DURECT Corporation

A Specialty Pharmaceuticals Company

March 2, 2015

DURECT

Forward-Looking Statements

The statements in this presentation regarding DURECT's and its collaborative partners' products in development, anticipated product benefits, anticipated product markets, clinical trial results and plans, DURECT's future business plans and projected financial results and DURECT's emergence as a specialty pharmaceutical company are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, DURECT's (and that of its third-party collaborators', where applicable) abilities to successfully enroll and complete clinical trials, complete the design, development, and manufacturing process development of the product candidates, obtain product and manufacturing approvals from regulatory agencies and manufacture and commercialize the product candidates and marketplace acceptance of the product candidates, as well as DURECT's ability to fund its growth and operations. Further information regarding these and other risks is included in DURECT's most recent Annual or Quarterly Report on Form 10-K or 10-Q filed with the SEC under the heading "Risk Factors."

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DURECT Corporation
Building a Leading Specialty Pharmaceutical Company

- 2 late (NDA) stage assets leveraging drug delivery: REMOXY® and POSIDUR™
  - Addressing large market opportunities ($1+ billion)
  - Unique products for chronic pain and post-surgical pain
  - Distinct approaches to proper use of opioids
  - Other programs pursuing 505(b)2 path to approval
- Epigenomic Regulator Program yielding endogenous new chemical entities (NCE's)
  - DUR-928: endogenous small molecule with novel mechanism, compelling data from multiple animal models, and successful initial Phase 1 study
  - Potential orphan and broad indications for acute organ injury and chronic metabolic disorders
- Balanced business model
  - Some programs partnered, others with rights retained

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Pipeline from Drug Delivery Programs
Multiple Products and Partnerships to Drive Value

	PROJECT	Pre Clinical / Phase 1 / Phase 2 / Phase 3 / NDA	Potential Market[1]	Commercialization Company
	REMOXY® (ORADUR®-Oxycodone)	Phase 3	$1+ Billion	Pain Therapeutics, Inc.
	POSIDUR™ (SABER®-Bupivacaine)	Phase 3	$1+ Billion	DURECT
	ELADUR® (TRANSDUR®-Bupivacaine Patch)	Phase 2	Orphan - PHN	IMPAX LABORATORIES, INC.
	Relday™ (Risperidone)	Phase 1	$1+ Billion	Zogenix
	ORADUR®-ADHD (Methylphenidate)	Phase 1	$1+ Billion	DURECT / orientPHARMA co. Ltd. 東亞生技醫藥股份有限公司
	ORADUR®-Hydromorphone	Phase 1	$1+ Billion	Pain Therapeutics, Inc.
	Ophthalmic Product (API not disclosed)	Pre Clinical	Not disclosed	Santen — A Clear Vision For Life

1) Estimates for potential market opportunities are based on publicly available information, research reports and company reports

DUR-928: Potential clinical indications

Currently in Phase 1

Chronic indications

Oral

- NAFLD/NASH
  AFLD/ASH
- Others ★

Acute indications

Injectable

- Acute kidney injury ★
- Others ★

★ Orphan indications

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Opioids Remain Major Focus of FDA

- Abuse of opioids remains top of mind for the FDA and the pain division – a hot, important and highly visible topic
- Our two lead programs both address this issue, but in different ways
- We think we should ultimately benefit from the FDA's actions and concerns

- REMOXY® - tamper-resistant formulation of oxycodone
- POSIDUR™ - benefits of reducing opioid use after surgery

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ORADUR®-Opioids
REMOXY®

REMOXY®

Crushed

Long Acting Oxycodone Tablets

Intact

Crushed

Tamper Resistant

- Snorting ⊘
- Smoking ⊘
- Injecting ⊘
- Chewing ⊘
- Dissolving in drinks

Minimal Impact

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ORADUR®-Opioids

REMOXY® Likeability Study – Met All Pre-specified Primary Endpoints

Pain Medicine 2011; 12: 618–631

The Abuse Potential of Remoxy®, an Extended-Release Formulation of Oxycodone, Compared with Immediate- and Extended-Release Oxycodone

Beatrice Setnik, PhD,* Carl L. Roland, PharmD,* Jody M. Cleveland, MS,* and Lynn Webster, MD†

- Drug Liking was significantly lower ($p<0.05$) for REMOXY
  - REMOXY (whole) vs. oxycodone ER (whole) or oxycodone IR
  - REMOXY (chewed) vs. oxycodone ER (crushed) or oxycodone IR
- Time to Peak Drug Liking was significantly delayed ($p<0.05$) for REMOXY (chewed) vs. oxycodone ER (crushed) or oxycodone IR
- No patient could chew REMOXY for more than 1.5 minutes (mean = 45 seconds) due to taste/texture

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ORADUR®-Opioids

REMOXY®: NDA Status post-CRL on June 23, 2011

- The issues in the Complete Response Letter relate primarily to manufacturing

- Pfizer met with FDA re: resubmission

- Various studies posted to ClinicalTrials.gov, now completed

- Meeting provided a path forward, following the outline Pfizer requested
  - No need to re-do Phase III studies
    - A pivotal bioequivalence (BE) study with the modified formulation can be used to bridge back to data with the original formulation
    - Similar to, but larger than, the BA studies already done by Pfizer
  - Also need to conduct additional abuse potential studies with the modified formulation
    - Such data may now potentially be used in the product label

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ORADUR®-Opioids

REMOXY®: Studies on Clinicaltrials.gov as of Sept 24, 2014

Study Purpose	Study Number	Number Subjects	Start Date	Estimated Completion Date	Status
Effect of food on PK of chewed versus non-chewed capsule - Formulation K	NCT02117583 Phase 1	N=34 healthy volunteers	April 2014	August 2014	Completed ✓
Dose proportionality of 5, 20 and 40 mg capsules - Formulation K	NCT02089295 Phase 1	N=18 healthy volunteers	April 2014	June 2014	Completed ✓
Bioavailability of Formulation K to Original Formulation	NCT02059915 Phase 1	N=134 healthy volunteers	April 2014	July 2014	Completed ✓
Abuse potential, after taking intact and chewed capsule	NCT01986283 Phase 1	N=67 recreational opioid users	Nov 2013	August 2014	Completed ✓
Effects of Ethanol on Oxycodone Pharmacokinetics in Healthy Volunteers	NCT02165930 Phase 1	N=17 healthy volunteers	July 2014	August 2014	Completed ✓

- All required studies are completed
- Program and data to be transferred back to Pain Therapeutics
- Pain Therapeutics will focus on resubmission and re-partnering

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Patent Protection for ORADUR® technology

- 7 issued U.S. patents covering ORADUR® technology platform
  - 6 composition of matter (opioid or oxycodone formulations) patents and 1 covering methods of making opioid-containing formulations
- U.S. patent coverage (oxycodone only) to at least 2031, U.S. patent coverage (opioid or oxycodone formulations) to at least 2025
- European patent coverage to at least 2023
- Other pending applications would go to 2034, plus any eligible patent term adjustments and extensions

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REMOXY®: Potential Financial Impact to DURECT
(dollars in millions)

- OxyContin® sales in 2013: ~$3.0 billion
- Blended royalties on net sales: 6% to 11.5%

Illustrative Royalty Calculations:
(in millions)

% of 2013 OxyContin Sales	**10%**	**20%**	**30%**
REMOXY Annual Sales	$ 314	$ 628	$ 941
Royalties to DURECT *	**$ 21**	**$ 47**	**$ 76**

* Does not include revenue / profits associated with manufacturing mark-up of key excipients.

