Transforming the Experience of Chemotherapy for Cancer Patients

CORPORATE PRESENTATION

September 2020

Forward Looking Statements

Statements in this presentation about Aileron's future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements about the Company's strategy and clinical development plans. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including whether Aileron's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; whether results obtained in preclinical and nonclinical studies and clinical trials will be indicative of results obtained in future clinical trials; whether preliminary or interim results from a clinical trial such as the interim data referenced in this presentation will be indicative of the final results of the trial; whether Aileron's product candidates will advance through the clinical trial process on a timely basis, or at all; whether the results of such trials will warrant submission for approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether Aileron's product candidates will receive approval from regulatory agencies on a timely basis or at all; whether, if product candidates obtain approval, they will be successfully distributed and marketed; whether the coronavirus pandemic will have an impact on the timing of our clinical development, clinical supply and our operations; and other factors discussed in the "Risk Factors" section of Aileron's quarterly report on Form 10-Q for the period ended June 30, 2020, filed on August 5, 2020, and risks described in other filings that Aileron may make with the Securities and Exchange Commission. Any forward-looking statements contained in this presentation speak only as of the date hereof, and Aileron specifically disclaims any obligation to update any forward-looking statement, whether because of new information, future events or otherwise.

Our Focus

Addressing a significantly overlooked and serious unmet need in oncology: Chemotherapy-induced toxicities and side effects that

- Severely diminish quality of life for cancer patients
- Often lead to dose reductions and delays, limiting probability of patients winning their battles against cancer

First-in-class therapeutic solution: ALRN-6924

- MDM2 + MDMX inhibitor that activates wild-type p53
- Biomarker approach: only healthy cells protected from chemotherapy, but cancer cells remain susceptible
- Phase 1b proof-of-concept study underway
  - Positive interim data ("-24h schedule") reported in Q2 2020
  - Presentation of full data ("-24h schedule") at EORTC-NCI-AACR conference October 25-26, 2020

LONG-TERM VISION

Protect patients with p53-mutated cancers from chemotherapy-induced side effects, regardless of cancer type or chemotherapy

50% of cancer patients have **P53-MUTATED CANCER**

We want to enable patients to fight cancer without the fear, quality-of-life burden and medical consequences of chemotherapy-induced side effects

MILLIONS OF PATIENTS

Need chemotherapy to fight cancer

SIDE EFFECTS

Impact all patients undergoing chemotherapy

UNSELECTIVE

Chemotherapy cannot distinguish between cancer cells and healthy cells, causing side effects

TODAY'S SUPPORTIVE CARE APPROACH:

Resignation / Side Effects Accepted

- Multiple drugs; typically address only one toxicity
- Often ineffective; associated with harmful toxicities
- No options for some side effects (like hair loss)

AILERON'S MISSION AND POTENTIAL:

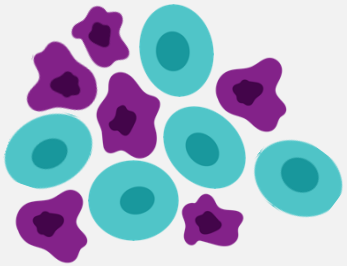
Proactive Prevention

- One medicine to protect multiple cell types
- Improved quality of life and better tolerance for chemotherapy, without dose reductions or delays

Basic principles to successfully protect against chemotherapy-induced side effects

CURRENT PARADIGM:

Chemotherapy targets both healthy cells and cancer cells that are cycling (undergoing cell division process)



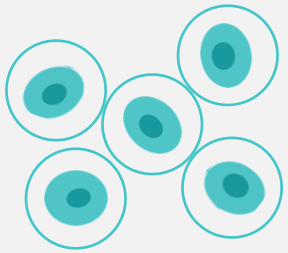
Both healthy cells and cancer cells are destroyed by chemotherapy

PARADIGM SHIFT

AILERON PARADIGM:

Temporarily pause cycling in healthy cells, shielding them

No interruption of cycling in cancer cells, leaving them fully susceptible to chemotherapy



