3-4
Hematology	Decreased leukocytes	79%	29%
	Decreased lymphocytes	79%	43%
	Decreased hemoglobin	74%	10%
	Decreased neutrophils	71%	46%
	Decreased platelets	37%	7%
	<i>Febrile neutropenia</i> ²	5%	5%
Chemistry	Increased creatinine	69%	0
	Increased alanine aminotransferase	66%	4%
	Increased glucose	52%	5%
	Decreased albumin	32%	1%
	Decreased sodium	31%	7%
	Increased aspartate aminotransferase	26%	2%
	Decreased magnesium	22%	0

¹ Lurbinectedin Prescribing Information, ² Trigo J, et al. *Lancet Oncol.* 2020

Key Clinical Takeaways

- Lurbinectedin is active as single-agent in second line SCLC, ORR = 35%, median duration of response = 5.3 months¹
 - Platinum sensitive ORR = 45%, median duration of response = 6.2 months
 - Platinum resistant ORR = 22%, median duration of response = 4.7 months
- Lurbinectedin has a manageable and well-tolerated safety profile
 - Low rate of discontinuation: 1.9% due to adverse reactions
 - Low rate of Grade 3-4 anemia, neutropenia, thrombocytopenia and febrile neutropenia²
 - No Grade 5 adverse reactions reported
 - Dose reductions and interruptions due to adverse reactions occurred in 25% and 30.5% of patients, respectively

¹ Lurbinectedin Prescribing Information, investigator assessment ²Trigo J, et al. *Lancet Oncol.* 2020



LABEL OVERVIEW & MOA

ANNE BORGMAN, M.D.
VP, Hematology/Oncology

 **ZEPZELCA™**
(lurbinectin) for injection 4 mg



Jazz Pharmaceuticals®

Zepzelca™ (lurbinectedin) U.S. Prescribing Information

FDA Approval June 15, 2020

Indication	<p>ZEPZELCA is indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.</p> <p>This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).</p>
Dosage/ Administration	<p>The recommended dosage of ZEPZELCA is 3.2 mg/m² by intravenous infusion over 60 minutes every 21 days until disease progression or unacceptable toxicity.</p>
How Supplied	<p>For injection: 4 mg of lurbinectedin as a sterile, preservative-free, white to off-white lyophilized powder in a single-dose vial for reconstitution prior to intravenous infusion.</p>

Please see the full prescribing information at www.zepzelca.com



Zepzelca U.S. Prescribing Information

Tolerability and Warnings

Manageable Tolerability Profile

- Permanent discontinuation due to an adverse reaction occurred in two patients (1.9%)
- Dose reductions due to adverse reactions occurred in 25% of patients
- Dose interruptions due to adverse reactions occurred in 30.5% of patients

Warnings*

- No contraindications
- Myelosuppression
- Hepatotoxicity
- Embryo-Fetal toxicity

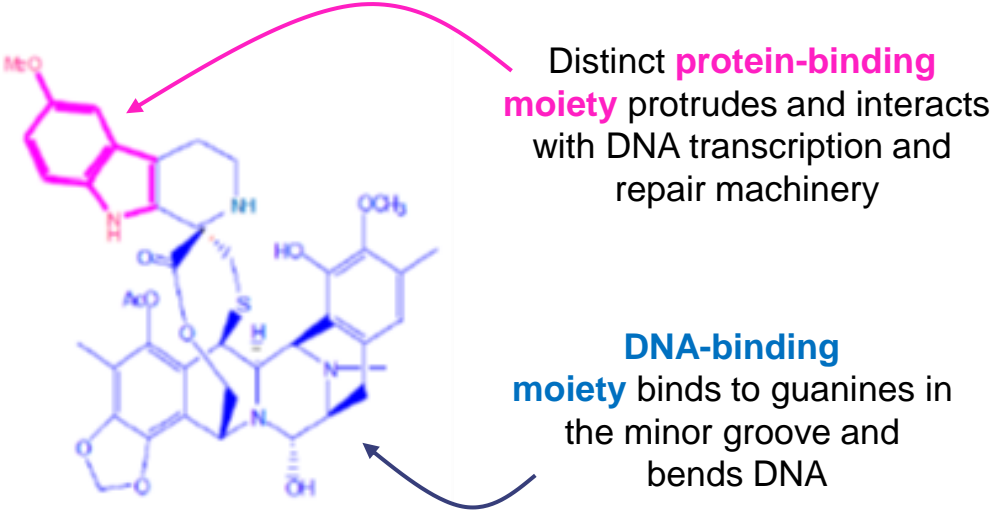
*Detailed information regarding warnings is available in the appendix and Zepzelca prescribing information

Zepzelca's Novel MOA

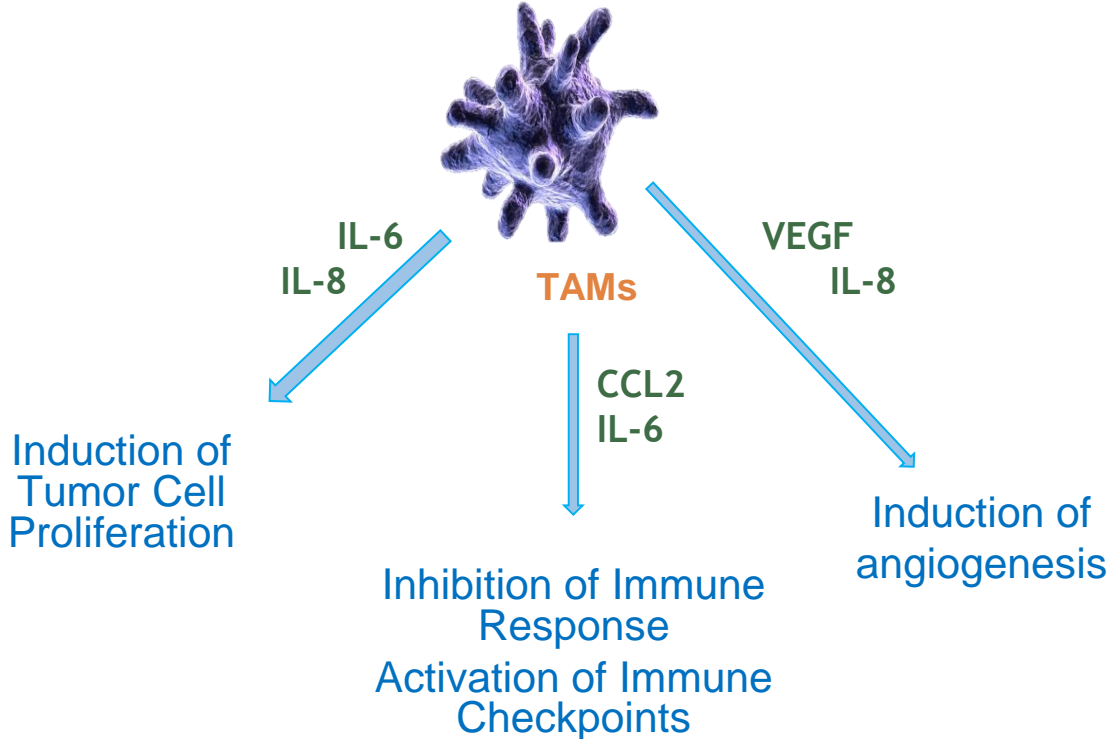
Cancer is frequently a transcriptional disease caused by deregulated oncogenic transcription factors¹

Lurbinectedin binds to GC-rich regulatory areas of gene promoters in minor groove of DNA, leading to:²

- Detachment of transcription factors and chromatin remodeling complexes from target promoters, and
- Degradation of RNA Pol II (not RNA Pol I/III) and blockade of trans-activated transcription



By inhibiting active transcription in Tumor Associated Macrophages (TAMs), lurbinectedin downregulates IL-6, IL-8, CCL2 and VEGF¹



¹ Presented by Dr. Luis Paz Ares at the 2019 ASCO Annual Meeting. Based on pre-clinical / animal models
² Nunez GS et al. *Mol Cancer Ther.* 2016;15(10):2399-2412.



