Building a Franchise in HDV

Sarasar® (lonafarnib)

Pegylated Interferon Lambda-1a

Forward-Looking Statements

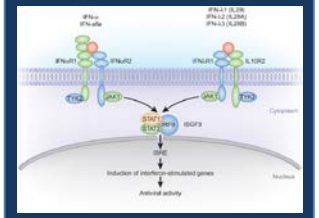
This presentation and the oral commentary contain “forward-looking” statements that involve substantial risks and uncertainties. All statements other than statements of historical facts, including statements regarding our future financial condition, timing for and outcomes of clinical results, business strategy and plans and objectives for future operations, are forward looking statements. These forward-looking statements include terminology such as “believe,” “will,” “may,” “estimate,” “continue,” “anticipate,” “contemplate,” “intend,” “target,” “project,” “should,” “plan,” “expect,” “predict,” “could,” “potentially” or the negative of these terms Forward looking statements are our current statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned clinical development, the timing of and our ability to initiate or enroll clinical trials, and our ability to make regulatory filings and obtain and maintain regulatory approvals for Sarasar, PEG IFN Lambda and our other product candidates, our intellectual property position, the potential safety, efficacy, reimbursement, convenience clinical and pharmaco-economic benefits of our product candidates, commercial opportunities, including potential market sizes and segments, our ability to commercialize, expectations regarding clinical trial data and FDA outcomes, our results of operations, cash needs, spending of the proceeds from this offering, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

Forward-looking statements involve known and unknown risks, uncertainties, assumptions and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements represent our beliefs and assumptions only as of the date of this presentation. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

PEG IFN Lambda

The Next Frontier in Interferon Therapy

Journal of Interferon & Cytokine Research



Interferon-Lambda: A New Addition to an Old Family

The discovery and initial description of the interferon-λ (IFN-λ) family in early 2003 opened an exciting new chapter in the field of IFN research. There are 3 IFN-λ genes that encode 3 distinct but highly related proteins denoted IFN-λ1, -λ2, and -λ3. These proteins are also known as interleukin-29 (IL-29), IL-28A, and IL-28B, respectively. Collectively, these 3 cytokines comprise the type III subset of IFNs. They are distinct from both type I and type II IFNs for a number of reasons, including the fact that they signal through a heterodimeric receptor complex that is different from the receptors used by type I or type II IFNs. Although type I IFNs (IFN-α/β) and type III IFNs (IFN-λ) signal via distinct receptor complexes, they activate the same intracellular signaling pathway and many of the same biological activities, including antiviral activity, in a wide variety of target cells. Consistent with their antiviral activity, expression of the IFN-λ genes and their corresponding proteins is inducible by infection with many types of viruses. Therefore, expression of the type III IFNs (IFN-λs) and their primary biological activity are very similar to the type I IFNs. However, unlike IFN-α receptors which are broadly expressed on most cell types, including leukocytes, IFN-λ receptors are largely restricted to cells of epithelial origin. The potential clinical importance of IFN-λ as a novel antiviral therapeutic agent is already apparent. In addition, preclinical studies by several groups indicate that IFN-λ may also be useful as a potential therapeutic agent for other clinical indications, including certain types of cancer.

Donnelly R et al, J Interferon Cytokine Res, 2010, 30(8): 555.

PEG IFN Lambda

Background

- *First developed by Zymogenetics*
  - *Clinical Development into Phase 2 in early 2000's*
- *Proposed benefit: improved safety and tolerability vs PEG IFN alfa*
- *Target indication: HCV*
- *Acquired by Bristol-Myers Squibb in 2010*
- *Greater than 3,000 patients in 17 clinical trials*
  - *Phase 2 and Phase 3 studies in HCV and HBV*
- *Discontinued following advent of all oral HCV combinations*