Healthy cells are not destroyed

Cancer cells are destroyed

A COUNTERINTUITIVE APPROACH:

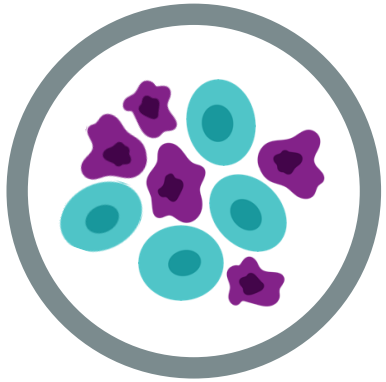
Treat healthy cells, not cancer cells

ALRN-6924 activates p53 to pause the cell cycle in healthy cells, but not cancer cells

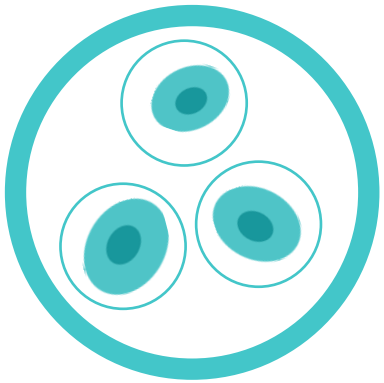
Patient with p53-mutant cancer receives ALRN-6924 before chemotherapy

IV administration;
1-hour infusion

→

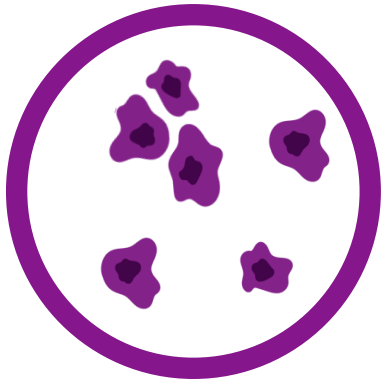


ALRN-6924 activates p53 in healthy cells



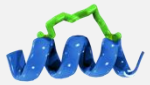
Activated p53 pauses cell cycling in healthy cells