DEVELOPMENT OVERVIEW

ROBERT IANNONE, M.D., M.S.C.E.
EVP, Research & Development

 **ZEPZELCA™**
(lurbinectedin) for injection 4 mg



Jazz Pharmaceuticals®

Antitumor Activity of Lurbinectedin and Doxorubicin in Relapsed SCLC from a Phase I Study

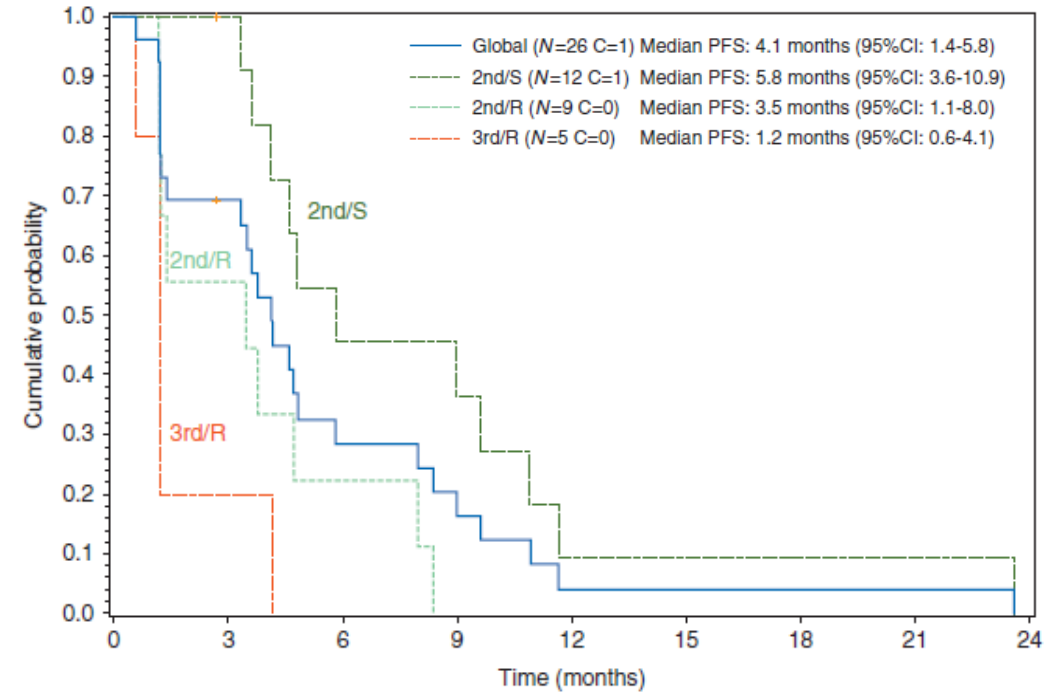
Lurbinectedin 4 mg (flat) plus Doxorubicin 50 mg/m² iv day 1 q3wks

	N	Response rate, %	Median PFS, mos
Overall	21	58*	4.1
2L, sensitive	12	91.7	5.8
2L, resistant	9	33.3	3.5
3L+	6	20	1.2

*2 CR; 13 PR

- Transient and reversible myelosuppression was the main toxicity
- Common AE (most < G3): fatigue (79%), N/V (58%), ↓ appetite (53%), mucositis (53%), alopecia (42%), D/C (42%), creatinine (68%), ALT/AST (42/32%)

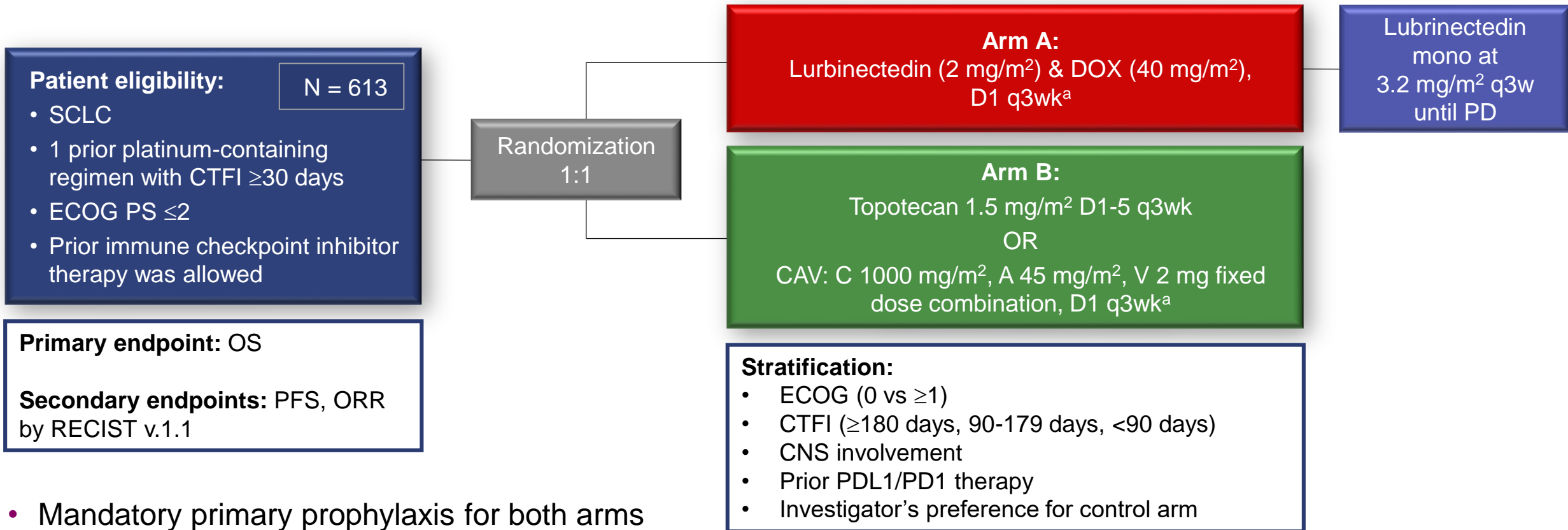
Progression Free Survival



ATLANTIS Trial

Phase 3 Randomized Study of Lurbinectedin and Doxorubicin in 2L SCLC – Expect Data 2H20

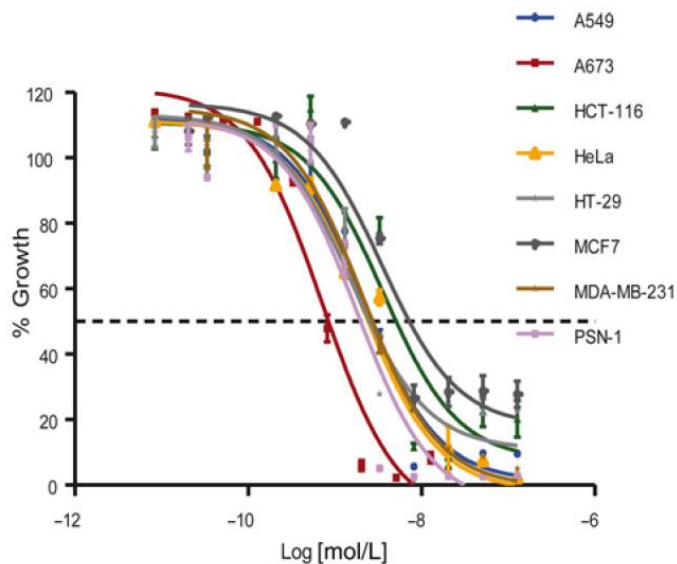
Open-label, randomized, Phase 3 trial of lurbinectedin in combination with doxorubicin versus investigator's choice chemotherapy (topotecan or CAV) in 2L SCLC



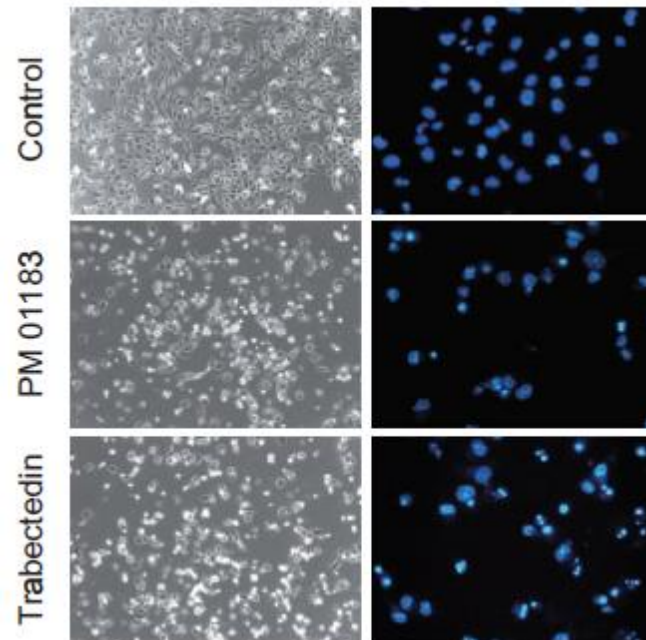
^a Maximum 10 cycles

Lurbinectedin Shows Preclinical Antitumor Activity Across Multiple Tumor Types

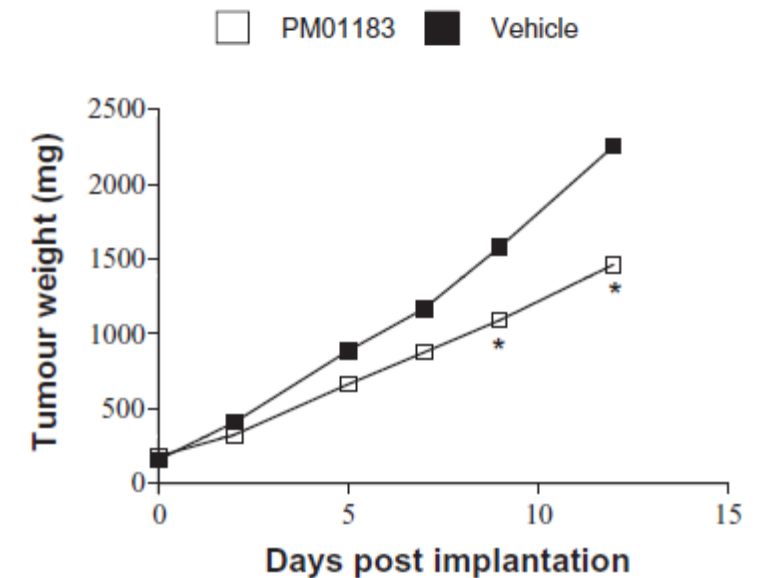
Lurbinectedin showed antiproliferative activity with IC_{50} values in the low nanomolar range in human lung (A549), Ewing sarcoma (A673), colon (HCT-116, HT-29), breast (MCF7, MDA-MB-231), cervix (HeLa), and pancreas (PSN-1) cancer cell lines¹



Exposure of A549 lung cancer cells to 150 nM lurbinectedin for 24 hours induced cell death by apoptosis²



Lurbinectedin (0.18 mg/kg in 3 consecutive weekly doses) showed statistically significant inhibition of tumor growth *in vivo* in an NCI-H460 lung xenograft model compared with vehicle-treated animals²



¹ Santamaría Nuñez G, et al. *Mol Cancer Ther.* 2016;15(10):2399-2412

² Leal JF, et al. *Br J Pharmacol.* 2010;161(5):1099-1110.