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POSIDUR™: Post-Operative Pain Control

SABER®-Bupivacaine

POSIDUR™
Bupivacaine Sterile Solution for Instillation

True 3 Days of Post-Op Pain Control

- Unmet need: non-narcotic analgesia, 24-72 hours after surgery
- Designed for local control of post-surgical pain
- Plus reduced narcotic use and associated side-effects / costs
  - Nausea, vomiting, ileus, constipation, respiratory suppression
  - Potential for earlier hospital discharge

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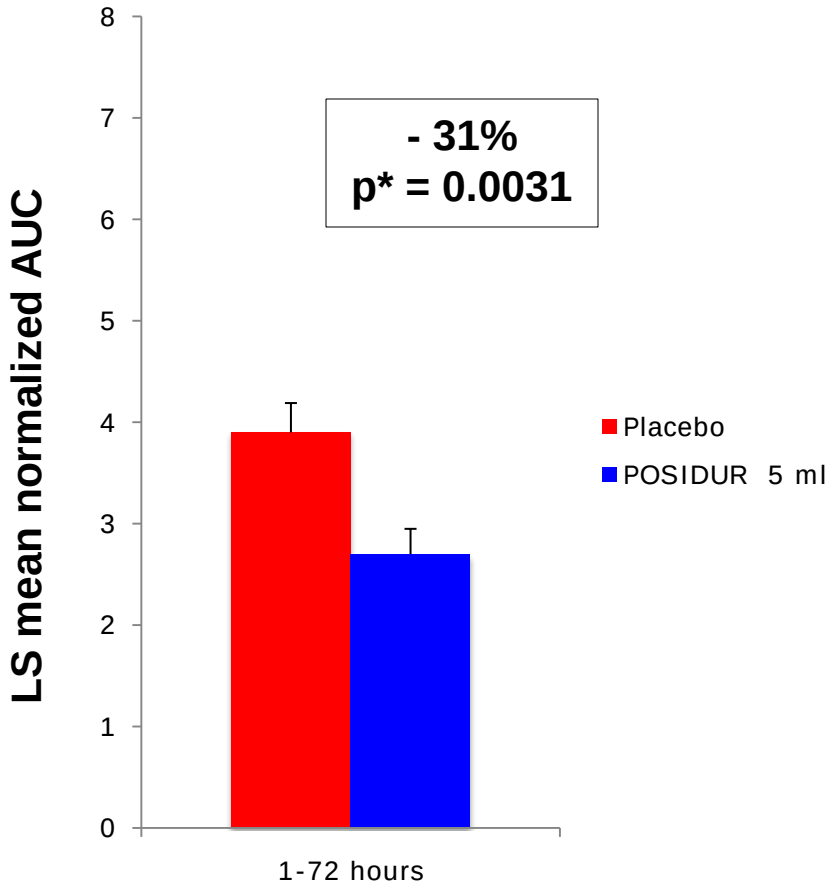
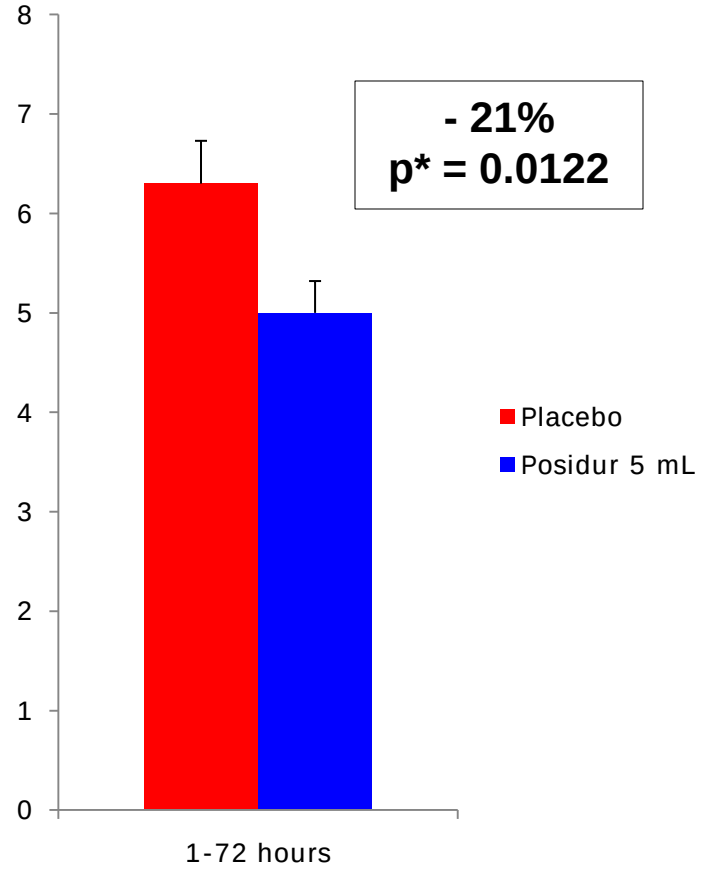
POSIDUR™:
Reduction in Pain on Movement

Hernia Surgery



Shoulder Surgery



* P-values are derived from ANOVA.

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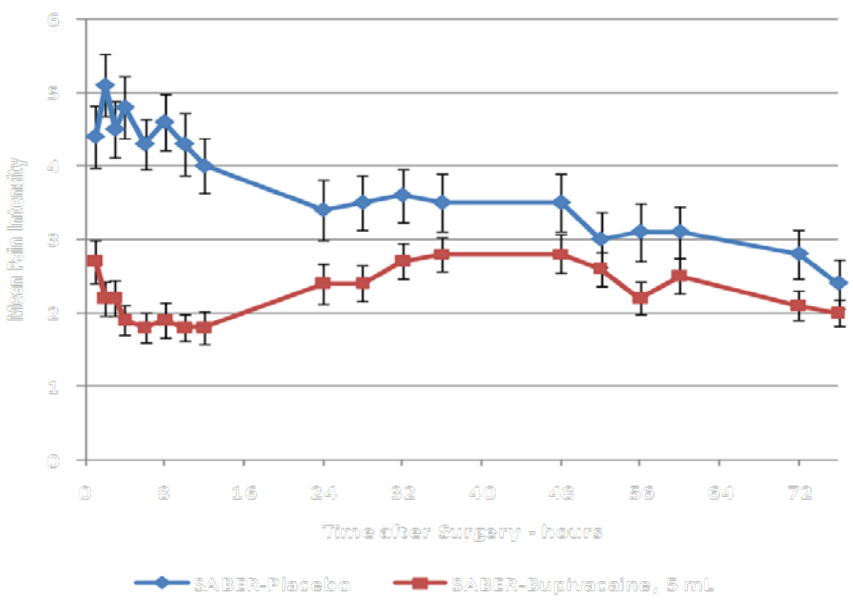
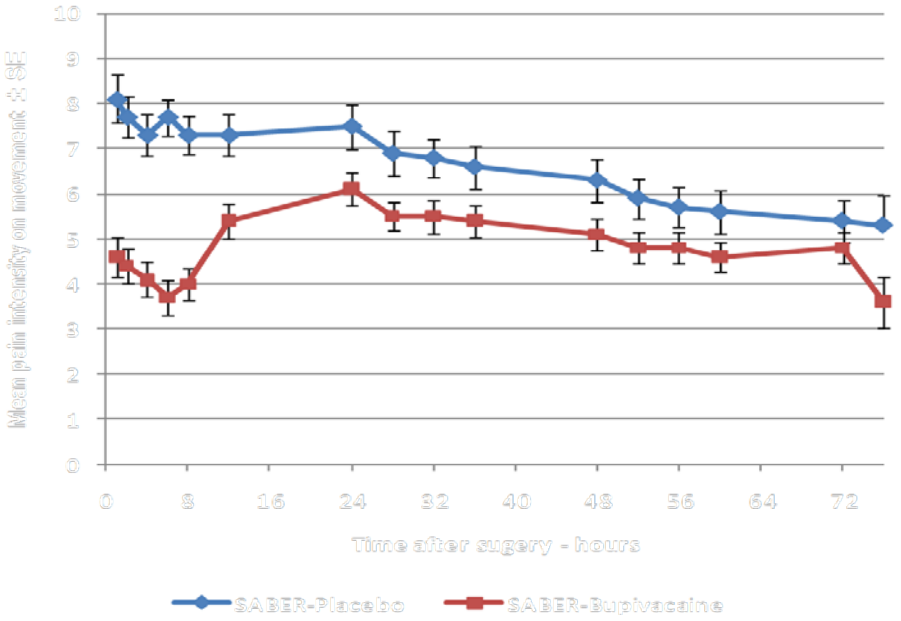
POSIDUR™:
Repeated Measures Analysis