Patient with p53-mutant cancer receives chemotherapy



Chemotherapy's attack on cancer cells is uninterrupted

ALRN-6924 window of protection for healthy cells

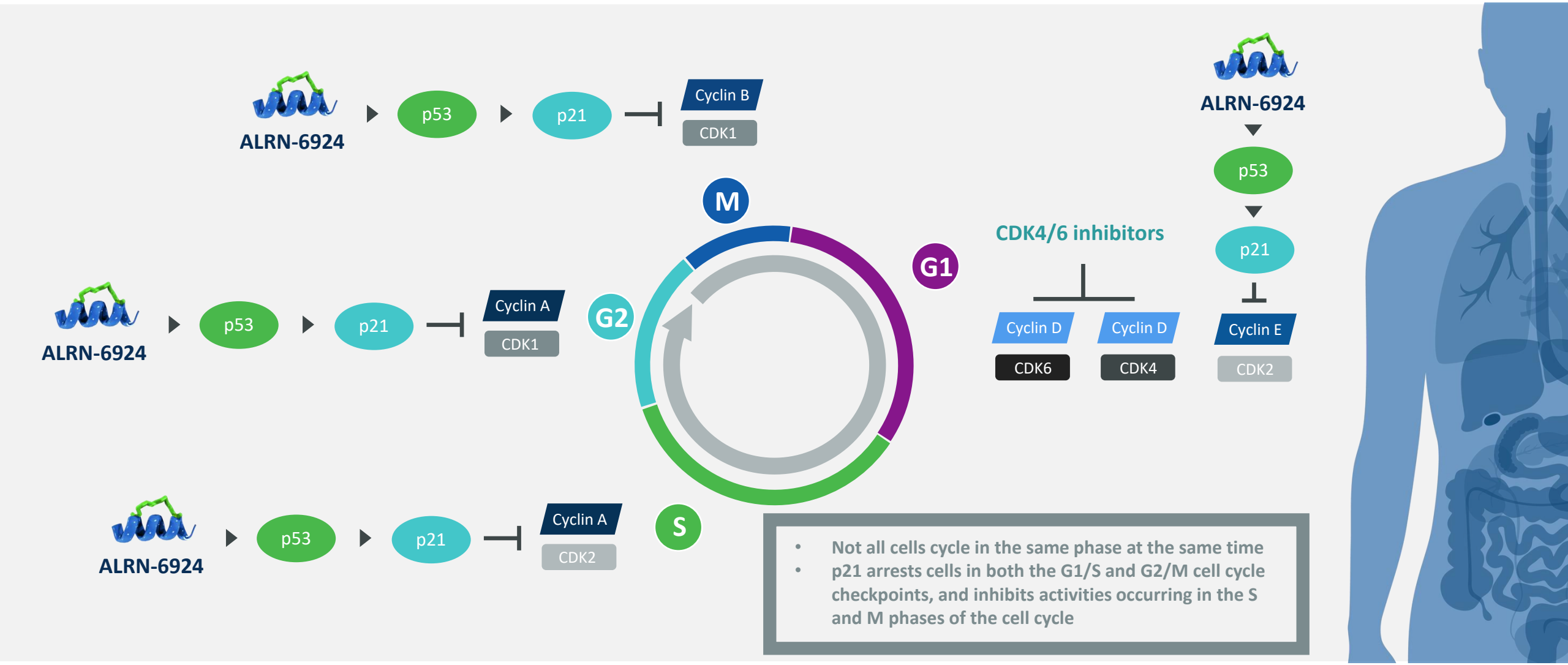


ALRN-6924

Selectively and temporarily activates normal p53 in healthy cells, not in cancer cells

Can not work in p53-mutated cancer cells because p53 has lost its function in those cancer cells

ALRN-6924 best-in-class potential: Effects on all phases of the cell cycle



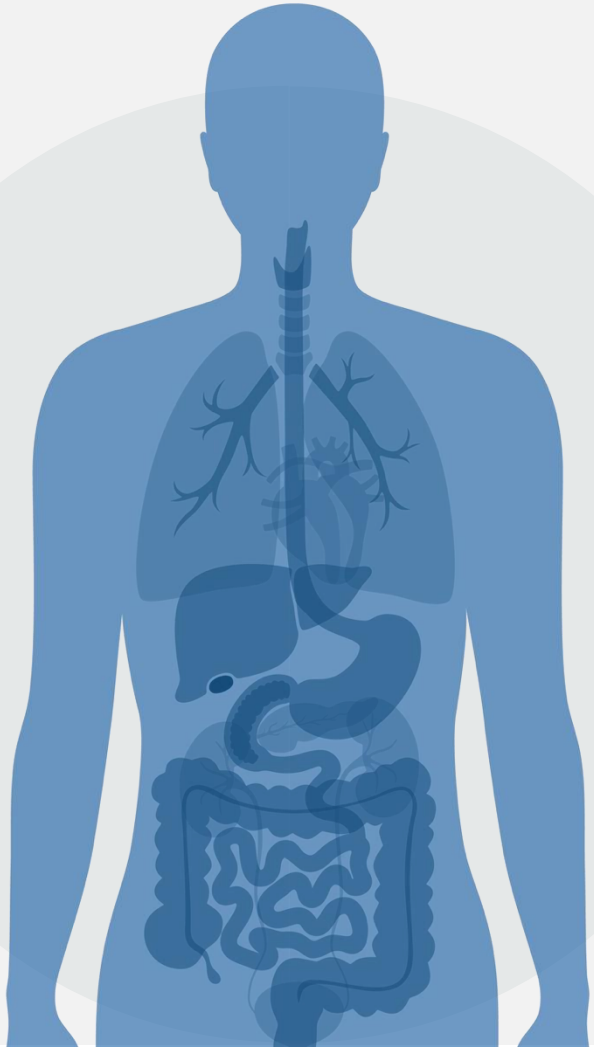
ALRN-6924: A systemic therapeutic approach to a systemic issue

