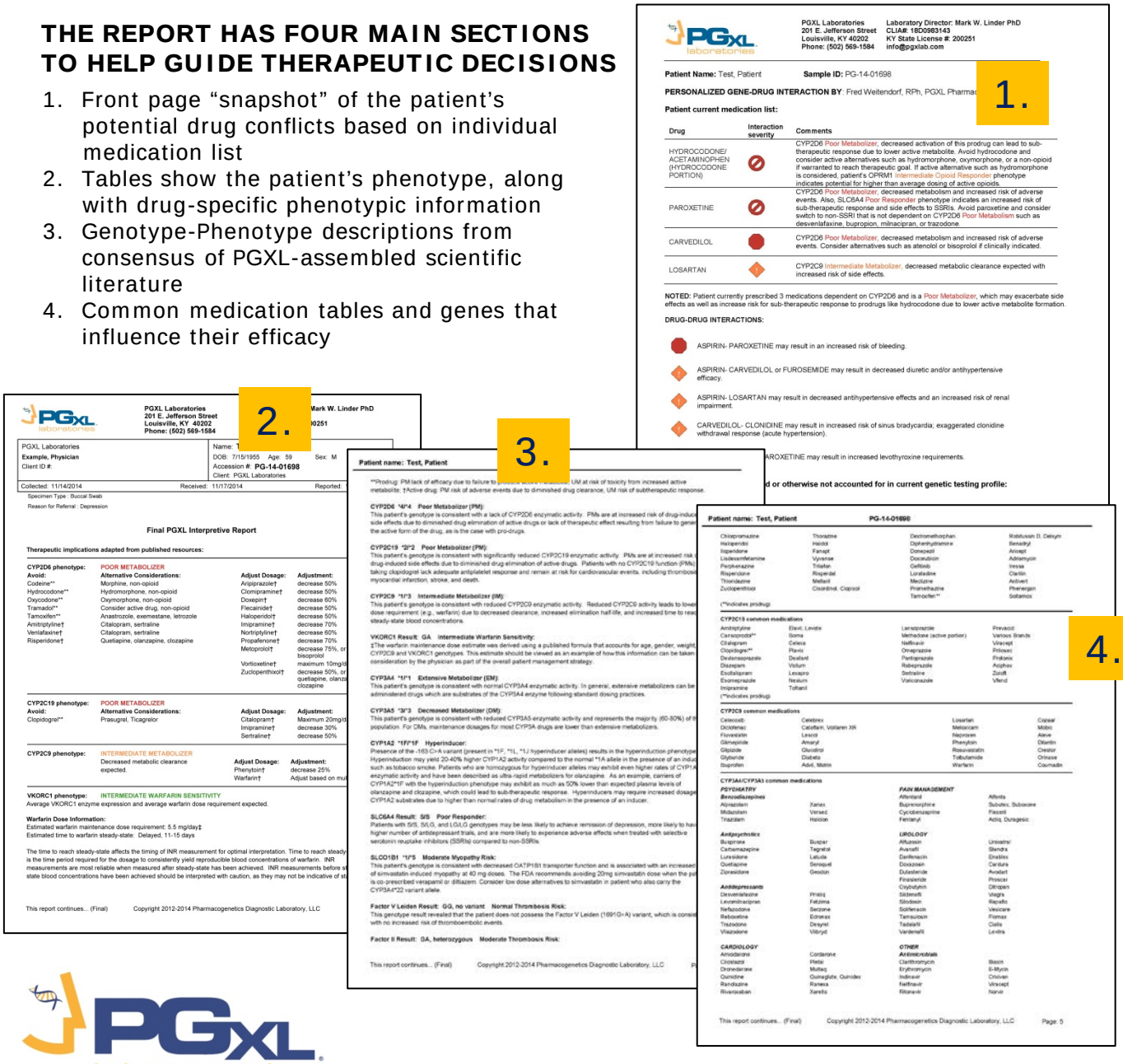
How to Read the
PGXL Drug Sensitivity Report

The PGXL Drug Sensitivity Panel provides insight into the metabolism and response of commonly prescribed drugs. In addition, when provided with your patient's current medication list and demographic information, PGXL's analytics identify potential medication conflicts.

(The reports used in this presentation are for demonstration purposes only and should not be used to make medical decisions.)