Phase 2 Trial: Lurbinectedin in Selected Advanced Solid Tumors

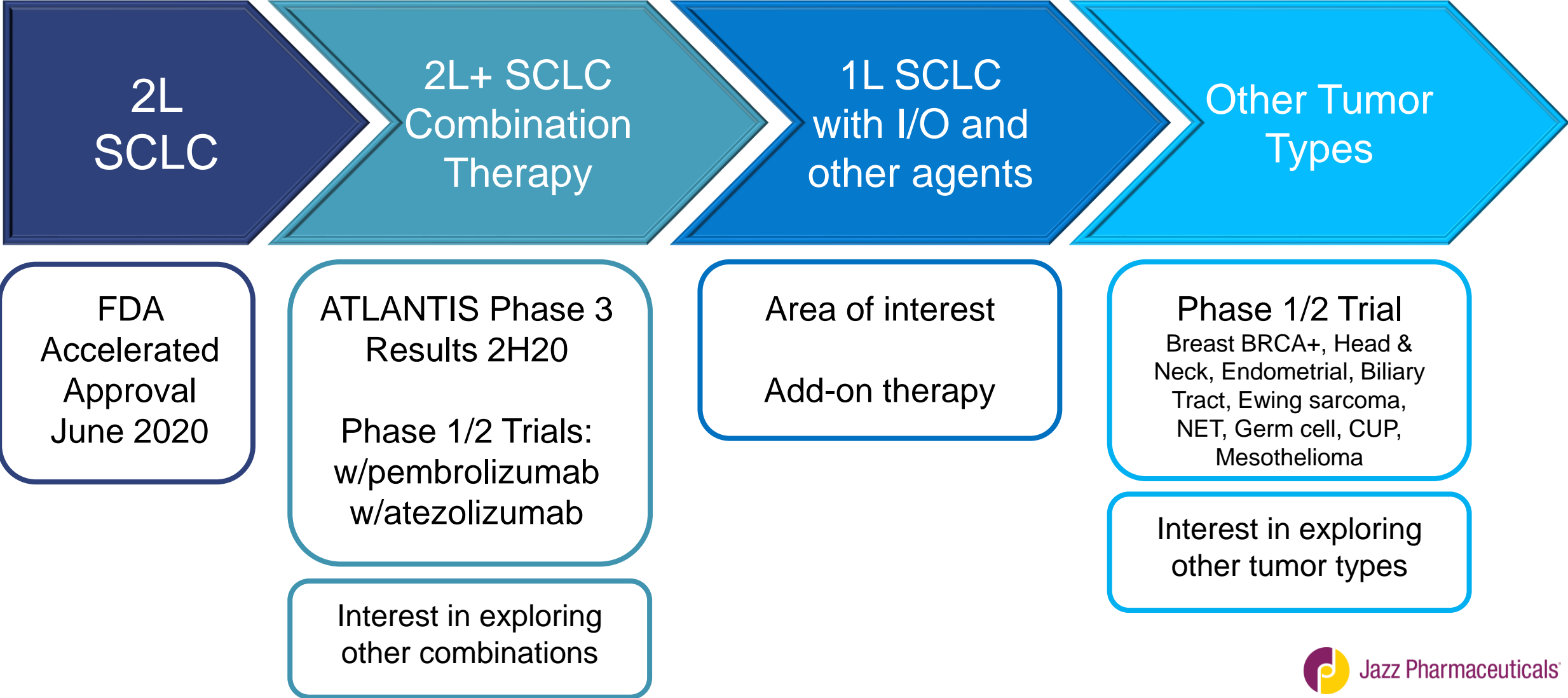
8 Other Tumor Types Being Studied

Tumor type	SCLC	Endo-metrial	NET	Biliary Tract	Head & Neck	CUP	Breast BRCA 1/2	Germ Cell Tumor	EFTs
Enroll	105	Up to 50	Up to 25 in each cohort						
Prior therapy	1 prior chemotherapy line	1 or 2 prior chemotherapy lines				1 – 3 prior chemo	No limit	Max 2 prior chemo	

Approved June 15

- Fully enrolled
- Estimated primary completion date: January 2021 (final data collection for primary outcome measure)
- Primary endpoint: Overall response rate
- Secondary endpoints: DoR, PFS, OS, Clinical Benefit

Lurbinectedin Future Development Opportunities





LAUNCH & COMMERCIAL LANDSCAPE

DAN SWISHER
President and
Chief Operating Officer

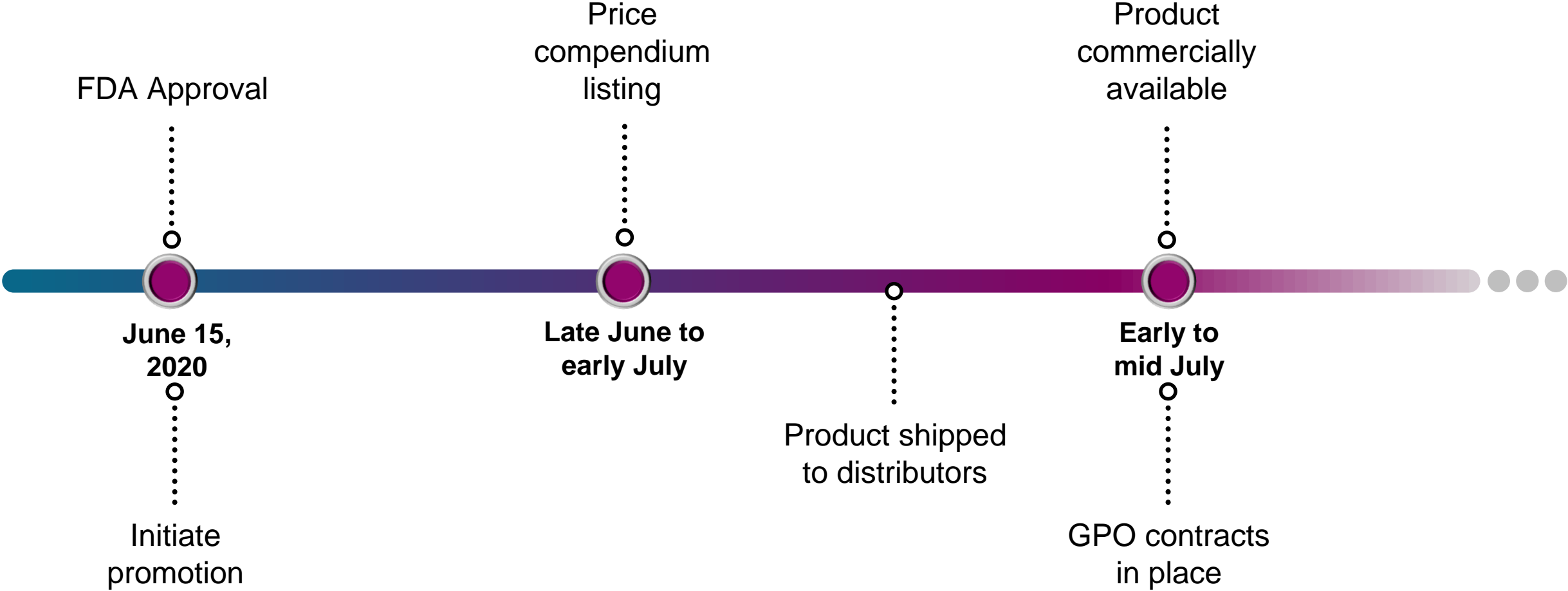
 **ZEPZELCA™**
(lurbinectedin) for injection 4 mg