Hernia Surgery



Shoulder Surgery



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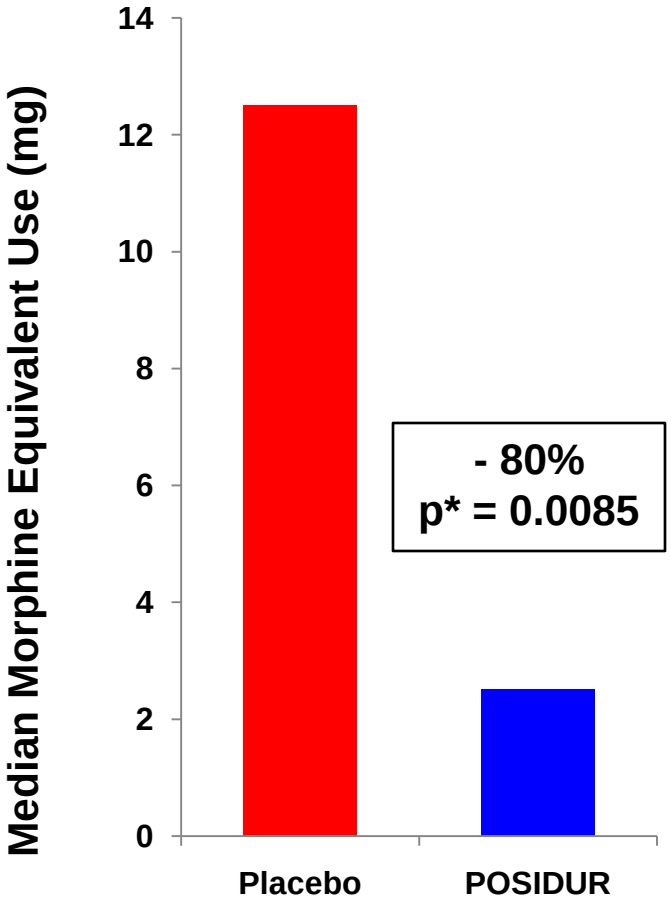
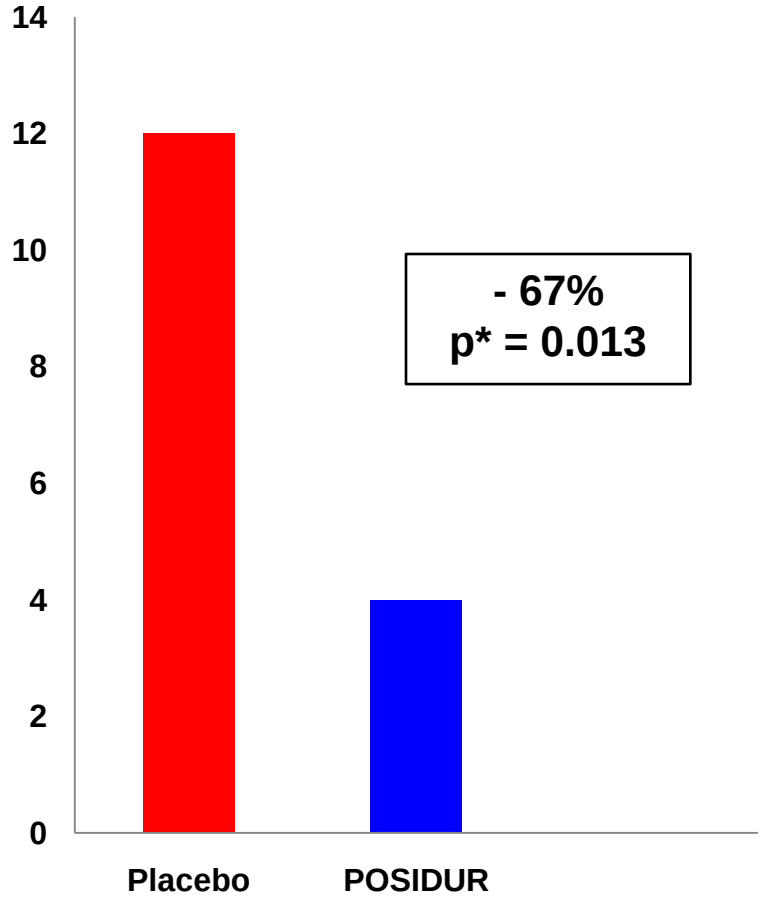
POSIDUR™:
Reduction in Opioid Use

Hernia Surgery



Shoulder Surgery



*P-value is derived from non-parametric Wilcoxon Rank Sum test

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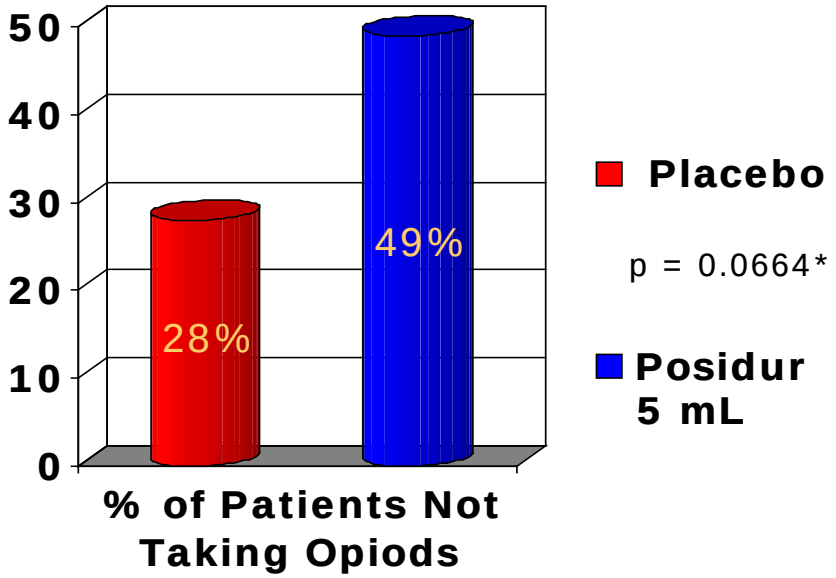
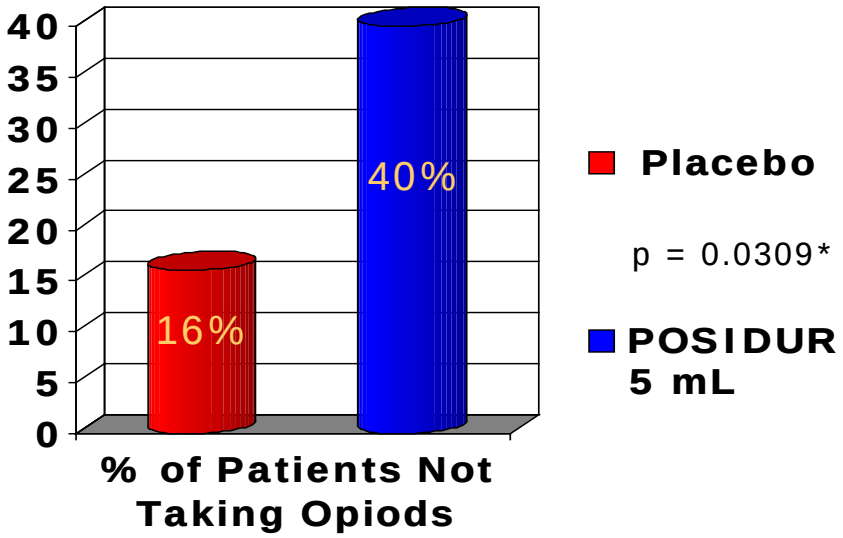
POSIDUR™:

Proportion of Patients NOT Taking ANY Supplemental Opioid 0-72 Hrs

Hernia Surgery



Shoulder Surgery



> 20% more patients didn't require a single opioid

* Using CMH Chi-Square test adjusted by study sites

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POSIDUR™: Clinical Program

- Extensive clinical program
  - 13 studies completed (+ 1 safety extension C803-017e)
  - 683 POSIDUR exposures
  - 951 SABER-Vehicle exposures
  - Multiple surgical models
  - No significant systemic safety concerns observed, some increase in temporary local discoloration

Surgical Model	Protocol No.	Phase	Patients Dosed	Received POSIDUR
Normal Subjects	CLIN005-0008	Phase 1	5	5
Hernia	CLIN004-0001	Phase 2	81	61
Hernia	CLIN004-0009	Phase 2	43	32
Hernia	CLIN005-0010	Phase 2	89	54
Hernia	CLIN005-0007	Phase 2	12	12
Appendectomy	CLIN005-0002	Phase 2	21	14
Shoulder	CLIN005-0006	Phase 2	106	62
Shoulder	C803-017	Phase 2	60	40
Hysterectomy	BU-001-IM	Phase 2	114	60
Abdominal	C803-027	Phase 2	10	10
Abdominal	C803-025	Phase 3	305	189
Hernia	CLIN 803-006-0006	**Pivotal**	123	91
Shoulder	BU-002-IM	**Pivotal**	107	53
Total Patients			1,075	683

