

# Addressing the Billion-Dollar Problem of Drug-Induced Liver Injury

Ultra-sensitive hepatotoxicity assays for the development of safer drugs



Drug-induced liver injury (DILI) is frequently detected in post-marketing resulting in drug withdrawals and box warnings that shrink the market and cost drug developers billions.

**40%**

Of drugs fail due to toxicity

**#1**

DILI is the #1 cause of toxicity

**23%**

Of drug withdrawals are caused by DILI

**60%**

Of drugs carry DILI box warnings

Lena Biosciences' hepatotoxicity assays predict DILI with high sensitivity using a single drug treatment

	Drug	Approval status	DILI status	DILI type	1 dose 1 day study IC50/Cmax	Predicted
<b>Structurally similar drugs</b>	Troglitazone	Withdrawn	Positive	Idiosyncratic	0.09	Yes
	Pioglitazone	✓	Negative/low DILI	Intrinsic	> 34	Yes
	Tolcapone	Withdrawn	Positive	Intrinsic	0.06	Yes
	Entacapone	✓	Positive/lower DILI	Intrinsic	9.48	Yes
	Sitax(s)entan	Withdrawn	Positive	Intrinsic	4.15	Yes
	Ambrisentan	✓	Negative	Intrinsic	> 1025	Yes
	Clozapine	✓	Positive	Intrinsic	11.4	Yes
	Olanzapine	✓	Negative	Intrinsic	> 625	Yes
	Trovafloxacin	Withdrawn	Positive	Idiosyncratic	1.48	Yes
	Levofloxacin	✓	Negative/low DILI	Intrinsic	> 32	Yes
Nefazodone	Withdrawn	Positive	Intrinsic	1.84	Yes	
Trazodone	✓	Negative/low DILI	Intrinsic	32.93	Yes	
Buspirone	✓	Negative	Intrinsic	26010	Yes	
Diclofenac	✓	Positive	Intrinsic	8.49	Yes	
Zileuton	✓	Positive	Intrinsic	14.91	Yes	
Isoniazid	Box Warning	Positive	Idiosyncratic	21.28	Yes	

DILI positive: IC50/Cmax < 25

# De-Risking Drug Development

with Perfused Organ Panel and proprietary assay services

Lena Biosciences' hepatotoxicity assays isolate early toxicity signals and provide actionable insights for drug developers



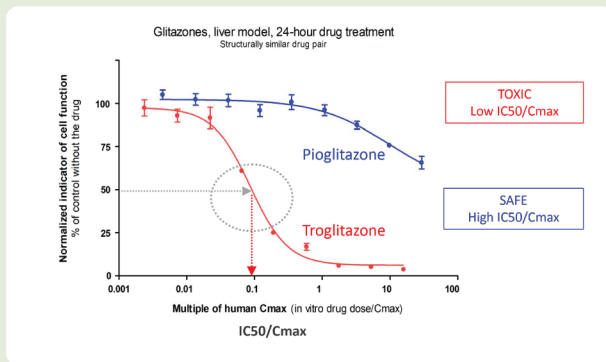
- ✔ Detect DILI early
- ✔ Understand what causes the toxicity
- ✔ Find active mechanisms for a given dose
- ✔ Identify safe doses
- ✔ Exclude at-risk patient groups



Cutting-edge services to predict and mitigate DILI using the Perfused Organ Panel microphysiological system which combines 3D cell cultures with in-well perfusion using synthetic hemoglobin, Blood Substitute.

## Case Studies Involving Structurally Similar Drugs

### Detecting toxicity at low dose for a withdrawn Type II diabetes drug

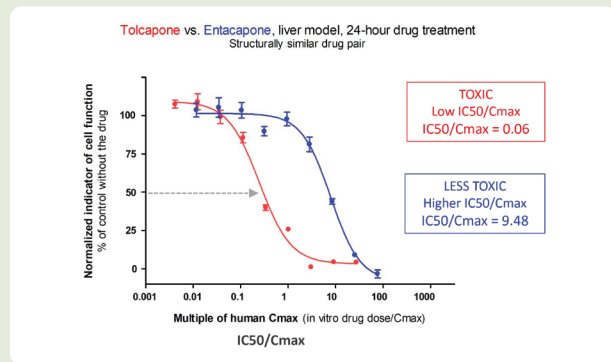


#### Troglitazone was withdrawn

- \$1.3 B annual sales loss
- 63 patients died from DILI

#### Pioglitazone is approved

### Differentiating severity of DILI symptoms for Parkinson's disease drugs



#### Tolcapone was withdrawn

- Later approved with careful monitoring

#### Entacapone is approved

- Prescribing information lists hepatitis in post-marketing

Contact us for additional case studies including Isoniazid, Phenformin, Metformin, and Diclofenac in liver and brain models, and mitochondrial complex-specific toxicity for Nefazodone, Trazodone and Buspirone.