Jazz Pharmaceuticals®

Zepzelca Key Events Timeline

U.S. Commercial Product Availability Goal Early July



Physicians Seeking Robust Options Following Platinum Therapy

1

**Treatment
Options for
Post-Platinum
Patients**

2

**Strong and
Durable
Response
Rates
in 2L+**

3

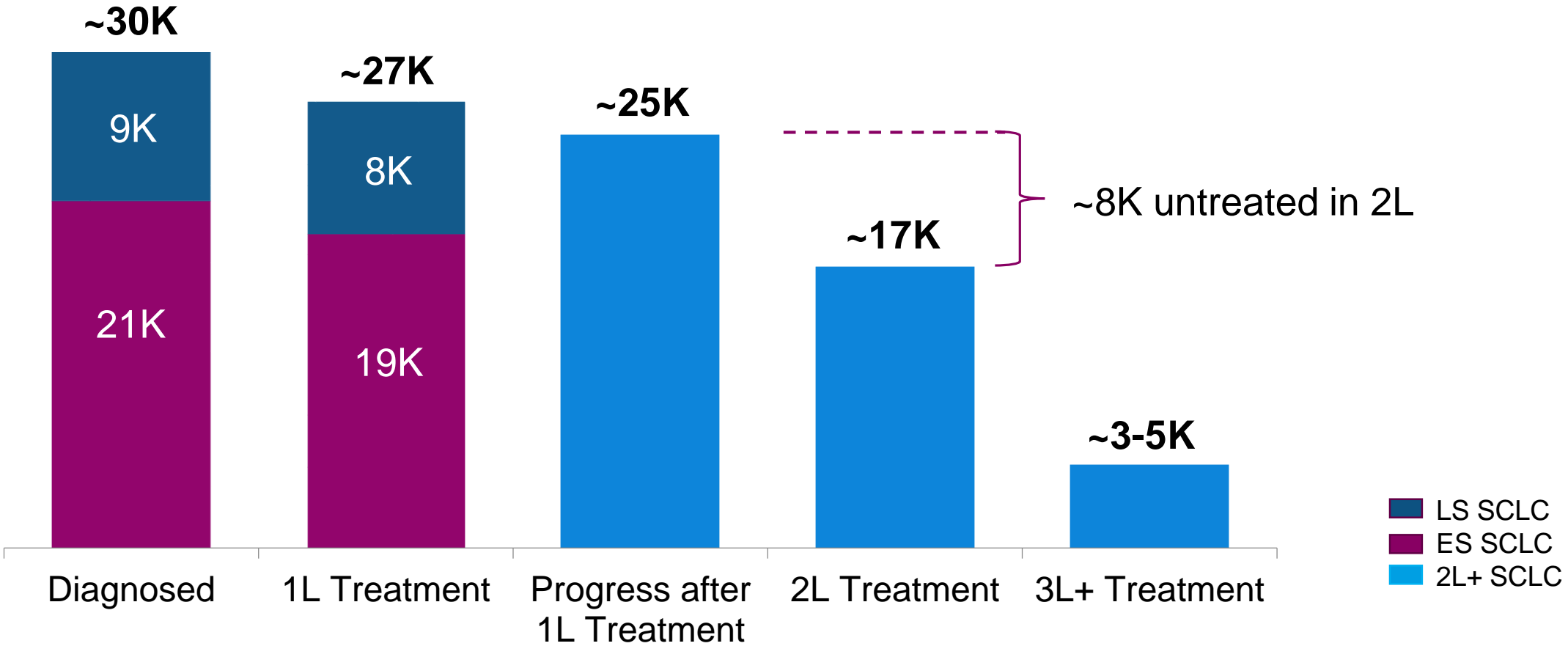
**Therapies
With Novel
MOAs in 2L+**

4

**Improved
Tolerability
and Ease of
Administration**

SCLC U.S. Market Opportunity

Of the ~17K 2L SCLC Patients, ~30% have CTFI < 90 days and ~70% have CTFI ≥ 90 days¹

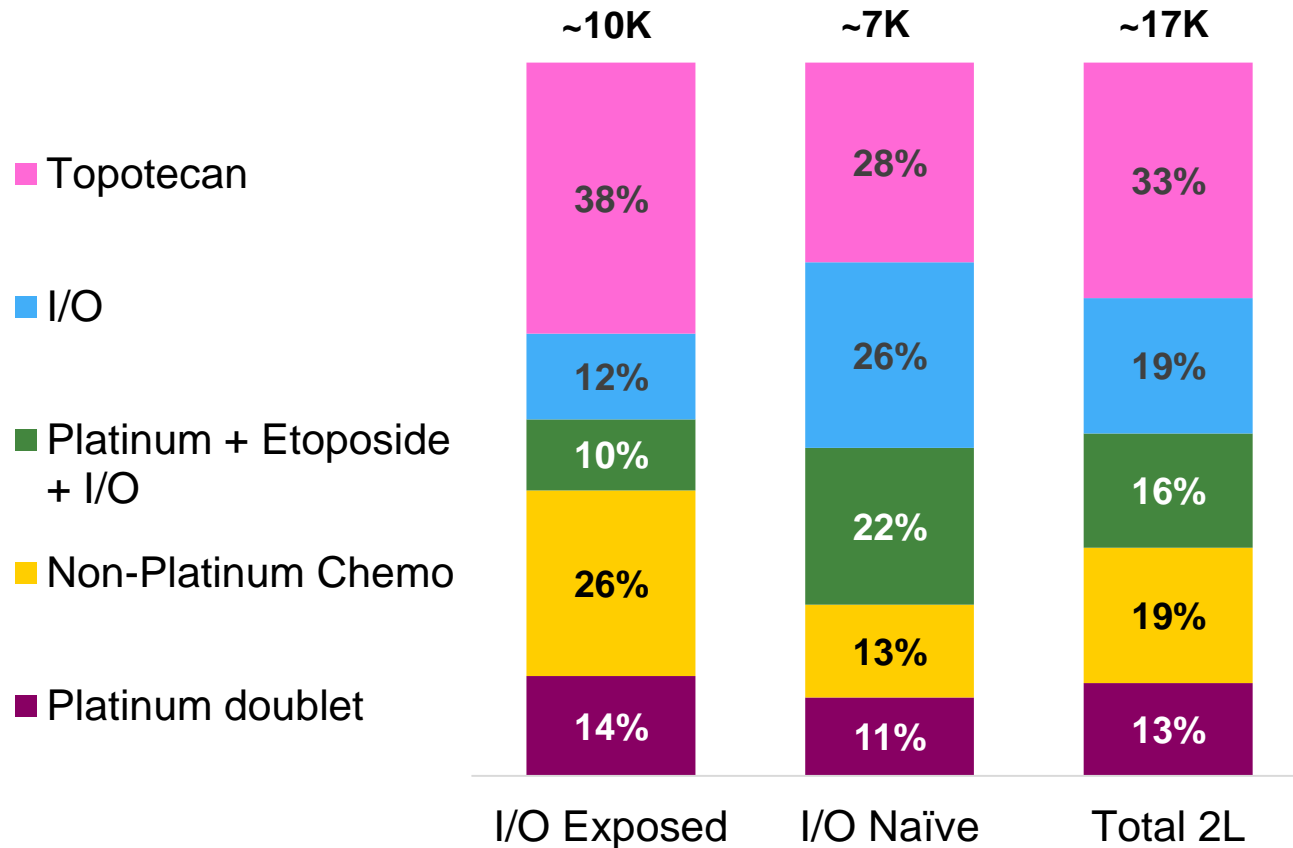


¹ Jazz market research, SHS claims data; Other sources: SEER Cancer Stat Facts <https://seer.cancer.gov/statfacts/html/lungb.html>, accessed April 19, 2019; American Cancer Society, <https://www.cancer.org/cancer/small-cell-lung-cancer/about/what-is-small-cell-lung-cancer.html>, accessed April 12, 2019; Kantar Health Treatment Architecture SCLC July 2018

Treatment Landscape

Opportunity to Change the Metastatic SCLC Treatment Paradigm

2L SCLC Treatment Paradigm



- Delivering a new, efficacious solution with a manageable safety profile
- Initiatives focused on
 - 2L treatment of choice for all patient segments
 - Topotecan replacement
 - New option for the ~8,000 untreated 2L patients
- I/O expansion in 1L is expected to further reduce I/O use in 2L

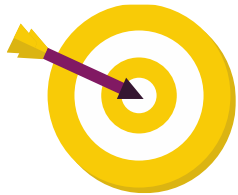
Source: Jazz market research. Other treatments include non-platinum based therapies reflecting divergence in opinions of standard of care. Chemo includes both platinum and non-platinum regimens. IO includes IO alone and Platinum doublet + IO.