Aileron Proof-of-Concept Focus

Severe Anemia
(weakness, fatigue)
Red blood cells

Severe Thrombocytopenia
(excessive bleeding)
Platelets

Severe Neutropenia
(serious infection, fever, sepsis)
White blood cells



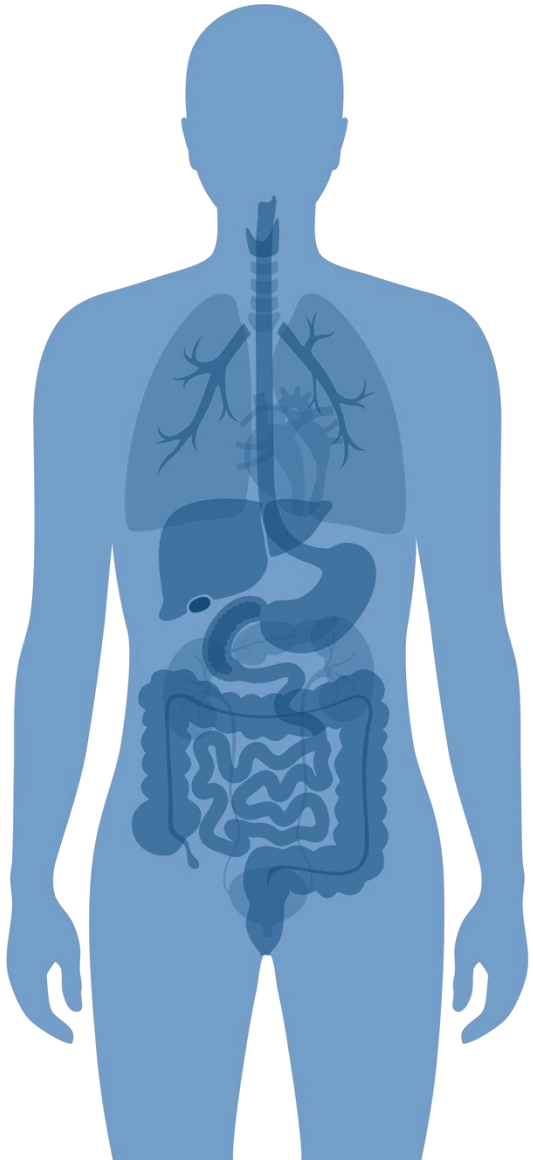
Potential Other Benefits

Alopecia (hair loss)
Hair follicle cells

Stomatitis (mouth sores)
Cells lining the oral cavity

Vomiting, Diarrhea, Bloating
Cells lining the stomach and intestines

Bone Marrow Toxicities: Proof-of-Concept Focus for ALRN-6924



SEVERE ANEMIA

Standard of Care: "EPOs" (e.g., Aranesp®/Epogen®); Blood transfusions

Safety Concerns:

- EPOs: promote tumor growth and thrombo-embolic events (black box warning ⚠)
- Transfusions: risk of infection; limited supply

SEVERE NEUTROPENIA

Standard of Care: G-CSF (e.g. Neulasta® /Neupogen®)

Safety Concerns:

- Can promote tumor growth and cause bone pain

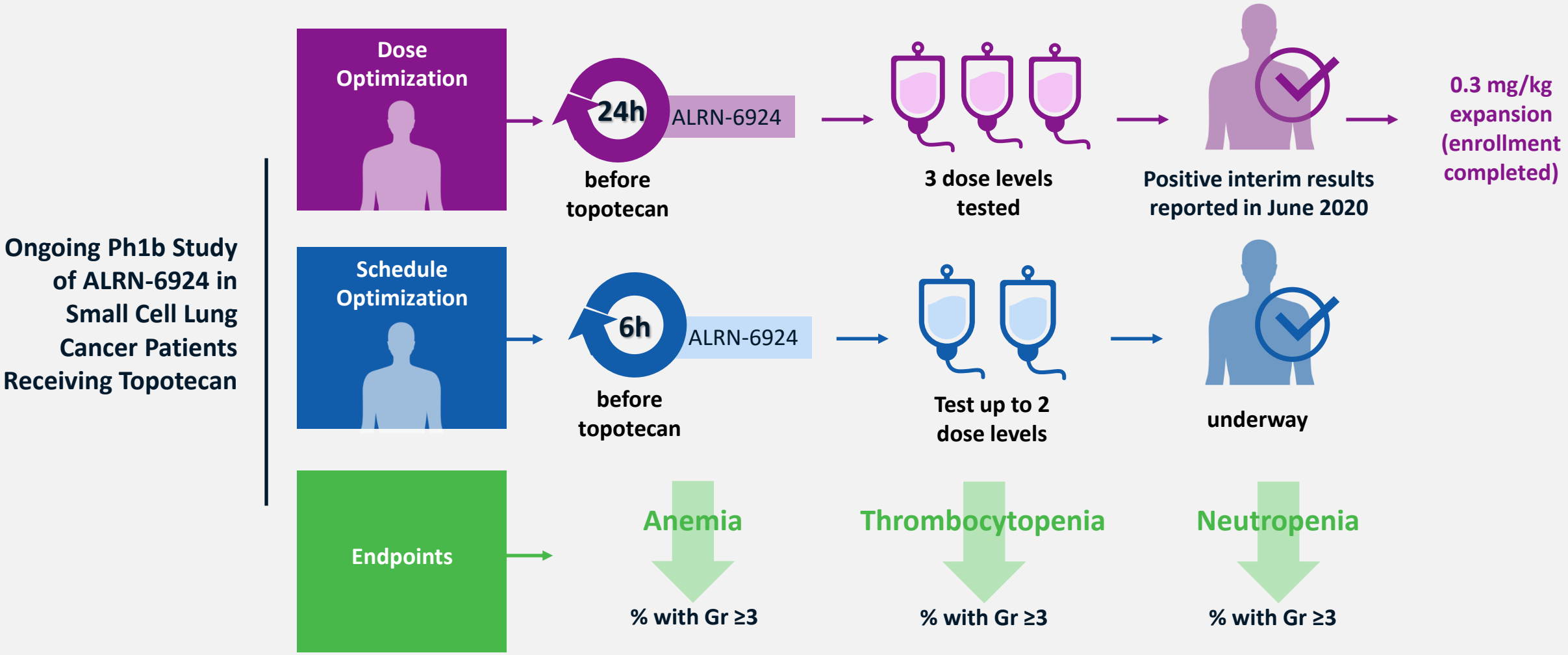
SEVERE THROMBOCYTOPENIA

Standard of Care: No drugs used as standard of care – platelet transfusions instead

Safety Concerns:

- Effects limited to 2-5 days maximum
- Patients can become transfusion-refractory
- Transfusion-related risk of infection; limited supply

ALRN-6924 Proof-of-Concept Phase 1b Study



ALRN-6924 Phase 1b Study

Dose Optimization: Positive Interim Results

REPORTED JUNE 2020

Interim Clinical Results: Highlights

- Demonstrated clinically meaningful protection against multiple hematological side effects when administering ALRN-6924 24-hours prior to chemotherapy
- 0.3 mg/kg dose level achieved most robust and consistent chemoprotection effects of 3 dose levels
- Patients treated with 0.3 mg/kg met protocol-defined criterion for reduction of NCI CTC Grades 3/4 neutropenia to ≤% 50% in 1st treatment cycle, triggering 0.3 mg/kg expansion cohort

Demographics and Key Baseline Characteristics

		0.3 mg/kg N (%) N=6	0.6 mg/kg N (%) N=5	1.2 mg/kg N (%) N=6	Total N (%) N=17
AGE	Median	69.5	67	58	65
GENDER	Male	6 (100)	2 (40)	4 (67)	12 (71)
ECOG PS	0	6 (100)	2 (40)	3 (50)	11 (65)
	1	-	3 (60)	3 (50)	6 (35)
BASELINE LDH	≥ULN	2 (33)	3 (60)	2 (33)	7 (41)
TIME SINCE PREVIOUS THERAPY	<60 days	3 (50)	1 (20)	5 (83)	9 (53)
STAGE AT INITIAL TUMOR DIAGNOSIS	Extensive Disease	6 (100)	5 (100)	6 (100)	17 (100)
P53 MUTATION STATUS	Mutated	6 (100)	5 (100)	6 (100)	17 (100)

Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 of 17 patients on-going

Study Drug Exposure

	0.3 mg/kg N=6	0.6 mg/kg N=5	1.2 mg/kg N=6	Total N=17
DURATION OF EXPOSURE (DAYS)				
Mean (SD)	49	41	61	51
Median (Min, Max)	31 (6, 103)	27 (6, 90)	42 (27, 157)	28 (6, 157)
NUMBER OF CYCLES COMPLETED				
Mean (SD)	2.8	2	3.3	2.8
Median (Min, Max)	2 (1, 5)	1 (1, 4)	2.5 (1, 8)	2 (1, 8)
TOPOTECAN DOSE REDUCTIONS				
Patients with any dose reductions (N, %)	-	-	1 (17)	1 (6)
ALRN-6924 DOSE REDUCTIONS				
Patients with any dose reductions (N, %)	-	-	-	-

Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going

Historical Data for Topotecan Hematological Toxicity in Small Cell Lung Cancer

Trial	Phase	N*	Cycles median	Hematological Toxicity Grade ≥3				Comments
				Neutropenia (%)	Febrile N-penia (%)	Thrombo-cytopenia (%)	Anemia (%)	
Hematological toxicity reported by laboratory values								
Hart et al. ASCO 2019	2	28	3	86	17	70	63	Chemosensitive population not reported GCSF not prophylactic in C1 Transfusions: Plt 31%, RBC 41%
Hematological toxicity reported as AEs								
Pawel et al. JCO 2014	3	213	5	54	3	54	31	Chemosensitive population 55% RBC transfusions 53% Mandatory prophylactic growth factors
Eckardt et al. JCO 2007	3	151	4	88	5	43	31	Chemosensitive population 100% RBC transfusions 43%, GCSF 16%
Jotte et al. JCO 2011	2	26	2	78	9	61	30	Chemosensitive population 100% Growth factors as necessary Worst toxicities in cycle #1
Inoue et al. JCO 2008	2	30	2	87	3	40	30	Chemosensitive population 63% GCSF not prophylactic

ALRN-6924 protected against key side effects of topotecan in multiple cell types relative to historical controls

	Topotecan + ALRN-6924 in SCLC patients				Topotecan ± Trilaciclib in SCLC patients‡	
	Topotecan 1.5 mg/m² + ALRN-6924				Topotecan 1.5 mg/m² + Placebo	Topotecan 1.5 mg/m² + Trilaciclib
	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg	Total		
	N (%) N=6	N (%) N=5	N (%) N=6	N (%) N=17	N (%) N=28	N (%) N=32
All AEs* (NCI CTC Grade ≥3)	5 (83)	5 (100)	6 (100)	16 (94)	27 (96)	28 (88)
Neutropenia	4 (67)	5 (100)	6 (100)	15 (88)	24 (86)	22 (69)
Thrombocytopenia	2 (33)	2 (40)	2 (33)	6 (35)	20 (70)	22 (68)
Anemia	1 (17)	2 (40)	1 (17)	4 (24)	18 (63)	10 (39)
Fatigue	-	-	-	-	2 (7)	3 (9)
Nausea	-	-	-	-	1 (4)	0 (0)
Neutropenia NCI CTC Grade 4**	2 (33)	5 (100)	1 (17)	8 (47)	21 (76)	13 (41)

*AEs based on laboratory values, as applicable
** in the first treatment cycle

‡ Hart et al. ASCO 2019 – G1 Therapeutics; Phase 2 Clinical Trial

Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going

Other results support chemoprotection signal with ALRN-6924 treatment

Serious Adverse Events

SAE	0.3 mg/kg N (%) N=6	0.6 mg/kg N (%) N=5	1.2 mg/kg N (%) N=6	Total* N (%) N=17
NEUTROPENIA	-	1 (20)	2 (33)	3 (18)
LEUKOPENIA	-	-	2 (33)	2 (12)
THROMBOCYTOPENIA	-	-	2 (33)	2 (12)
ANEMIA	-	-	2 (33)	2 (12)
FEBRILE NEUTROPENIA	-	-	-	-