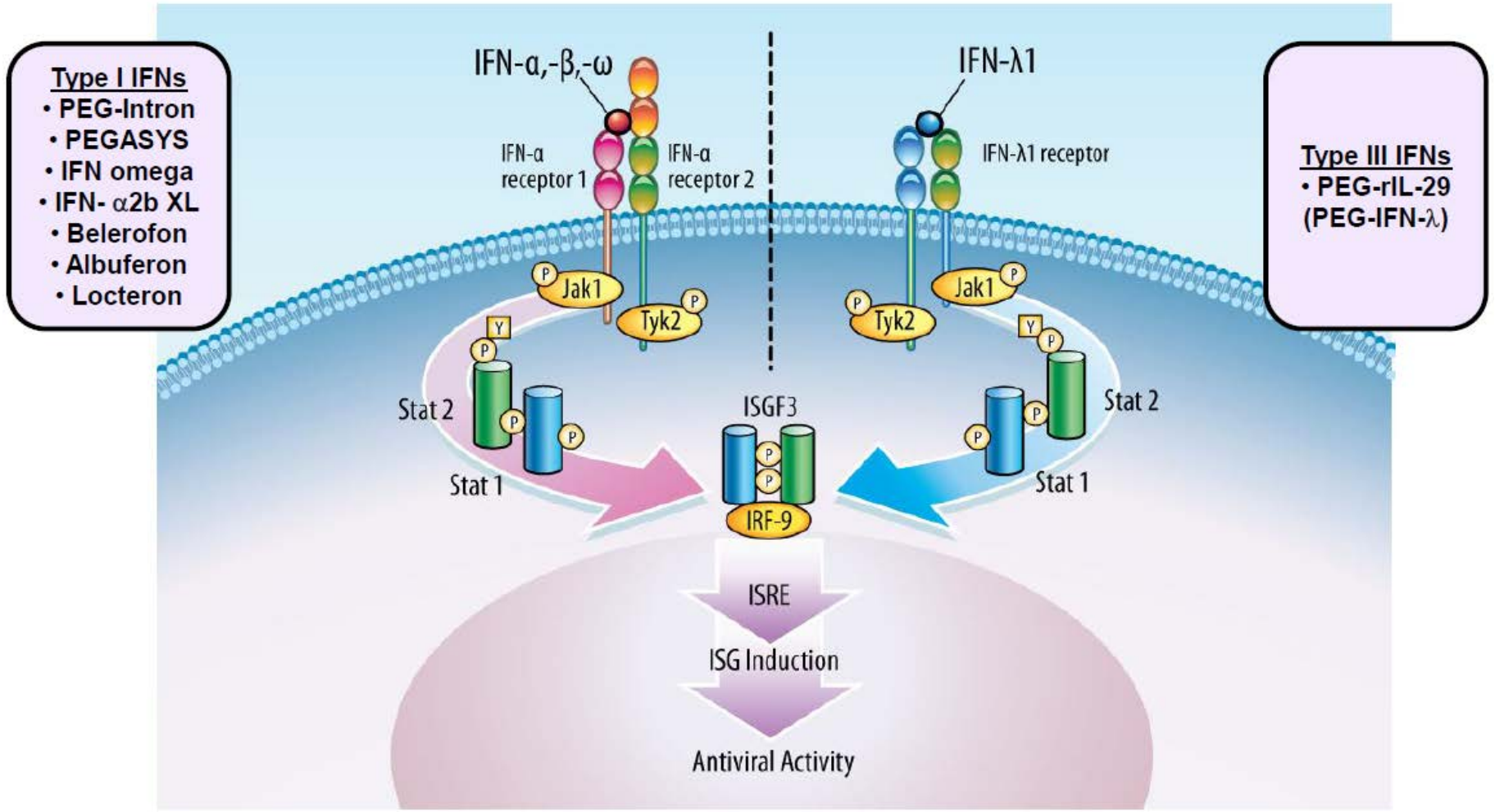
PEG IFN Lambda

A targeted interferon for HDV

- *A novel, first in class Type III interferon*
  - *Native Lambda is generated by human immune system in viral infections*
- *Binds to a unique receptor versus Type I interferons*
  - *Highly expressed on hepatocytes*
  - *Limited expression on hematopoietic cells and CNS cells*
- *Uses similar downstream signaling pathway as Type I interferons*
- *Anti HCV / Anti HBV activity demonstrated in clinical studies*
- *Antiviral activity with less of the typical IFN alfa related side effects*
- *Anti HDV activity demonstrated in humanized liver mouse model*