SCLC Prescriber Universe

~63% of Treatment is Undertaken by Top 1,500 Prescribers



~6,000 Medical and Thoracic oncologists

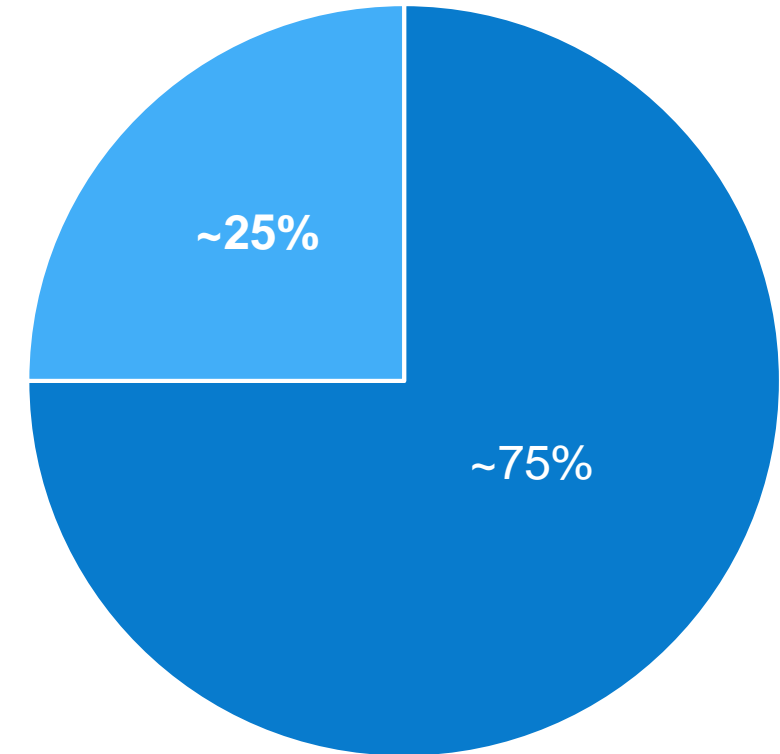


~5,000 **Target prescribers**
~87% of SCLC treatment



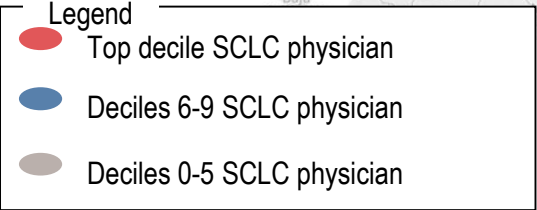
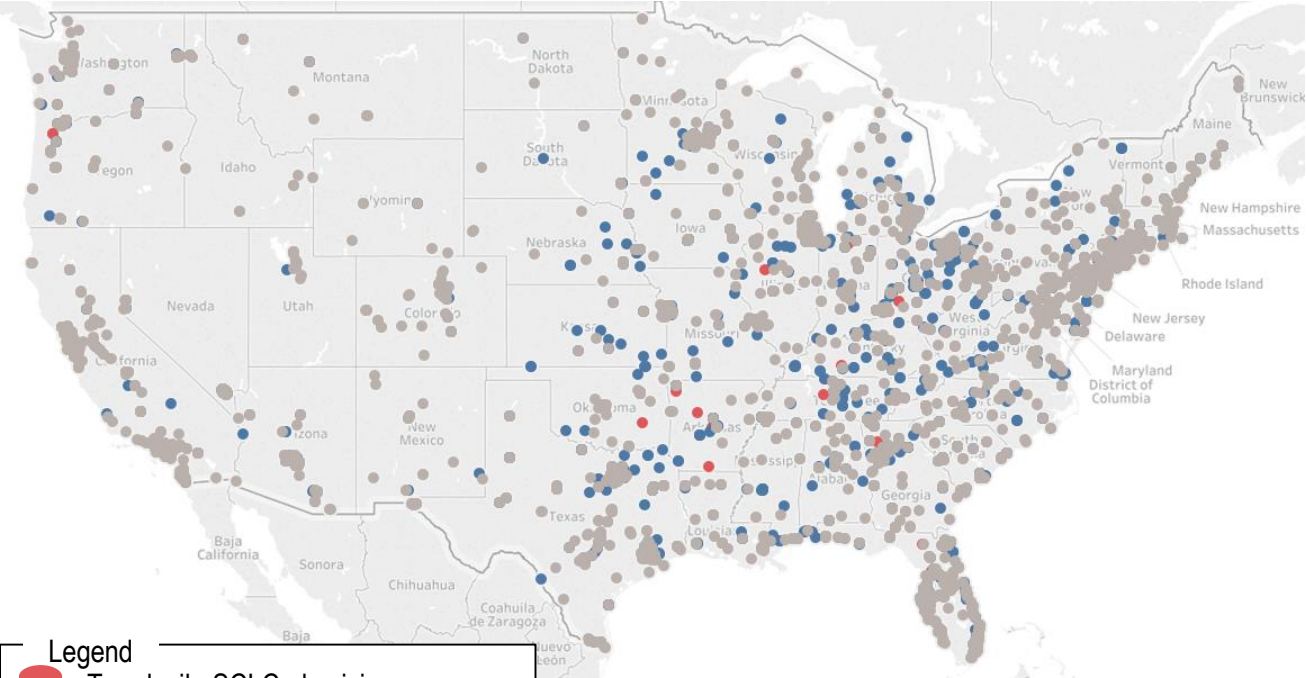
~1,500 **Laser Focus**
~63% of SCLC treatment

Treatment setting



■ Community ■ Academic

SCLC U.S. Prescriber Distribution

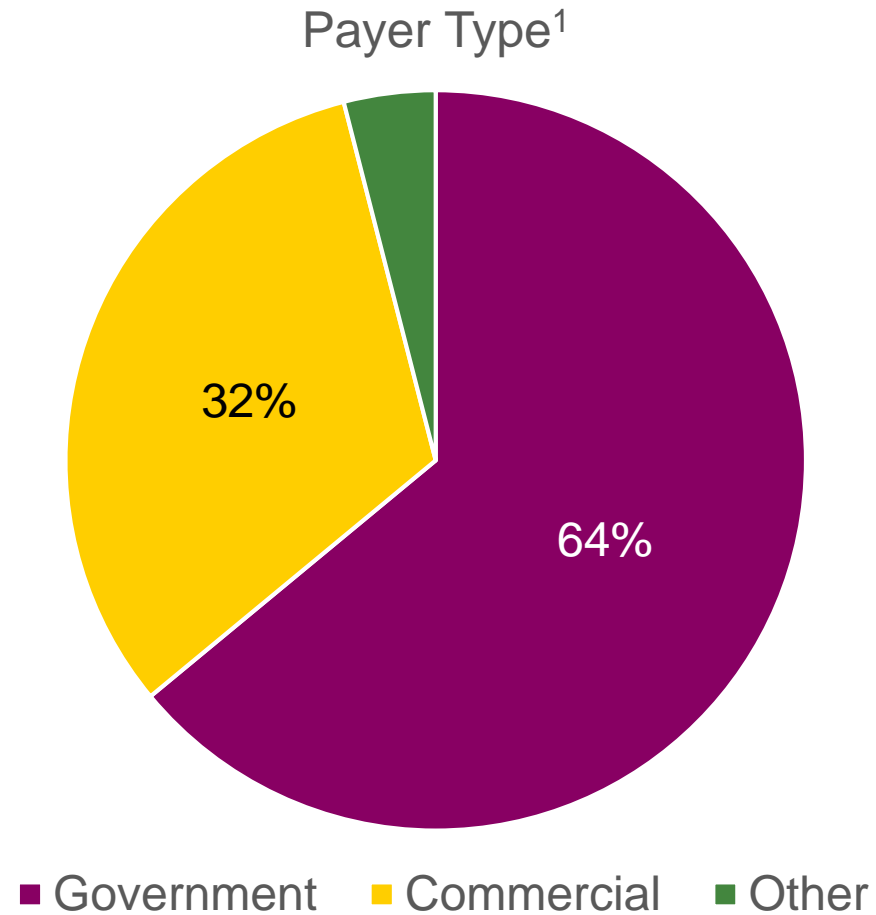


Resource Concentration Aligned to Geo-Distribution

- 28 Additional Sales Representatives
- 72 Combined Vyxeos / Zepzelca Sales Force
- 10 Zepzelca MSLs
- 13 Reimbursement Specialists

Payer Landscape

The Majority of Patients are Covered by Government Programs



¹JAMA Netw Open. 2020;3(4):e203277. doi:10.1001/jamanetworkopen.2020.3277, 'Other' (4%) relates to self-pay or uninsured patients