Transfusions

	0.3 mg/kg N=6	0.6 mg/kg N=5	1.2 mg/kg N=6	Total N=17
RBC transfusions (% of patients, N of transfusions)	-	3 (60)	3 (50)*	6 (35)
Platelet transfusions (% of patients, N of transfusions)	-	2 (40)	1 (17)	3 (18)

*One patient received multiple RBC transfusions with Hb NCI CTC Grade 2

Performance Status

	0.3 mg/kg N=6	0.6 mg/kg N=5	1.2 mg/kg N=6	Total N=17
ECOG PS at baseline (Mean, Median)	0, 0	0.5, 0.5	0.5, 0.5	0.3, 0
ECOG final PS (Mean, Median)	0, 0	1, 1	0.5, 0.7	0.6, 0

Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going

Interim Clinical Results: Key Takeaways

Evidence of clinically meaningful protection against multiple hematological side effects

Early data suggests broad chemoprotection as indicated by absence of febrile neutropenia, blood transfusions, severe nausea, vomiting, diarrhea, and fatigue

Enrollment completed into 0.3 mg/kg expansion cohort on 24-hour schedule; presentation of full data from patients on 24-hour schedule at EORTC-NCI-AACR conference Oct. 24-25, 2020

Expansion strategy to multiple cancers and multiple chemotherapies

Phase 1b Proof-of-Concept Study in SCLC

- Exploring dose & timing of ALRN-6924 prior to chemotherapy (-24h and -6h schedules)

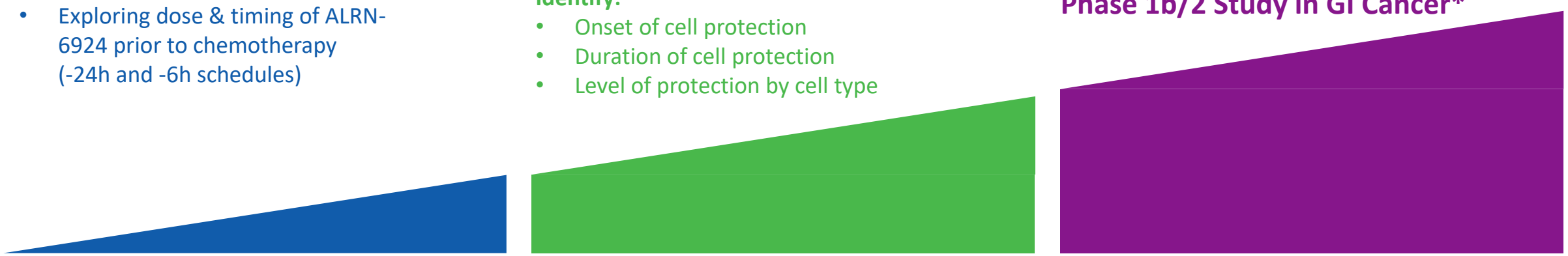
Healthy Volunteer Study

Identify:

- Onset of cell protection
- Duration of cell protection
- Level of protection by cell type