Type I Interferons versus Type III Interferons

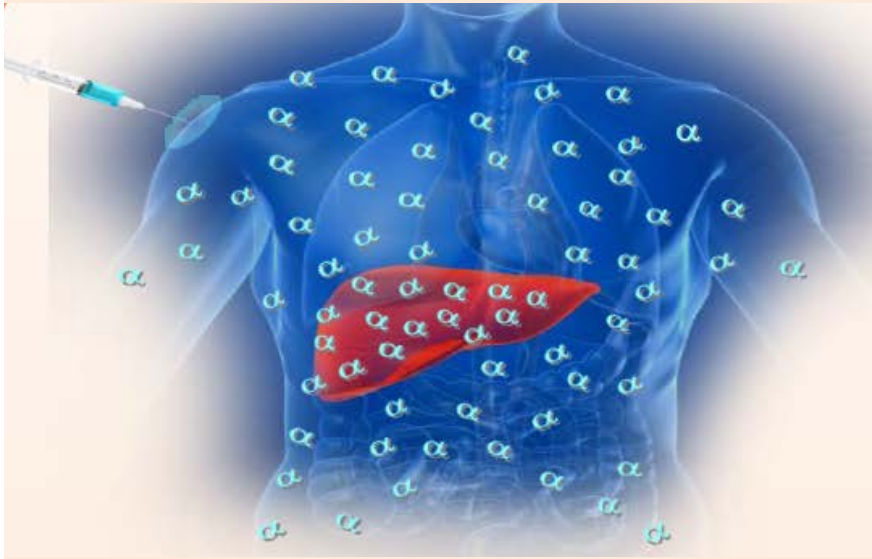
alfa, beta, omega versus lambda



Miller et al, Cytokine Therapies, Ann NY Acad Sci 2009.

Potential Impact of Lambda Receptor Distribution

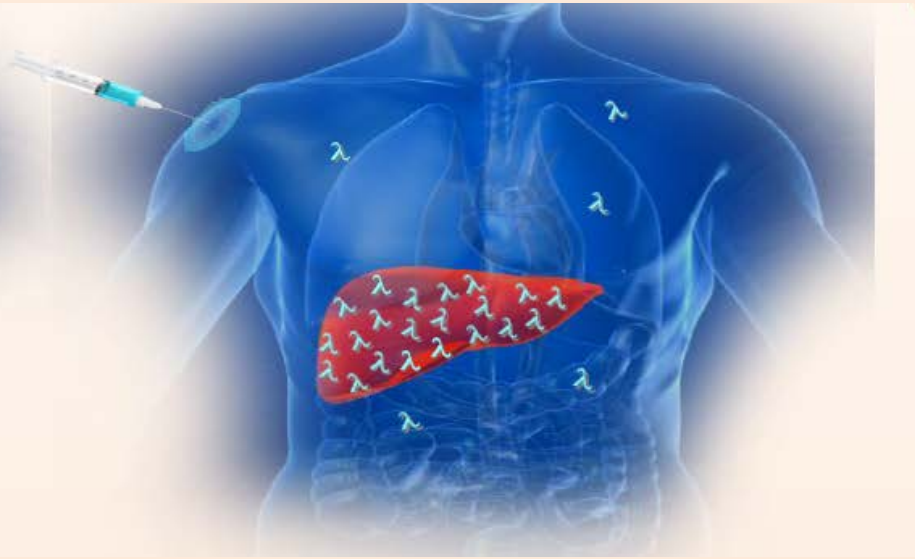
IFN-α receptors **widely** distributed throughout body.



Potential for **MORE** IFN-associated abnormalities:

- ↑ Neutropenia
- ↑ Thrombocytopenia
- ↑ Flu-like Symptoms
- ↑ Musculoskeletal Symptoms

Lambda receptors NOT **widely** distributed throughout body.