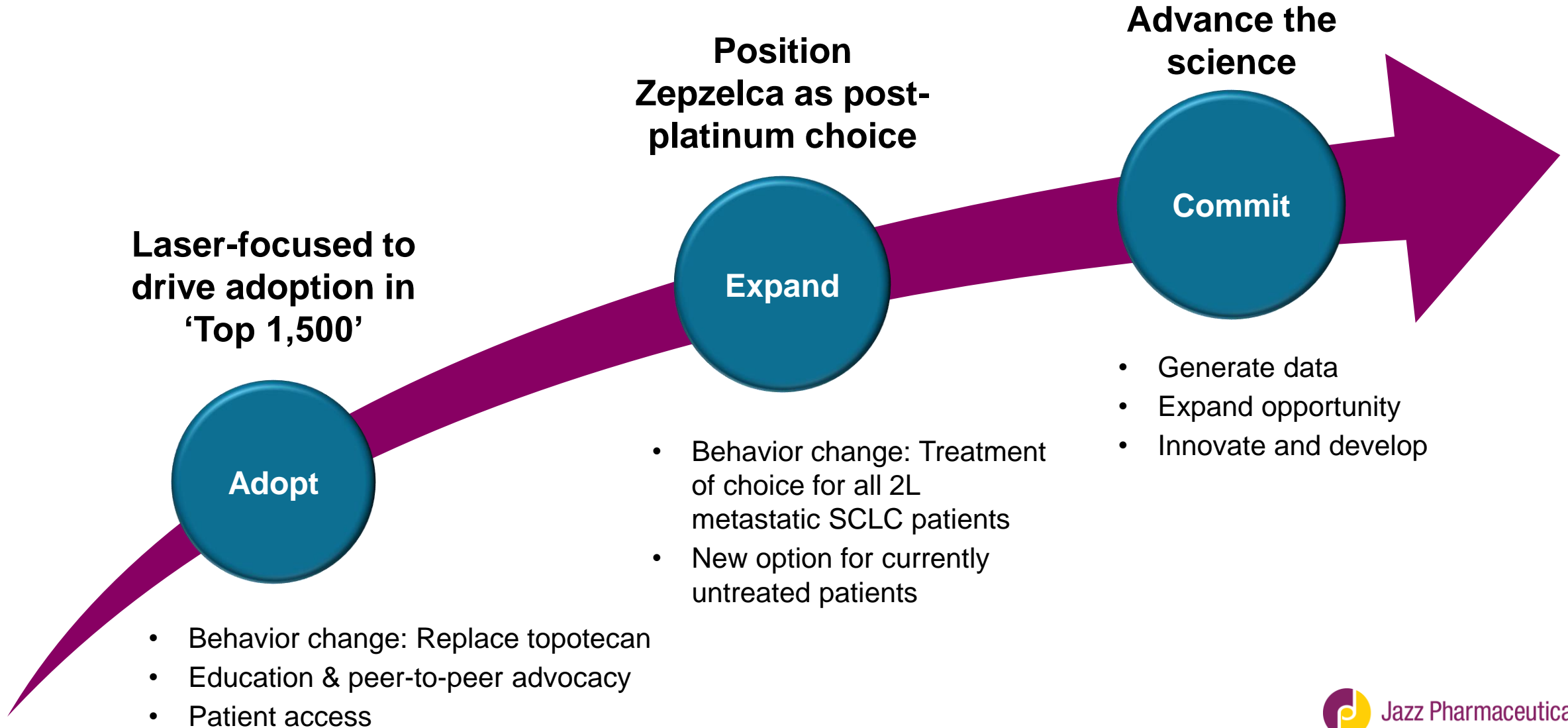
Manufacturing and Distribution



- PharmaMar to provide product for launch
- Future supply post-launch
 - Jazz contracting with CMOs
 - PharmaMar to provide lurbinectedin API
- Specialty distributors
 - AmerisourceBergen, Cardinal Health, McKesson

Executing a Successful Launch

Driving Knowledge and Treatment Behaviors Across the SCLC Prescriber Community





FINANCIAL OVERVIEW

RENÉE GALÁ
EVP and Chief Financial Officer

 **ZEPZELCA™**
(lurbinectedin) for injection 4 mg



Jazz Pharmaceuticals®

Zepzelca

Leveraging External Innovation to Achieve Our Strategic Objectives

Provide innovative and life-changing medicines for patients



Meaningful revenue diversification



Partner of choice



First new treatment in 2L SCLC > 20 years



Multi-hundred million dollar opportunity with 3-5 year route to peak*



Harness our oncology expertise and capabilities

*In the current indication

Zepzelca Cost of Treatment Considerations

First New Treatment Option in 2L SCLC in > 20 Years

- Dose: 3.2 mg/m² every 21 days as a 1-hour IV infusion¹
- Based on average BSA, a patient would require 2 vials per 21-day cycle
- In Phase 2 basket study, # cycles patients received:^{1,2}

Median = 4	IQR = 2-8
<ul style="list-style-type: none">• 56% of patients received < 6 cycles• 44% of patients received ≥ 6 cycles	

- The cost per patient per course of therapy will vary based on patient size and treatment duration
 - Based on median of 4 cycles in the Phase 2 study, the WAC cost would be ~\$53K (\$6,633 x 2 vials x 4 cycles)
- WAC = \$6,633 per 4 mg vial

Total cost of therapy will vary based on patient size and treatment duration

The WAC cost per course of therapy, based on median of 4 cycles, would be ~\$53K

¹ Zepzelca U.S. Prescribing Information
² Trigo J, et al. *Lancet Oncol.* 2020

Transaction Terms and Key Financial Considerations

Transaction terms

Exclusive License Agreement for U.S. Rights to Lurbinectedin Across All Indications*

- All amounts payable to PharmaMar:
 - Up to \$150M on full approval within certain timelines
- \$200M upfront; paid January
- \$100M milestone on accelerated SCLC approval; expect to pay 2Q20
- Up to \$550M in potential commercial milestones
- Tiered royalties; high teens to 30%

Accounting

- All post-approval milestones capitalized and amortized over estimated useful life
- Royalties recorded in COGs
- GTNs in the 20% to 30% range, consist primarily of:
 - Government rebates
 - Distributor fees
 - GPO discounts
 - Patient services

*Jazz has the right to co-fund (50%) any pivotal trials in new indications or pay a milestone on FDA approval. These payments can be offset against any future commercial milestones. Any additional confirmatory trial for the current indication will be funded and undertaken by PharmaMar.

Zepzelca

Aligned with Our Expanding Capabilities and Corporate Strategy



- ~25K patients in the 2L population; ~8K untreated
- First new treatment in 2L SCLC in more than 20 years
- Committed to further development



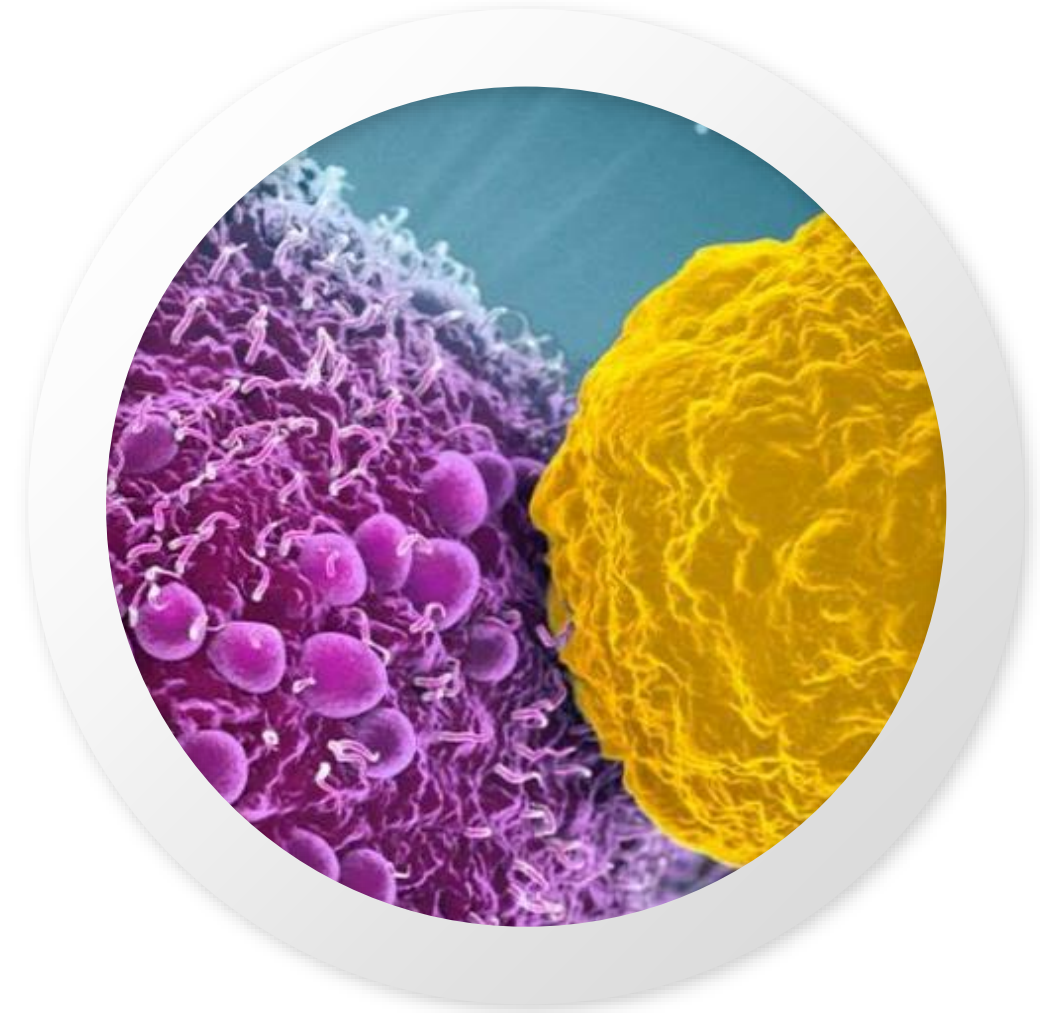
- Laser-focus on the top 1,500 prescribers, accounting for 63% of patients
- Leveraging existing capabilities and infrastructure