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Patent Protection for POSIDUR™

- 2 granted patent families in the U.S. - coverage to at least 2025
  - Pharmaceutical composition
  - Method for providing sustained local anesthesia
- 1 granted patent in Europe - coverage to at least 2025
- 1 granted patent in Japan - coverage to at least 2025

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POSIDUR™: Commercial Opportunity

POSIDUR™
Bupivacaine Sterile Solution for Instillation

- >70 million surgeries per year in the U.S.
- 10-20 million procedures as a potential available market
- Targeting ~$300 / procedure based on strong pharmacoeconomics
  - Driven by reduction in opioid use and side-effects

- Easy product concept for surgeons, anesthesiologists and payers to get behind
  - Better for patients
  - Potentially large healthcare cost savings
  - Benefits to administration technique
  - Underlying desire for non-opioid, extended post-surgical pain relief

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POSIDUR™ Complete Response Letter
February 12, 2014

- Complete Response Letter: FDA has determined that they cannot approve the NDA in its present form, stating the NDA does not contain sufficient information to demonstrate that POSIDUR is safe when used in the manner described in the proposed label, and the FDA indicated that additional clinical safety studies need to be conducted

- We met with the FDA on September 23, 2014 to discuss path forward and have had subsequent interactions
  - FDA is reviewing our protocol synopsis for a soft tissue Phase 3 trial to generate the efficacy and safety data required for approval

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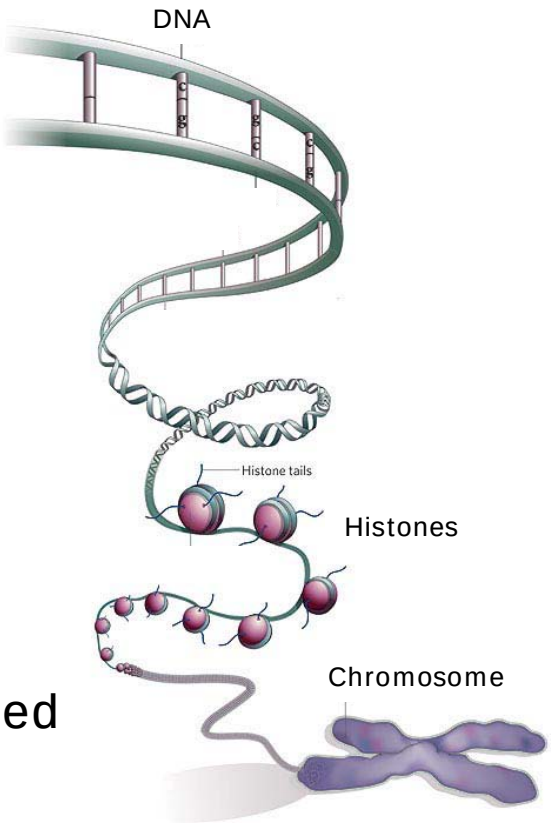
Epigenomic Regulator Program

- Lead molecule: DUR-928
  - Endogenous small molecule
- Epigenomic modulator
  - Lipid homeostasis
  - Inflammation
  - Cell survival
- Family of compounds
  - Additional endogenous molecules discovered
  - Ongoing analogue program



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Improvement in Hepatic Morphology after 6 Weeks

Chow diet

High fat diet (HFD)

10 weeks

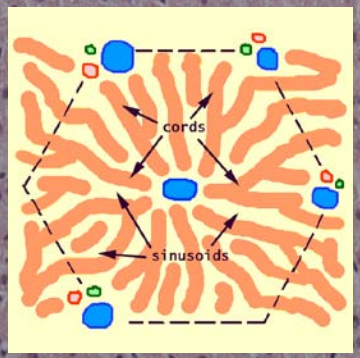
+ Placebo

6 weeks

+ Placebo

+ DUR-928

Chow + Placebo



HFD + Placebo

HFD + DUR-928

- ↑ Insulin sensitivity
- ↑ Glucose tolerance
- ↓ Liver TG & cholesterol
- ↓ Serum ALT, AST
- ↓ Plasma cholesterol

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Epigenomic Regulator Program Highlights

- Family of endogenous regulators and analogues
- Novel mechanisms, with compelling data from multiple animal models
- Potential orphan and broad-based indications
  - Acute organ injury: injectable formulation
  - Chronic metabolic and lipid disorders: oral formulation

- Program in-licensed in 2012; exclusive worldwide rights with issued and pending patents
- Successful initial Phase I study, with further clinical studies planned for 2015

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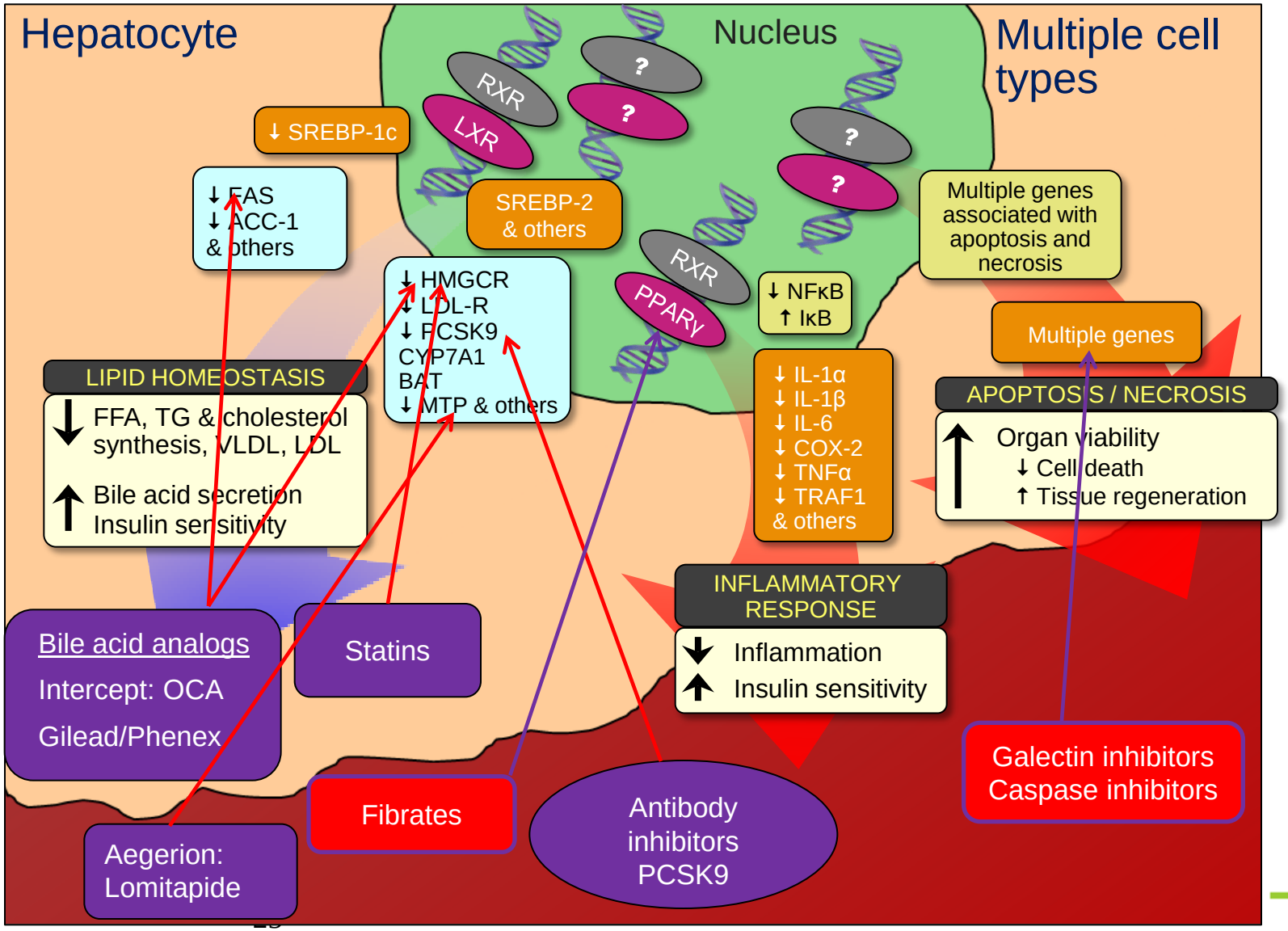
Observed Biochemical Activity