Potential for **LESS** IFN-associated abnormalities:

- ↓ Neutropenia
- ↓ Thrombocytopenia
- ↓ Flu-like Symptoms
- ↓ Musculoskeletal Symptoms

PEG IFN Lambda Safety versus PEG IFN Alfa

Results of Clinical Study in HBV Infected Patients

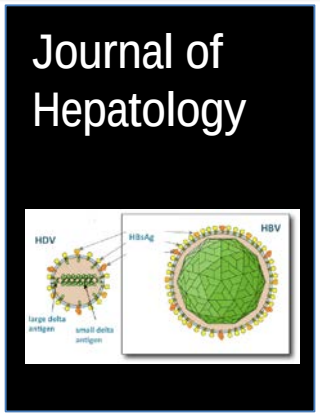
Type of Event	Event	Lambda 180 mcg (N = 80)	Alfa 180 mcg (N = 83)
		# of patients (%)	
Serious adverse events		7 (8.8)	5 (6.0)
Adverse events leading to discontinuation		6 (7.5)	8 (9.6)
Adverse events (any grade) in >15% in any group	Pyrexia	8 (10.0)	38 (45.8)
	Alopecia	9 (11.3)	25 (30.1)
	Fatigue	26 (32.5)	24 (28.9)
	Headache	11 (13.8)	24 (28.9)
	Neutropenia	0	20 (24.1)
	Myalgia	3 (3.8)	18 (21.7)
	Dizziness	5 (6.3)	13 (15.7)
	Pruritus	7 (8.8)	13 (15.7)
	ALT Increase	15 (18.8)	8 (9.6)
Adverse event categories of special interest	Constitutional	28 (35.0)	26 (31.3)
	Neurological	18 (22.5)	30 (36.1)
	Flu-like	13 (16.3)	45 (54.2)
	Musculoskeletal	5 (6.3)	23 (27.7)
	Psychiatric	11 (13.8)	15 (18.1)

Chan, HLY et al, J Hepatology 2016.

PEG IFN Lambda Safety versus PEG IFN Alfa

Results of Clinical Study in HBV Infected Patients

Type of Event	Event	Lambda 180 mcg (N = 80)	Alfa 180 mcg (N = 83)
		# of patients (%)	
Grade 3-4 laboratory abnormalities	ALT increases (>5 x ULN)	33 (41.3)	19 (23.3)
	AST increases (>5 x ULN)	27 (33.8)	15 (18.3)
	Hyperbilirubinemia (>2.5 x ULN)	3 (3.8)	0
	Neutropenia (<750 cells / mm^3)	2 (2.5)	17 (20.7)
	Thrombocytopenia (<50,000 cells / mm^3)	0	1 (1.2)
	Hemoglobin (<9 g/dL or 4.5 g/dL decrease from baseline)	0	0
ALT flares		13 (16.3)	6 (7.2)
Dose reductions		12 (15.0)	23 (27.7)
Dose interruptions		8 (10.0)	4 (4.8)

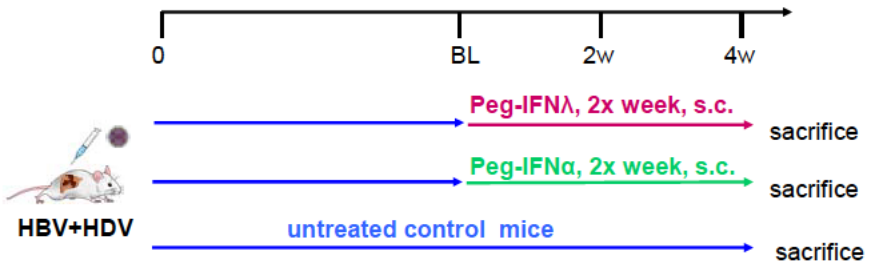


Chan, HLY et al, J Hepatology 2016.