- Revenue diversification
- Multi-hundred million dollar revenue opportunity

JAZZ's Demonstrated Value Proposition

- 1 Diverse portfolio of commercialized products
- 2 Multiple growth drivers 2020-2021
 - ✓ Sunosi European approval
 - ✓ Zepzelca U.S. approval
 - JZP-258 PDUFA July 21, 2020
 - JZP-458 BLA submission as early as 4Q20
- 3 Disciplined capital allocation
 - Focused investments in the business
 - Investing to diversify portfolio
- 4 Robust and expanding R&D portfolio
 - Enhanced R&D capabilities
 - Expanding our portfolio through internal and corporate development efforts
 - 4 corporate development transactions in 2019
- 5 Strong operational efficiency and globalization





APPENDIX

 **ZEPZELCA™**
(lurbinectedin) for injection 4 mg



Jazz Pharmaceuticals®

Zepzelca U.S. Prescribing Information

Warnings

Myelosuppression	In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 or 4 neutropenia occurred in 41% of patients. Febrile neutropenia occurred in 7% of patients. Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm ³ and platelet count of at least 100,000/mm ³ .
Hepatotoxicity	In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA Grade 3 elevations of ALT and AST were observed in 6% and 3% of patients, respectively, and Grade 4 elevations of ALT and AST were observed in 0.4% and 0.5% of patients, respectively.
Embryo-Fetal Toxicity	Based on animal data and its mechanism of action ZEPZELCA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 6 months after the final dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the last dose.

ATLANTIS Trial: Key Eligibility Criteria and Treatment Protocol

Key Eligibility Criteria

- Adults ≥ 18 years with a histologically or cytologically confirmed diagnosis of limited- or extensive-stage SCLC^a
- Must have failed 1 prior platinum-containing regimen and have had a CTFI of ≥ 30 days
- ECOG PS of 0 to 2
- Washout of ≥ 3 weeks since last prior anticancer treatment, ≥ 4 weeks since completion of whole brain radiation therapy, and ≥ 2 weeks since completion of prophylactic cranial irradiation or palliative radiation
- Adequate renal and hepatic function
- Must *not* have received >1 prior chemotherapy-containing regimen or prior treatment with lurbinectedin, topotecan, or anthracyclines; patients who had never received prior platinum-containing regimen for SCLC were also excluded

^aPatients who had received prior-intervening immune checkpoint inhibitor therapy are eligible.

Treatment Administration and Cycles Received

- **Experimental arm:**
 - Doxorubicin 40 mg/m² on Day 1, followed by lurbinectedin 2 mg/m² on Day 1 of each 21-day cycle
- **Control arm:**
 - Topotecan 1.5 mg/m² daily on Days 1–5 of each 21-day cycle

OR

- Cyclophosphamide 1,000 mg/m², doxorubicin 45 mg/m², and vincristine 2 mg fixed dose on Day 1 of each 21-day cycle

Up to 10 cycles of doxorubicin-containing regimens will be allowed. For patients in the experimental arm, lurbinectedin will be continued as maintenance therapy at a dose of 3.2 mg/m² (or 2.6 mg/m² if >1 dose reduction was applied during combination therapy) on Day 1 of each 21-day cycle. All patients will receive primary G-CSF prophylaxis.

Key Differences Between the Basket and ATLANTIS Trials

	Basket trial ¹	ATLANTIS trial ²
Trial design	Phase 2, single-agent trial	Phase 3, open-label, randomized trial
Patient population	Patients with SCLC who have failed 1 prior line of chemotherapy	Patients SCLC who have failed 1 prior line of platinum-based chemotherapy
Treatment regimen	Lurbinectedin monotherapy	Lurbinectedin/doxorubicin VS standard-of-care chemotherapy (topotecan OR CAV)
Primary study endpoint	Overall response rate by RECIST v.1.1	Overall survival
CNS Metastases	Excluded	Allowed if stable

¹ Trigo J, et al. *Lancet Oncol.* 2020, [Epub ahead of print].

² Farago AF, et al. *Future Oncol.* 2019;15(3):231-239.

Other Agents in Relapsed SCLC

Regimen*	Topotecan ¹	CAV ²	Platinum Based ^{3,4}
Patient population	All CTFI (n = 213)	CTFI > 60 days (n = 104)	CTFI ≥ 90 days
Response rate (95% CI)	17% (12% - 23%)	18% (11% - 26%)	45% - 49%
Median DoR (months) (95% CI)	4.2 (N/A)	3.5 (1.9 – 16.1)	
Disease control rate (95% CI)	62% (55% - 68%)	30% (N/A)	
Median OS (months) (95% CI)	7.8 (6.6 – 8.5)	5.7 (0.3 – 23.3)	7.5 – 7.9

*These are not head-to-head comparisons with Zepzelca – trial designs vary by study.

¹ von Pawel J, et al. J Clin Oncol. 2014;32:4012-4019; ² von Pawel J, et al. J Clin Oncol. 1999;17:658-667; ³ Genestreti G, et al. Clin Lung Cancer. 2015;16:e223-e228; ⁴ Monnet I, et al. Presented at IASLC 2019 World Conference on Lung Cancer; Barcelona, Spain. Abstract OA15.02.

Topotecan Efficacy & Safety in 2L SCLC

Select Efficacy Parameters

Select Hematological AEs

Efficacy	Overall (n=213)	Resistant CTFI < 90 days (n=93)	Sensitive CTFI ≥ 90 days (n=120)	Safety	Overall (n=197)
ORR, %	16.9	9.4	23.1	Neutropenia, G3-4, %	53.8
OS months, median (95% CI)	7.8 (6.6-8.5)	5.7 (4.1-7.0)	9.9 (8.5-11.5)	Thrombocytopenia, G3-4, %	54.3
PFS months, median (95% CI)	3.5 (2.9-4.2)	2.6 (1.8-3.3)	4.3 (3.8-5.4)	Anemia, G3-4, %	30.5

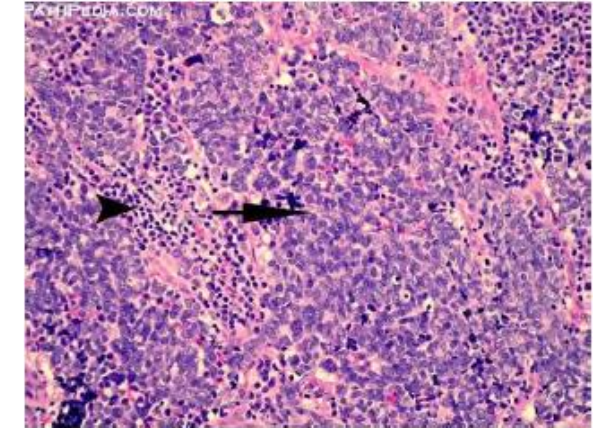
SCLC Diagnosis: Pathology¹

SCLC is Staged to Determine Prognosis and Identify Appropriate Treatment

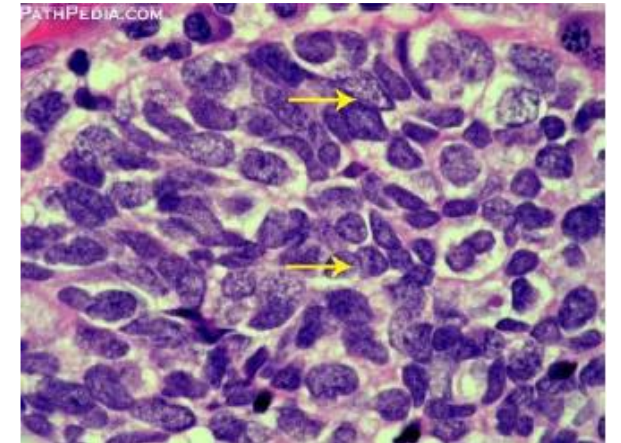
SCLC under the microscope (H&E stain):²

- Small blue cancer cells that are approximately double the size of lymphocytes
- Cells are round, oval, or spindle-shaped with nuclear molding and high mitotic counts
- Sparse cytoplasm
- Nuclei with finely dispersed chromatin and no distinct nucleoli
- Arrangements of cancer cells in clusters, sheets, or trabeculae that are separated by fibrovascular stroma

- Arrow points to an area of diffuse proliferation of small to intermediate-sized SCLC cells
- Arrowhead points to area of lymphocytic infiltration³



- Arrow points to an instance of “nuclear molding”
- In nuclear molding, the nucleus of one cell appears to be bumping into another one, causing them to appear as pieces of a jigsaw puzzle³



¹ Dowell JE, et al. In: Grippi MA, et al. eds. *Fishman's Pulmonary Diseases and Disorders*, Fifth Edition. New York, NY: McGraw-Hill; 2015, ² Glisson BS, et al. 2019. <https://www.uptodate.com/contents/pathobiology-and-staging-of-small-cell-carcinoma-of-the-lung>, ³ Pathopedia. https://www.pathpedia.com/education/eatlas/histopathology/lung_and_bronchi/small_cell_carcinoma.aspx Image_LU041.1, LU041.7.