Phase 1b/2 Study in NSCLC*

Phase 1b/2 Study in GI Cancer*



Establish chemoprotection against multiple hematological side effects

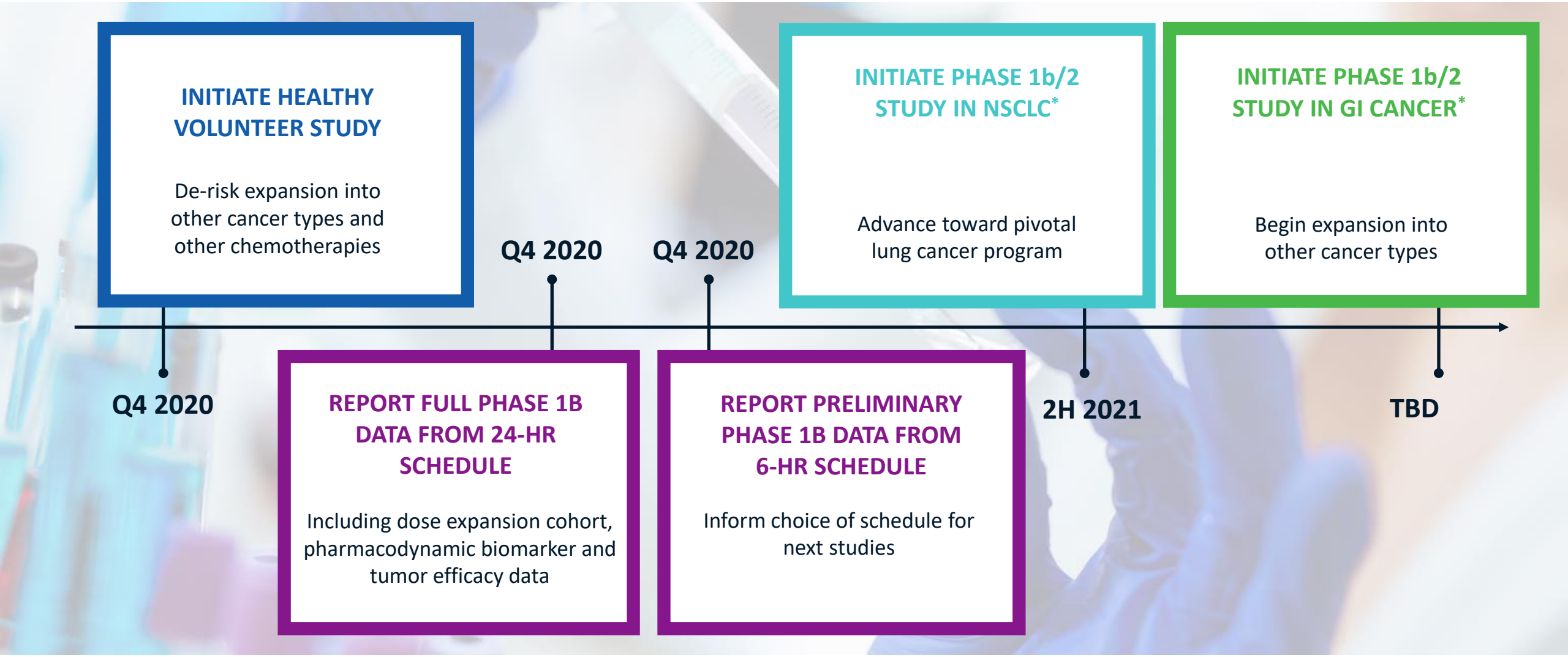
Informs rational design of future clinical trials

Begin expansion to other cancers and chemotherapies

One cancer w/ p53 mutation	→	Multiple cancers w/ p53 mutation
One chemotherapy w/ short half-life	→	Multiple chemotherapies w/ longer half-lives

* Conduct of future trials dependent on funding and results from ongoing dose and schedule optimization trial as well as subject to the impact of the Covid-19 pandemic

Multiple Key Value Drivers in 2020/2021



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Key Financial Highlights

Q2 2020	
Cash, Cash Equivalents and Investments *Expected to support operations into Q4 2021*	**$19MM**
Common Shares Outstanding	**39MM**
Common Warrants ($2.01)	**13MM**

Strategic Execution to Advance Broad Long-Term Vision

- ✓ Validated mechanism of action to pause cell cycle and protect healthy cells in patients with p53-mutated cancers
- ✓ Interim results demonstrated evidence for clinically meaningful protection against multiple hematological side effects
- Planned studies to assess expanded protective effects to other chemotherapies, cancers, and additional chemotherapy-induced toxicities

LONG-TERM VISION

- Chemoprotection for patients with P53-mutated cancers regardless of cancer type or chemotherapy

50% of cancer patients have **P53-MUTATED CANCER**

Transforming the Experience of Chemotherapy for Cancer Patients

NASDAQ: ALRN

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