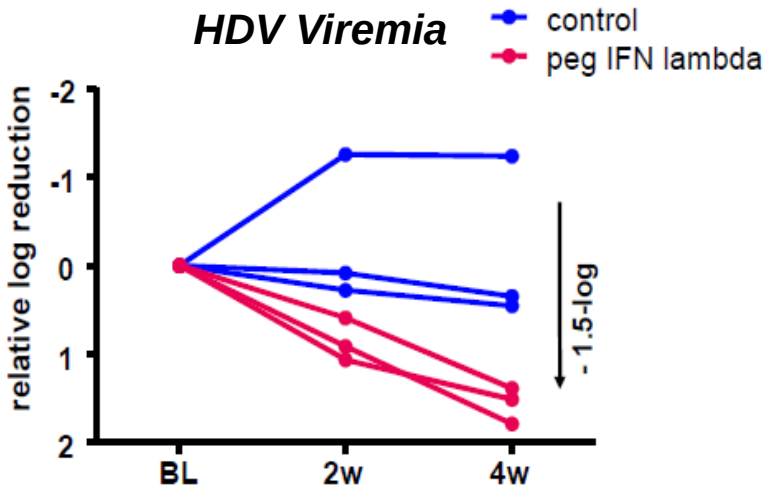
PEG IFN Lambda Suppresses HDV RNA

Strongly Enhanced Innate Immune Response of Human Hepatocytes

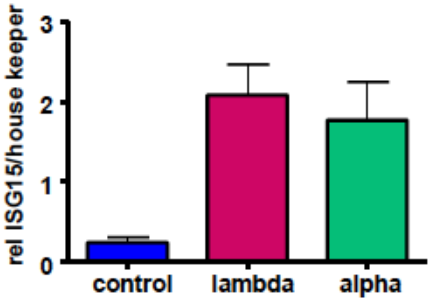
Experimental Design



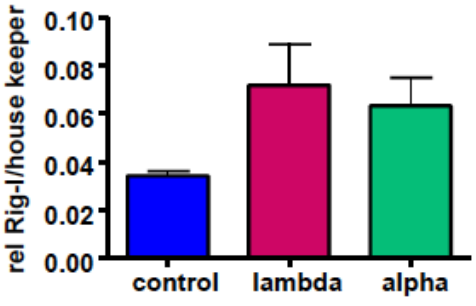
HDV Viremia



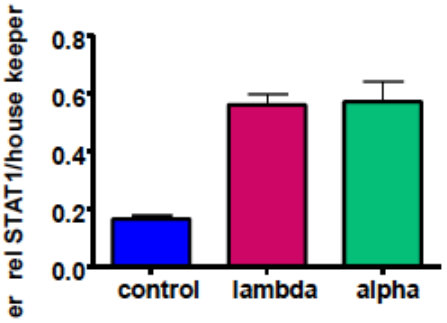
ISG15 = 6.2 Fold



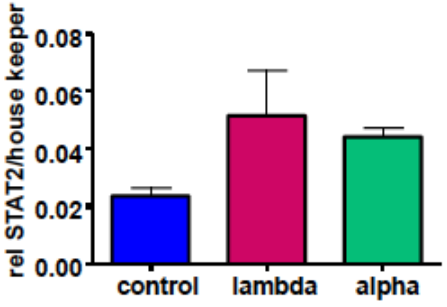
Rig-I = 1.9 Fold



STAT1 = 6.2 Fold



STAT2 = 11.2 Fold



Dandri et al, EASL 2013 Monothematic Conference, Poster

Sarasar® (lonafarnib) Phase 2 HDV Program

LOWR 1 and LOWR 2 Include PEG IFN α Combination Dosing

- ***Proof of Concept***
  - *Monotherapy* — *N = 14* — NIH — *Complete*
- ***LOWR HDV – 1***
  - *Combinations +/- PEG IFN α* — *N = 15* — *Complete*
- ***LOWR HDV – 2***
  - *Dose Finding +/- PEG IFN α* — *N = 37* — *Dosing*
- ***LOWR HDV – 3***
  - *Duration* — *N = 21* — NIH — *Dosing*
- ***LOWR HDV - 4***
  - *Titration* — *N = 15* — MHH Hannover Medical School — *Dosing*

PEG IFN Lambda

Plans

- *Replace PEG IFN alfa in next Eiger HDV studies*
- *Efficiently study potential use as:*
  - *An effective monotherapy in HDV*
  - *An effective combination therapy with Lonafarnib in HDV*
- *Identify potential for better tolerability versus PEG IFN alfa in HDV*
- *Offer a proprietary interferon with more optimal efficacy / tolerability*
- *Apply for Orphan Designation & Fast Track status*
- *Create an HDV franchise opportunity at Eiger*