SCLC Diagnosis: Stage

	Limited-Stage SCLC	Extensive-Stage SCLC
VALSG ¹	Disease limited to one hemithorax (including contralateral mediastinal and ipsilateral supraclavicular lymph nodes), if disease can be confined to one radiation port	Disease that cannot be classified as limited, including malignant pleural or pericardial effusions and hematogenous metastases
AJCC TNM	<p>Stage I-III (T any, N any, M0) that can be safely treated with definitive radiation doses.</p> <p><i>Excludes stage T3-T4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan</i></p>	<p>Stage IV (T any, N any, M1a/b) or T3-T4 due to multiple lung nodules that are too extensive or have tumor / nodal volume that is too large to be encompassed in a tolerable radiation plan</p>

The Veterans’ Administration Lung Study Group (VALSG) staging system has been the conventional classification used for SCLC¹

The AJCC TNM (primary tumor, regional lymph nodes, distant metastases) classification is used for SCLC¹

- This is the staging system used in the NCCN guidelines for the treatment of SCLC
- The IASLC has called for replacement of the VALSG classification with the AJCC TNM system

¹ Kalemkerian GP, Schneider BJ. *Hematol Oncol Clin N Am.* 2017;31:143-156.

² National Comprehensive Cancer Network. SCLC Guidelines Version 3.2020.



Lurbinectedin Publications

Name	Year	Publication	Authors
Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial	Mar-20	The Lancet, Oncology	Trigo J, et al.
From Seabed to Bedside: A Review on Promising Marine Anticancer Compounds	Feb-20	Biomolecules	Wang E, et al.
Lurbinectedin as Second- Or Third-Line Palliative Therapy in Malignant Pleural Mesothelioma: An International, Multi-Centre, Single-Arm, Phase II Trial (SAKK 17/16)	Jan-20	Annals of Oncology	Metaxas Y, et al.
A phase II multi-strata study of lurbinectedin as a single agent or in combination with conventional chemotherapy in metastatic and/or unresectable sarcomas	Dec-19	European Journal of Cancer	Cote G, et al.
Lurbinectedin synergizes with immune checkpoint blockade to generate anticancer immunity	Sept-19	Oncoimmunology	Xie W, et al.
Multicenter Phase II Study of Lurbinectedin in BRCA-Mutated and Unselected Metastatic Advanced Breast Cancer and Biomarker Assessment Substudy	Nov-18	Journal of Clinical Oncology	Cruz C, et al.
Looking Ahead to New Therapies in Small Cell Lung Cancer	Apr-18	Clinical Advances in Hematology & Oncology	Charles M. Rudin, MD, PhD
Lurbinectedin Reduces Tumour-Associated Macrophages and the Inflammatory Tumour Microenvironment in Preclinical Models	Aug-17	British Journal of Cancer	Belgiovine C, et al.
Phase II Randomized Study of PM01183 Versus Topotecan in Patients With Platinum-Resistant/Refractory Advanced Ovarian Cancer	Jun-17	Annals of Oncology	Poveda A, et al.
Phase I clinical and pharmacokinetic study of PM01183 (a tetrahydroisoquinoline, Lurbinectedin) in combination with gemcitabine in patients with advanced solid tumors.	Nov-16	Investigational New Drugs	Paz-Ares et al
Lurbinectedin induces depletion of tumor-associated macrophages, an essential component of its in vivo synergism with gemcitabine, in pancreatic adenocarcinoma mouse models.	Oct-16	Dis Model Mech	Céspedes et al

Lurbinectedin Publications

Name	Year	Publication	Authors
Lurbinectedin Inactivates the Ewing Sarcoma Oncoprotein EWS-FLI1 by Redistributing It within the Nucleus	Oct-16	Cancer Research	Harlow et al
Lurbinectedin Specifically Triggers the Degradation of Phosphorylated RNA Polymerase II and the Formation of DNA Breaks in Cancer Cells.	Sep-16	Molecular Cancer Therapeutics	Santamaría Nuñez et al
Combination of cisplatin and lurbinectedin as palliative chemotherapy in progressive malignant pleural mesothelioma: Report of two cases.	Jul-16	Lung Cancer (Netherlands)	Metaxas et al
Preclinical Investigations of PM01183 (Lurbinectedin) as a Single Agent or in Combination with Other Anticancer Agents for Clear Cell Carcinoma of the Ovary	Mar-16	PLoS One	Takahashi et al
Development of a liquid chromatography/tandem mass spectrometry assay for the quantification of PM01183 (lurbinectedin), a novel antineoplastic agent, in mouse, rat, dog, Cynomolgus monkey and mini-pig plasma.	May-16	Journal of Pharmaceutical and Biomedical Analysis	Pernice et al
Phase Ib/II study to evaluate the efficacy and tolerability of PM01183 (lurbinectedin) in combination with olaparib in patients with advanced solid tumors	Oct-16	European Journal of Cancer	Poveda et al
Lurbinectedin (PM01183) plus paclitaxel (P), recommended dose (RD) expansion results with or without the addition of bevacizumab (Bev) in patients (pts) with selected solid tumors	Oct-16	European Journal of Cancer	Drilon et al
PM01183 inactivates the EWS/FLI1 transcription factor by redistributing the protein within the nucleus	Jul-16	AACR American Association for Cancer Research	Harlow et al
CORAIL trial: Randomized phase III study of lurbinectedin (PM01183) versus pegylated liposomal doxorubicin (PLD) or topotecan (T) in patients with platinum-resistant ovarian cancer	Jun-16	ASCO American Society of Clinical Oncology	Harlow, M et al
Lurbinectedin reduces tumor-associated macrophages and the production of inflammatory cytokines, chemokines, and angiogenic factors in preclinical models	Jul-16	AACR American Association for Cancer Research	Allavena et al
Lurbinectedin specifically targets transcription in cancer cells, triggering DNA breaks and degradation of phosphorylated Pol II	Jul-16	AACR American Association for Cancer Research	Santamaria-Nuñez et al

Glossary of Abbreviations

1L, 2L, 3L = First, Second, Third-Line Treatment

AE = Adverse Event

ALL = Acute Lymphoblastic Leukemia

ALT/AST = Alanine Aminotransferase / Aspartate Aminotransferase

AJCC = American Joint Committee on Cancer

API = Active Pharmaceutical Ingredient

ASCO = American Society of Clinical Oncology annual meeting

ATLANTIS = Phase 3 Clinical Study of lurbinectedin in SCLC

BLA = Biologics License Application

BRCA = Breast Cancer Gene

BSA = Body Surface Area

CAV = Cyclophosphamide/Doxorubicin/Vincristine

CI = Confidence Interval

CMO = Contract Manufacturing Organization

CNS = Central Nervous System

COGS = Cost of Goods Sold

COVID-19 = Coronavirus Disease of 2019

CTFI = Chemotherapy Free Interval

CUP = Cancer of Unknown Primary

D/C = Diarrhea / Constipation

DNA = Deoxyribonucleic Acid

DoR = Duration of Response

DOX = Doxorubicin

ECOG = Eastern Cooperative Oncology Group

EDS = Excessive Daytime Sleepiness

EFTs = Ewing's Family of Tumors

ES SCLC = Extensive-Stage Small-Cell Lung Cancer

EU = European Union

FDA = U.S. Food and Drug Administration

G-CSF = Granulocyte Colony-Stimulating Factor

GI = Gastrointestinal

GPO = Group Purchasing Organization

GTNs = Gross-to-Nets

GvHD = Graft-vs-Host Disease

IA = Interim Analysis

IASLC = International Association For The Study of Lung Cancer

IC₅₀ = Half of maximal inhibitory concentration

IH = Idiopathic Hypersomnia

I/O = Immuno-Oncology

IRC = Independent Review Committee

IQR = Inter-Quartile Range

IV = Intravenous

LDH = Lactate Dehydrogenase

LPI = Last Patient In

LS SCLC = Limited-Stage Small-Cell Lung Cancer

MOA = Mechanism of Action

MSL = Medical Science Liaison

NCCN = National Comprehensive Cancer Network

NDA = New Drug Application

NET = Neuroendocrine Tumor

NSCLC = Non-Small Cell Lung Cancer

N/V = Nausea / Vomiting

ODD = Orphan Drug Designation

ORR = Overall Response Rate

OS = Overall Survival

PD = Progressive Disease

PDL1 = Programmed Death-Ligand 1

PDUFA = Prescription Drug User Fee Act

PFS = Progression Free Survival

PS = Performance Status

RNA = Ribonucleic Acid

Q3wk = Every 3 weeks

RECIST = Response Evaluation Criteria in Solid Tumors

SCLC = Small-Cell Lung Cancer

SHS = Symphony Health Solutions

TAM = Tumor Associated Macrophages

TNM = Tumor, Node, Metastasis

ULN = Upper Limit of Normal

VALSG = Veteran's Administration Lung Cancer Study Group

VEGF = Vascular Endothelial Growth Factor

WAC = Wholesale Acquisition Cost