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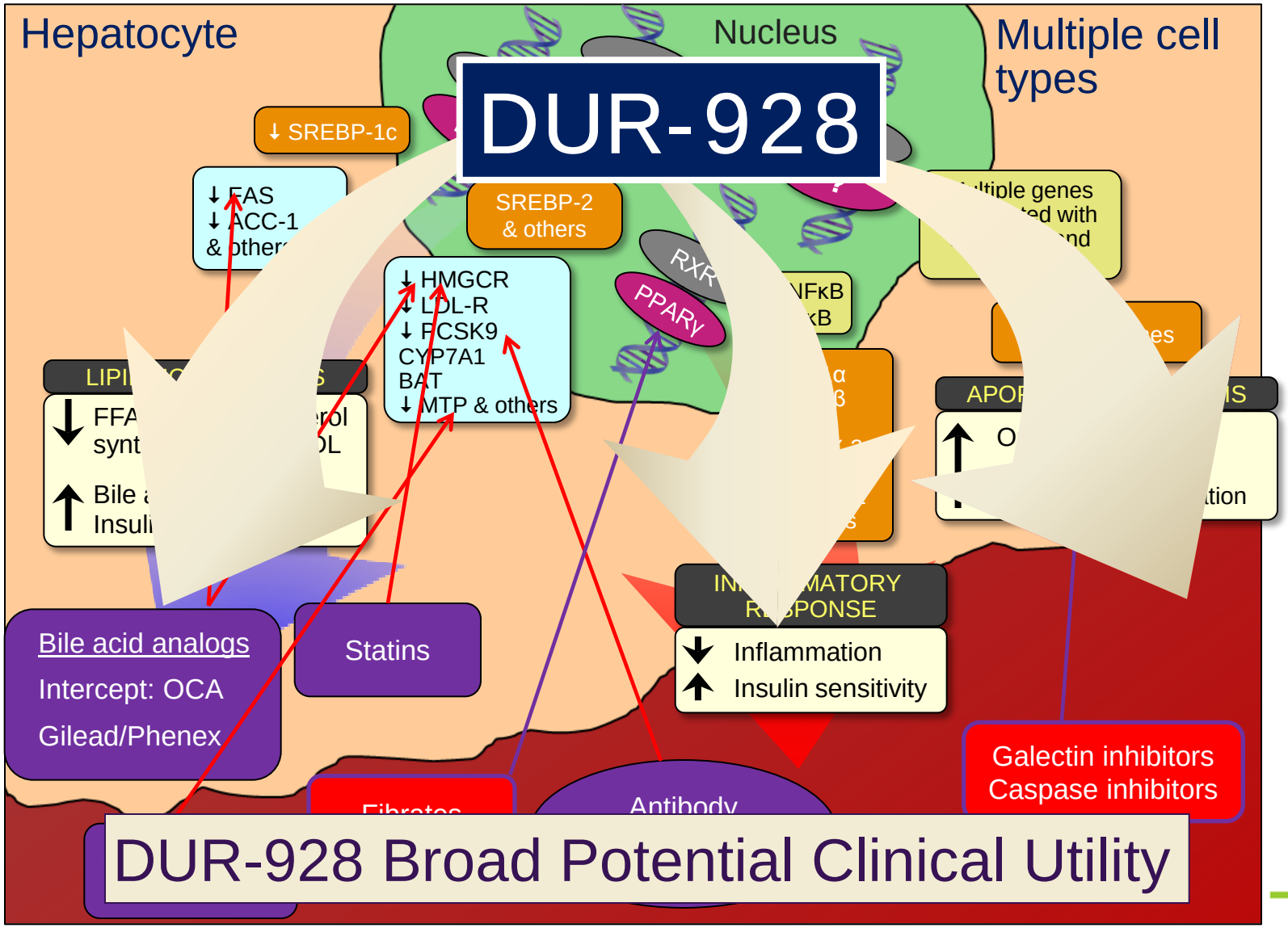
Observed Biochemical Activity



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Compelling Animal Data

Acute Organ Injury models

- Liver toxicity
- Endotoxin-induced septic shock
- Renal ischemia / reperfusion injury

Chronic Disease Models

- High fat diet mouse
- High fat diet hamster
- NAFLD / NASH mouse
  - Nonalcoholic fatty liver disease (NAFLD)
  - Nonalcoholic steatohepatitis (NASH)

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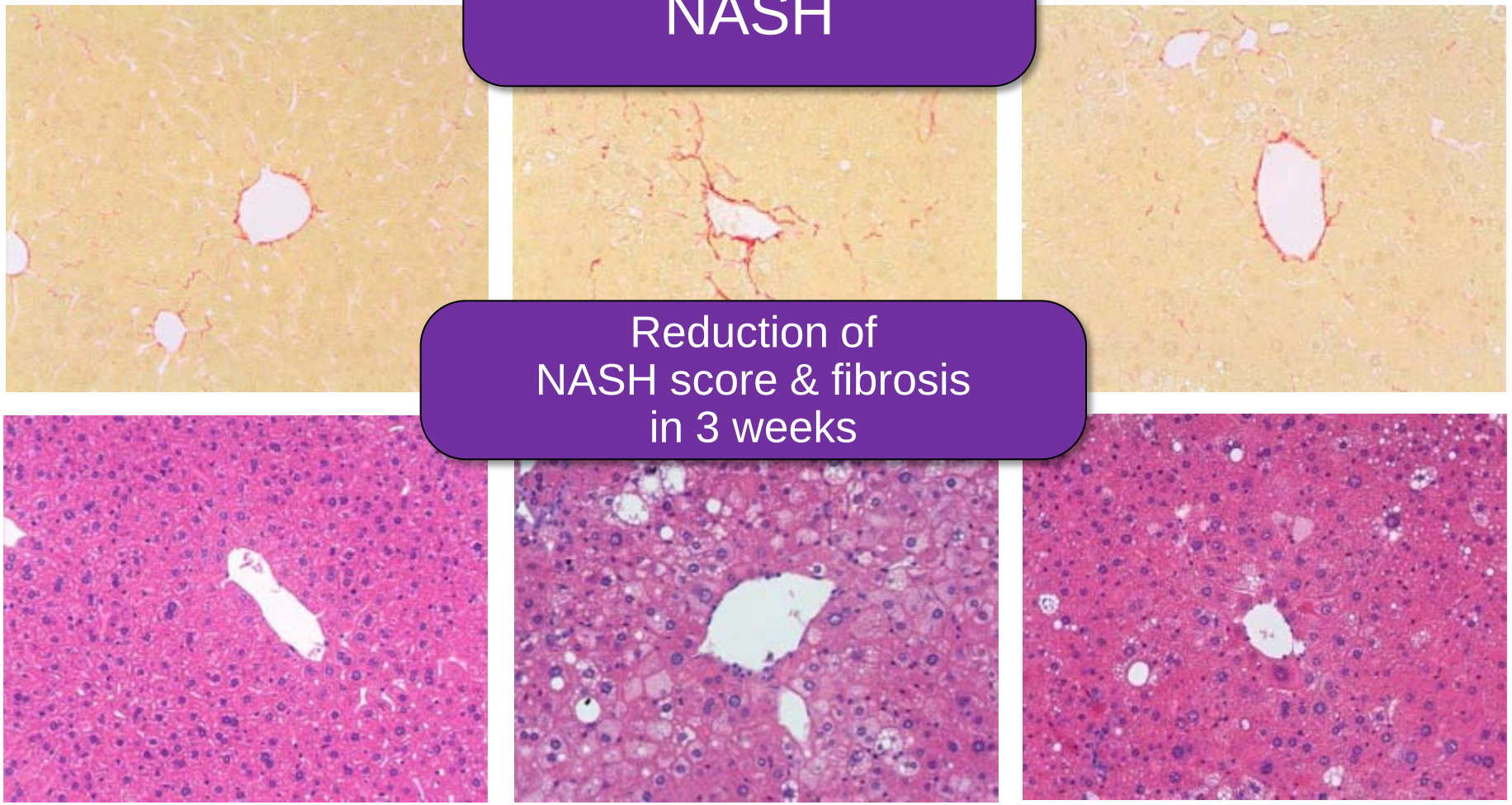
Broad Potential Clinical Utility Suggested by Multiple Animal Models