PEG IFN Lambda

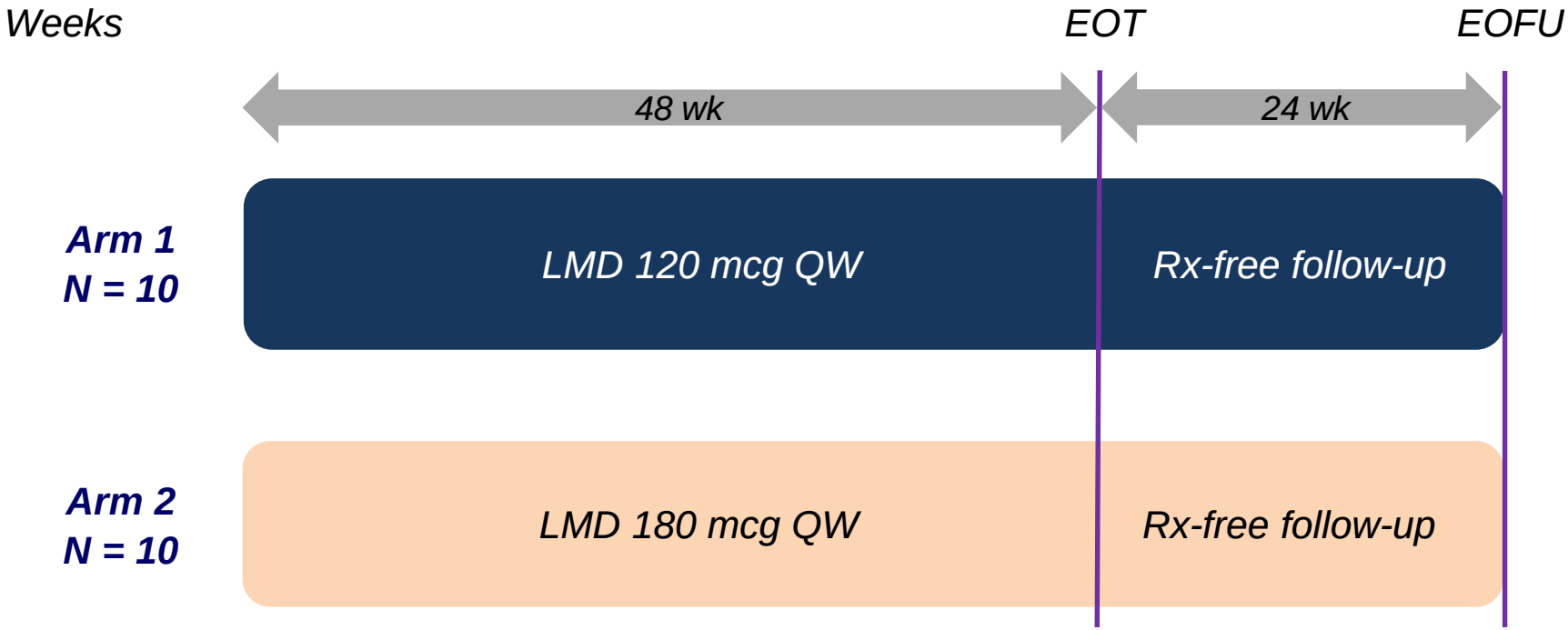
Expected Timelines

- *Drug Product on hand sufficient for Phase 2*
  - *Quantities may supply development through registration*
- *Monotherapy study in HDV to begin in 2H2016*
  - *Lambda alone dose ranging study*
- *Combination study in HDV to begin in 2H2016*
  - *Lonafarnib + Ritonavir + Lambda*
- *Efficient generation of Phase 2 POC data in 4Q2017*
  - *Multiple, international sites*

Monotherapy - Phase 2 POC Study in HDV

LMD 120 mcg QW vs LMD 180 mcg QW

Objective: Safety and Efficacy of LMD 120 mcg vs LMD 180 mcg



New Zealand: Ed Gane (Auckland)

Pakistan: Saeed Hamid (Karachi)