NASH



Reduction of
NASH score & fibrosis
in 3 weeks

Normal

NASH + Vehicle

NASH + DUR-928

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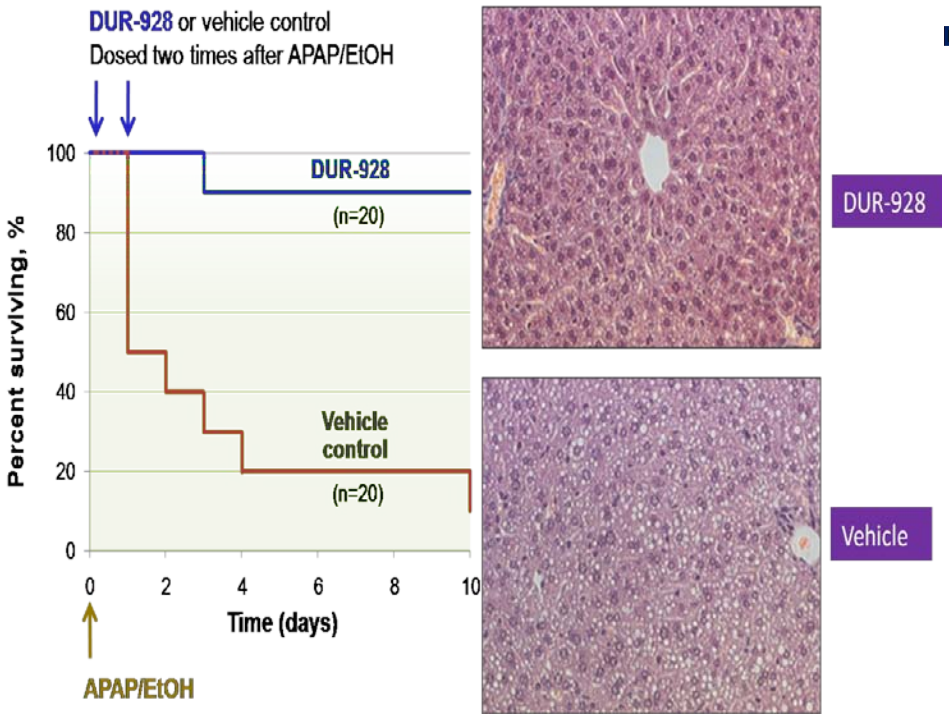
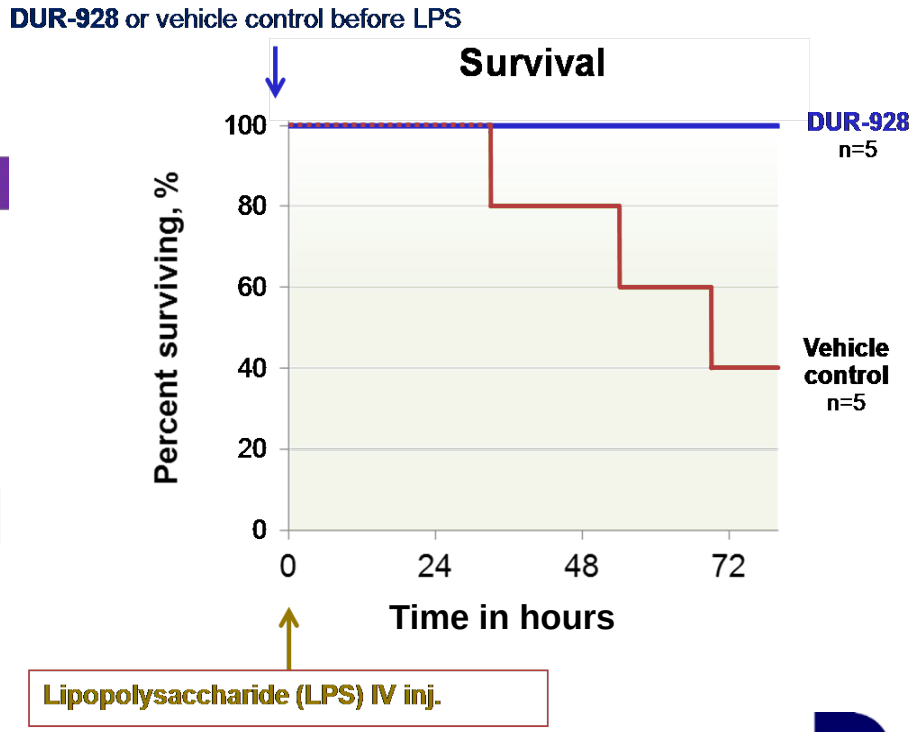
Broad Potential Clinical Utility Suggested by Multiple Animal Models

Chemical Injury
90% lived on DUR-928
90% died on vehicle



Endotoxin
100% lived on DUR-928
60% died on vehicle



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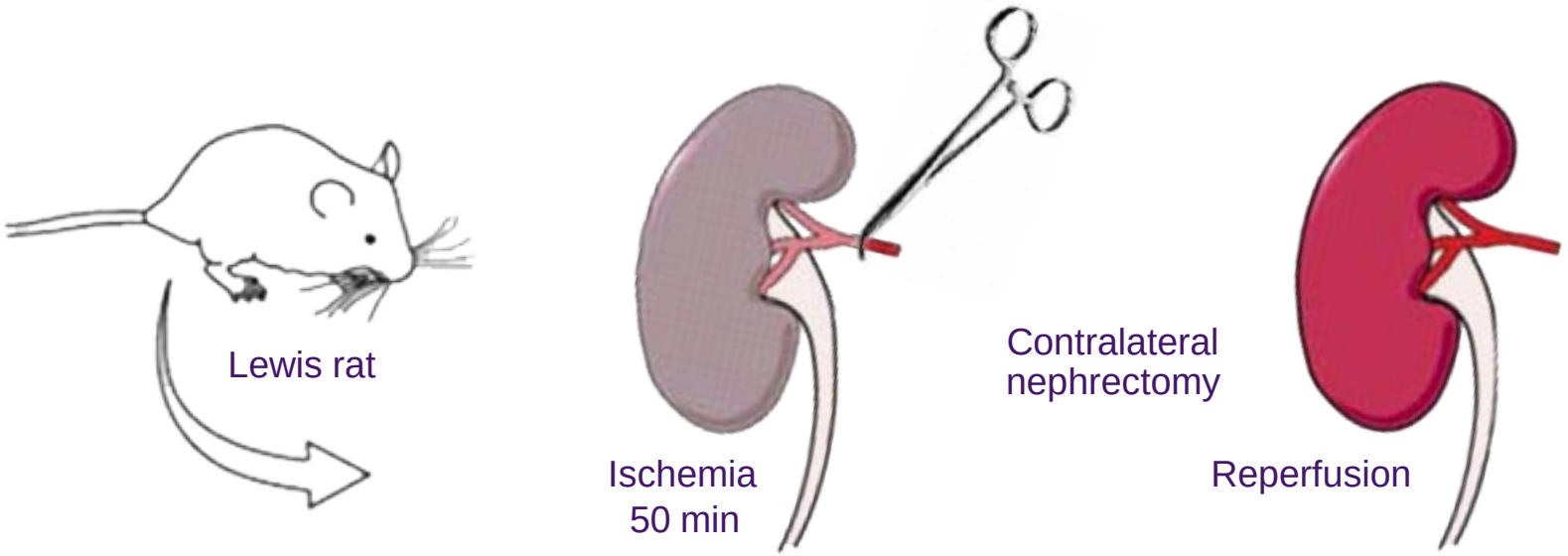
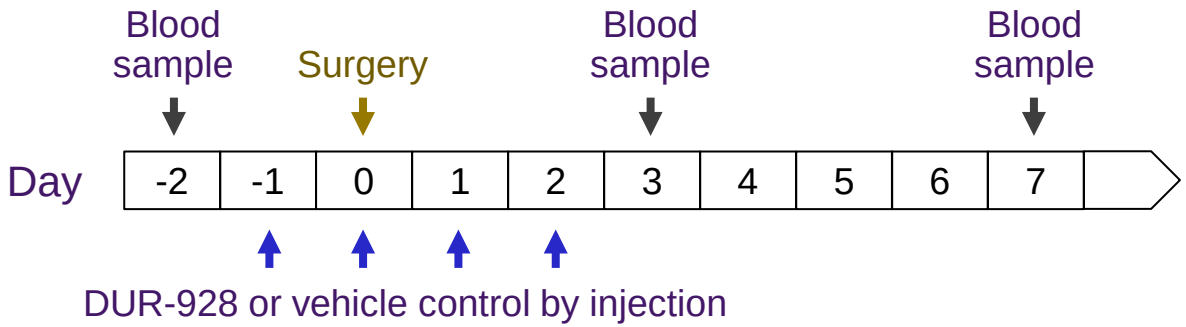
Broad Potential Clinical Utility Suggested by Multiple Animal Models