PEG IFN Lambda Monotherapy

Clinical / Regulatory POC Plan

2016	2017	2018

★ Regulatory Filings ✓

Enroll ☆

Dosing ☆

☆ EOT Data

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

2017

☆ Post TRx Data

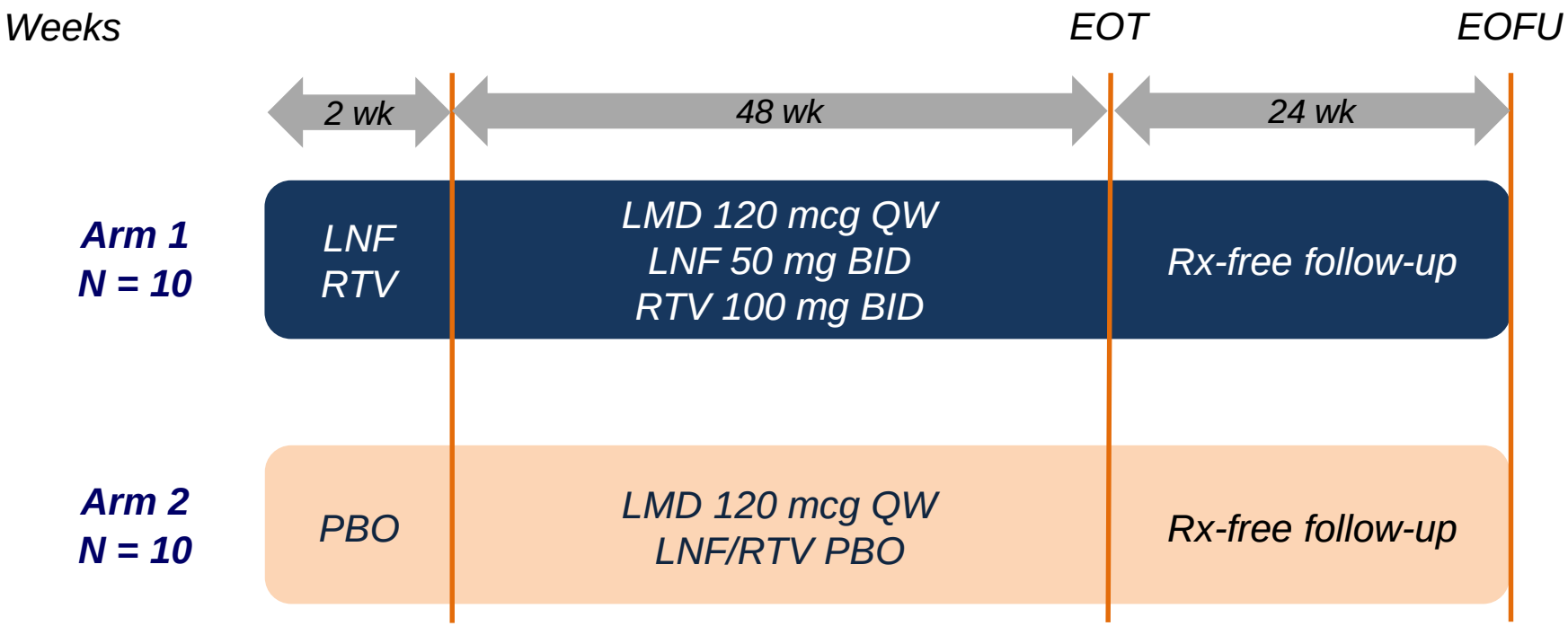
EASL
The Home of Hepatology

2018

Combination - Phase 2 POC Study in HDV

LNF 50 mg BID / RTV 100 mg BID + LMD 120 mcg QW

Objective: Safety and Efficacy of LNF + RTV + LMD vs LMD Alone



Planned Sites:

US: NIH

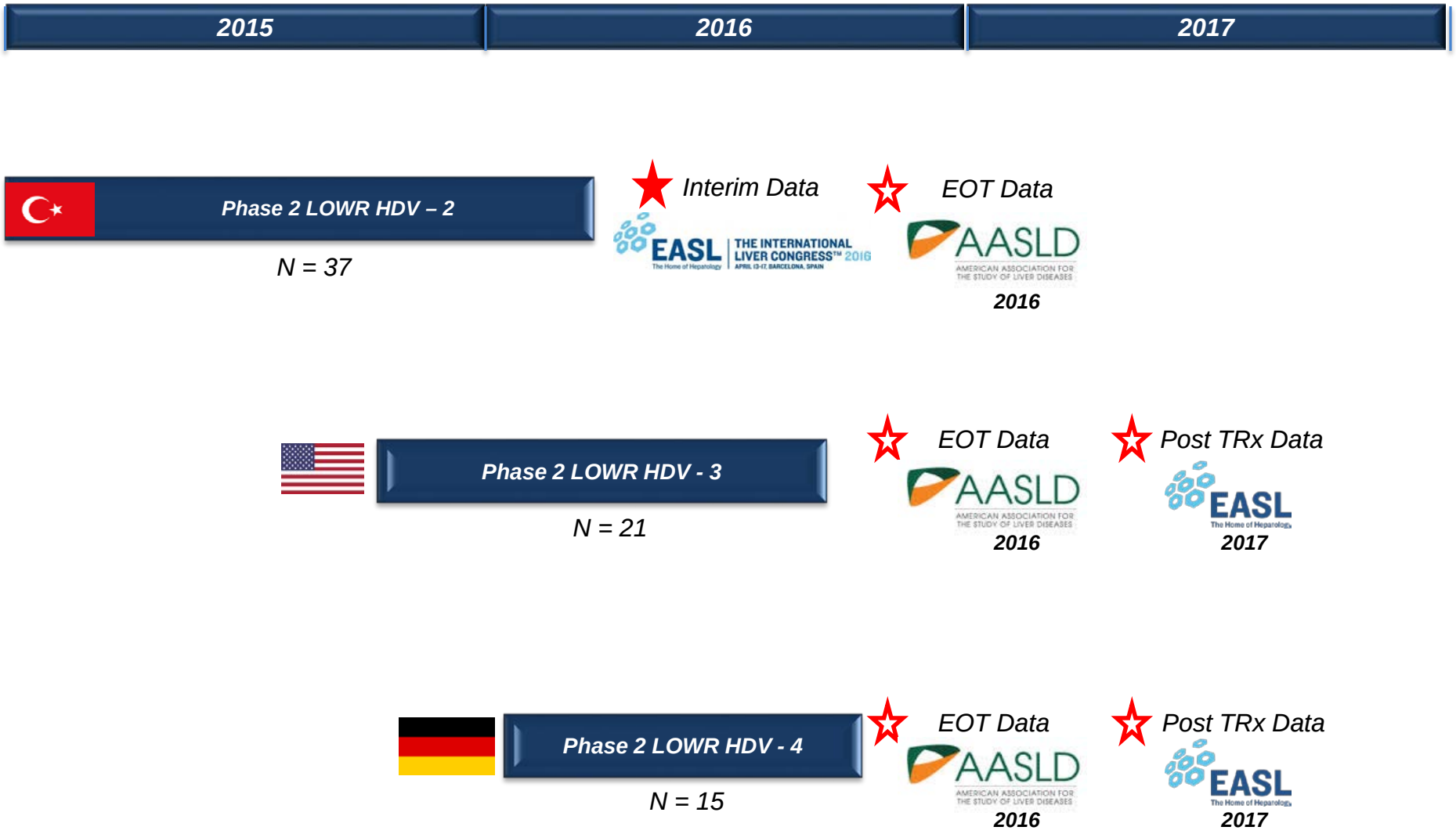
Turkey:

PEG IFN Lambda Combination

Clinical / Regulatory POC Plan

Sarasar® (lonafarnib) in HDV

Phase 2 Results Expected in 2016 / 2017



Potential Registration Pathways

Building an HDV Franchise

HDV Registration Options	*Clinical Description*	*Treatment Option* *All Oral*	*Treatment Option* *Triple Combo*	*Treatment Option* *Mono*
Cure	*HDV RNA Negativity* + *ALT Normalization*	*Lonafarnib* + *Ritonavir*	*Lonafarnib* + *Ritonavir* + *Lambda*	*Lambda*
Chronic Treatment	*HDV RNA Reduction* + *ALT Normalization*	*Lonafarnib* + *Ritonavir*		

Building a Franchise in HDV

Sarasar® (lonafarnib)

Pegylated Interferon Lambda-1a