Ischemic Injury





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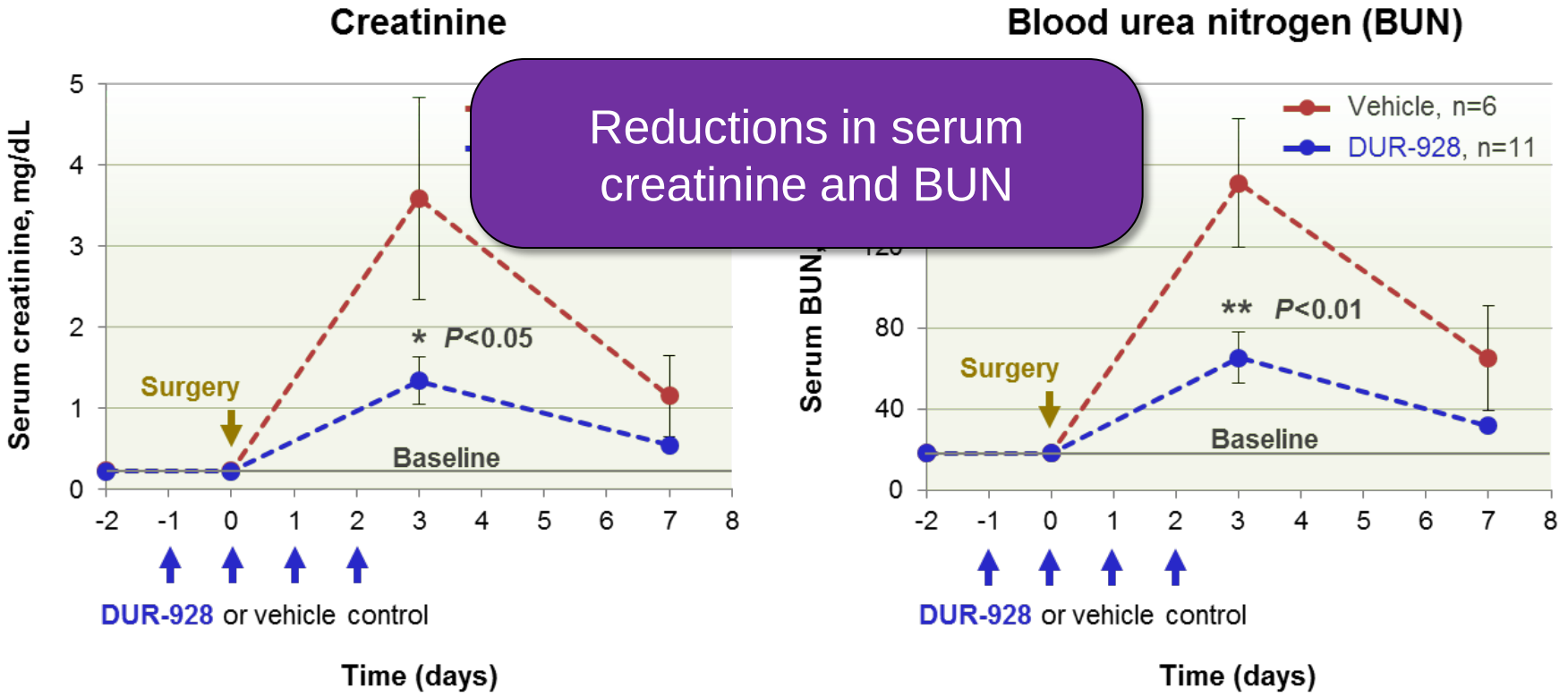
Broad Potential Clinical Utility Suggested by Multiple Animal Models

Ischemic Injury



Values are means ± SD

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Phase I: Safety in healthy human subjects

- Single-site, randomized, double-blind, placebo-controlled, single ascending oral dose in 30 subjects
- 5 doses, highest of which resulted in plasma levels >100-fold higher than endogenous levels
- No treatment-related side effects noted at any dose
- Half-life appears suitable for once-daily or less-frequent dosing
- Precursor to Phase I multiple-ascending-dose trial in mid-2015

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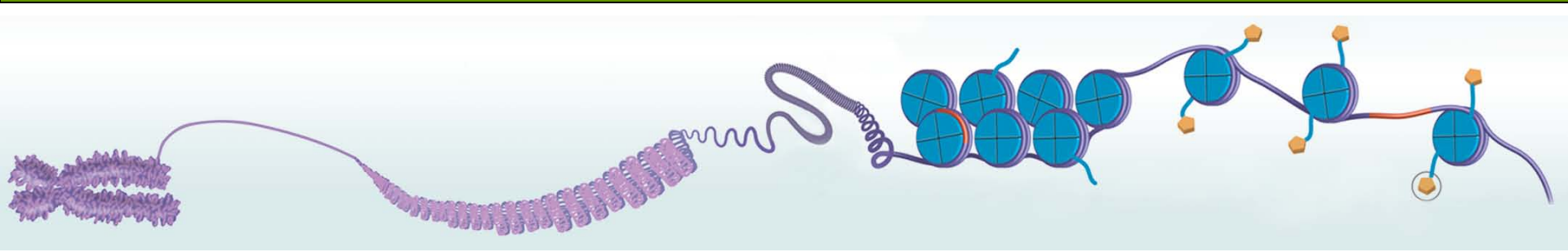
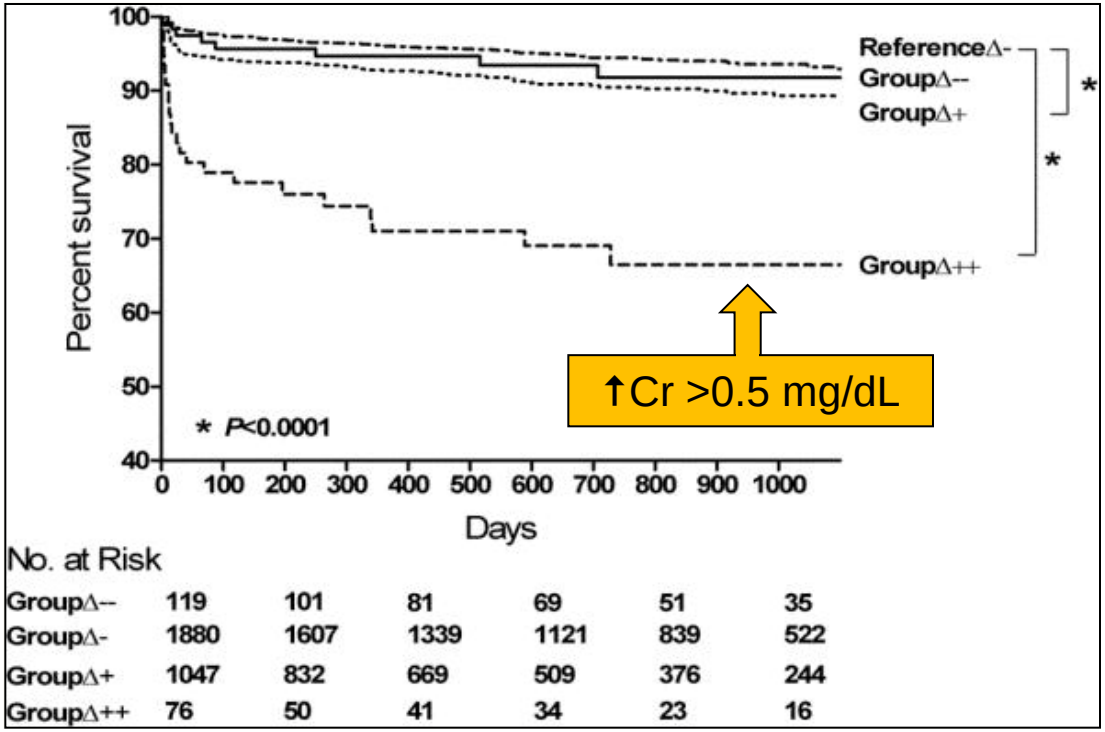


DUR-928
Therapeutic Opportunities

DURECT

Postoperative acute kidney injury (AKI) associated with cardiac surgery

- Increasing incidence of postoperative AKI
  - 5% to 25% of patients undergoing major surgery
- AKI portends a poor outcome
  - Even small elevations in creatinine are significant



- 3,123-patient cardiac surgery cohort study
- Primary endpoint: 30-day adjusted mortality rate

Lassnigg A, et al. *Crit Care Med*. 2008;36(4):1129-1137.

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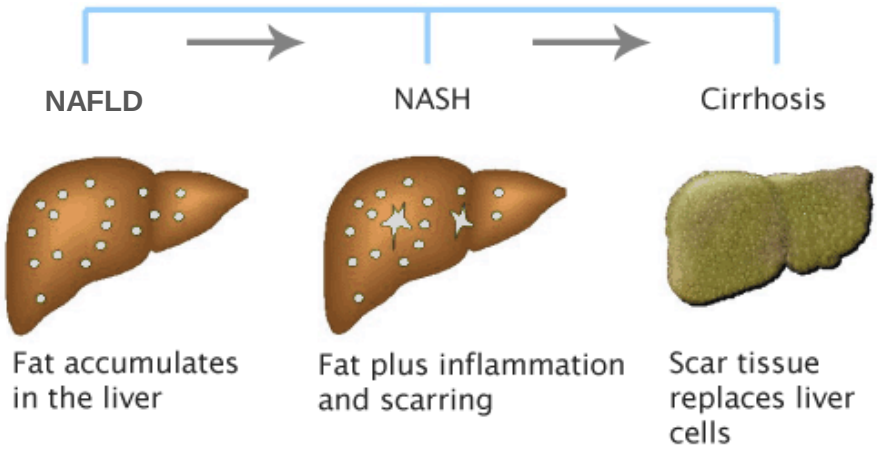
NAFLD and NASH: A growing epidemic

Metabolic Syndrome

Central obesity
High blood pressure
High triglycerides
Low HDL-c
Insulin resistance

Fatty Liver Disease



- NAFLD/NASH are hepatic manifestations of the metabolic syndrome
  - NAFLD prevalence doubled in the last 20 years to ~ 33% of the US population
  - 3%-5% of Americans (9-15 million people) have NASH, and ~20% of those will develop cirrhosis
  - By comparison, the 1999-2002 prevalence of hepatitis C virus (HCV) infection was 1.6%

Rinella ME. *Hepatology*. 2011;54:1118-1120

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Features of DUR-928

- Injectable formulation for acute dosing
- A novel, endogenous, small-molecule, epigenomic regulator of lipid homeostasis, inflammation, and cell survival
  - Regulates key enzymes & cell signaling mediators
    - Lipids: LXR, HMGCR, CYP7A1, PCSK9, FAS, ACC, BAT & others
    - Inflammation: PPARγ, NFκB/IκB, TNFα, IL-1α, IL-6, COX-2 & others
    - Cell survival: 24 genes associated with apoptosis/cell survival
- Compelling data from multiple animal models
  - Acute organ injury
    - Improved post-ischemia organ function
    - Improved survival
  - Chronic metabolic disease
    - Improved liver morphology and reduced liver TG & cholesterol
    - Reduced inflammation, fibrosis, and NASH score
    - Improved glucose tolerance and insulin sensitivity

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Features of DUR-928

- Injectable formulation for acute dosing
- Oral formulation for chronic dosing
- Once-daily or less-frequent dosing
- No toxicity observed in preclinical studies to date
- No adverse events observed in initial Phase I trial

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DUR-928: Next steps

- Multiple-ascending-dose oral Phase I to begin mid-2015
- Single-dose injectable Phase I to begin H2 2015
- Multiple-ascending-dose injectable Phase I to begin Q4 2015
- Phase II to begin 2016 in one or more patient populations
  - Acute organ injury with parenteral formulation (orphan)
  - Chronic indication with oral formulation (non-orphan, e.g., NAFLD/NASH)

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ELADUR® (TRANSDUR™-Bupivacaine) Pain Patch

- Targeting post-herpetic neuralgia (PHN)
- Features:
  - 3 days vs. 12 hours for lidocaine patches
    - 66% of patients experience pain during the 12-hour “rest period” *
  - Patient-friendly design
    - Ability to shower and exercise, won’t fall off as easily
  - Orphan Drug Designation
- 1 US patent issued (2031), 1 European patent (2027+)
- Positive Phase II data in PHN
- Licensed to Impax Pharmaceuticals
  - $61 million potential milestones, royalties

IMPAX LABORATORIES, INC.

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* Gammaitoni, AR et al., Journal of Clinical Pharmacology, 2003; 43:111-117

SABER®/CLOUD™ Technology for LT Injectables
Feasibility Projects leading to Development Programs

Relday™

- Opportunity = >$1 billion
- Features:
  - First once-a-month risperidone
  - Subcutaneous vs. IM injection
  - Simplified dosing regimen
- Positive single dose Phase I
  - Dose range expected for clinical practice
- Partnered with Zogenix
  - $103 mm milestones, royalties
  - Plans to initiate multi-dose clinical trial Q1 2015, data Q3 2015

Santen Ophthalmic Program

- Opportunity = LT injectable
- Features:
  - Long term delivery
  - Small gauge needle
  - High drug loading, low injection vol
- Positive feasibility project
- Partnered with Santen
  - $76 mm milestones, royalties
  - Development program January 2015

ALZET® and LACTEL®

(dollars in millions)

alzet® OSMOTIC PUMPS

LACTEL® Absorbable Polymers

- Strong financial performance and positive cash flow contribution

	2010	2011	2012	2013	2014 *
Revenue	$ 10.5	$ 10.6	$ 10.5	$ 11.4	$ 11.0
Gross Profit	6.6	6.2	5.9	6.8	7.0
Gross Margin	63%	58%	56%	60%	63%

*Gross profit and margin in 2014 excludes $1.6 million charge for excipients used in other product lines.

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DURECT Corporation
Company Financials

December 31, 2014			
Cash and Investments	$	34.9	MM
Debt		19.8	MM

Shares Outstanding (Feb 18, 2015)		113.7	
Recent Share Price	$	1.00	
Market Value	$	113.7	MM

Potential Milestone Payments			
REMOXY and ORADUR-Hydromorphone	$	3.4	MM
Relday		103.0	MM
ELADUR		61.0	MM
Santen ophthalmic product		76.0	
Total	$	243.4	MM

Federal NOL carryforward at 12/31/14	$	277	MM
State NOL carryforward at 12/31/14	$	204	MM

Insider buying 2012-2014	>1.4 MM	shares
Insider ownership (excl. options)	4.5%	
Options paid in lieu of cash bonuses 2011-2013	~$3.7 MM	
Reduced salaries / BOD fees for options 2012-2014	>$1 MM	
2013 cash bonus declined by Section 16 Officers	~$158,000	

DURECT

Potential Key Drivers Next 12-24 months

- REMOXY®
  - Tech transfer back to Pain Therapeutics (PTI), NDA resubmission by PTI
  - PTI seeking new commercialization partner
- POSIDUR™
  - Finalize design and initiate soft tissue safety/efficacy trial
  - Potential commercialization partner
- DUR-928
  - Additional Phase 1 studies in 2015, precursor to Phase 2 in 2016
  - Potential development and commercialization partner(s)
- Other Programs in Pipeline
  - ELADUR®: Initiation of Phase 3 by Impax
  - Relday™ (risperidone): Initiation of multi-dose clinical trial by Zogenix in Q1 2015 with data in Q3 2015, precursor to Phase 3 in 2016
  - Santen Ophthalmic Program: In development, details to be disclosed by Santen

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