THE REPORT HAS FOUR MAIN SECTIONS TO HELP GUIDE THERAPEUTIC DECISIONS

1. Front page "snapshot" of the patient's potential drug conflicts based on individual medication list
2. Tables show the patient's phenotype, along with drug-specific phenotypic information
3. Genotype-Phenotype descriptions from consensus of PGXL-assembled scientific literature
4. Common medication tables and genes that influence their efficacy



1. The front page gives a quick-read table of gene variants and their effect on the drugs your patient takes…

Drug	Interaction Severity	Comments
OXYCODONE/ ACETAMINOPHEN (OXYCODONE PORTION)		CYP2D6 Poor Metabolizer, decreased activation of this prodrug can lead to sub-therapeutic response due to lower active metabolite. Avoid oxycodone and consider active alternatives such as hydromorphone, oxymorphone, or a non-opioid if warranted to reach therapeutic goal. If active alternative such as oxymorphone is considered, patient's OPRM1 Intermediate Opioid Responder phenotype indicates potential for higher than average dosing of active opioids.
PAROXETINE		CYP2D6 Poor Metabolizer, decreased metabolism and increased risk of adverse events. Also, SLC6A4 Poor Responder phenotype indicates an increased risk of sub-therapeutic response and side effects to SSRIs. Avoid paroxetine and consider switch to non-SSRI that is not dependent on CYP2D6 Poor Metabolism such as desvenlafaxine, bupropion, milnacipran, or trazodone.
CARVEDILOL		CYP2D6 Poor Metabolizer, decreased metabolism and increased risk of adverse events. Consider alternatives such as atenolol or bisoprolol if clinically indicated.
LOSARTAN		CYP2C9 Intermediate Metabolizer, decreased metabolic clearance expected with increased risk of side effects.

…as well as identifying potential conflicts between that patient's medications.

	Drug Combination	Comments
	ASPIRIN-PAROXETINE	May result in an increased risk of bleeding.
	ASPIRIN-CARVEDILOL or FUROSIMIDE	May result in increase diuretic and/or antihyperintensive efficacy
	ASPIRIN-LOSARTAN	May result in decrease antihypertensive effects and an increaed risk of renal impairment.
	CARVEDILOL-CLONIDINE	May result in increased risk of sinus bradycardia; exaggerated clonidine withdrawal response (acute hypertension).

Medications not metabolized or otherwise not accounted for in genetic testing profile:

ASPIRIN
CARBIDOPA/LEVODOPA
CLONIDINE
CLOTRIMAZOLE
FUROSIMIDE
LEVOTHYROXINE
LYRICA
SULFASALAZINE

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2. Each gene has a discreet result and gets its own section on the report. That section contains information about the patient's genotype and phenotypic implications of that genotype.

Final PGXL Interpretive Report

Therapeutic implications adapted from published resources:

CYP2D6 phenotype: POOR METABOLIZER

Avoid:	Alternative Considerations:	Adjust Dosage:	Adjustment:
Codeine**	Morphine, non-opioid	Aripiprazole†	decrease 50%
Hydrocodone**	Hydromorphone, non-opioid	Clomipramine†	decrease 50%
Oxycodone**	Oxymorphone, non-opioid	Doxepin†	decrease 60%
Tramadol**	Consider active drug, non-opioid	Flecainide†	decrease 50%
Tamoxifen**	Anastrozole, exemestane, letrozole	Haloperidol†	decrease 50%
Amitriptyline†	Citalopram, sertraline	Imipramine†	decrease 70%
Venlafaxine†	Citalopram, sertraline	Nortriptyline†	decrease 60%
Risperidone†	Quetiapine, olanzapine, clozapine	Propafenone†	decrease 70%
		Metoprolol†	decrease 75%, or atenolol, bisoprolol
		Vortioxetine†	maximum 10mg/day
		Zuclopenthixol†	decrease 50%, or flupenthixol quetiapine, olanzapine, clozapine

CYP2C19 phenotype: POOR METABOLIZER

Avoid:	Alternative Considerations:	Adjust Dosage:	Adjustment:
Clopidogrel**	Prasugrel, Ticagrelor	Citalopram†	Maximum 20mg/day
		Imipramine†	decrease 30%
		Sertraline†	decrease 50%

CYP2C9 phenotype: INTERMEDIATE METABOLIZER

Decreased metabolic clearance expected.

Adjust Dosage:	Adjustment:
Phenytoin†	decrease 25%
Warfarin†	Adjust based on multiple factors

3. This part of the report explains in more detail the implications of each genotype. Along with the tables in section 2, this should provide information that can be used to guide drug and dosage for optimal treatment.

CYP2D6 *4/*4 Poor Metabolizer (PM):
This patient's genotype is consistent with a lack of CYP2D6 enzymatic activity. PMs are at increased risk of drug-induced side effects due to diminished drug elimination of active drugs or lack of therapeutic effect resulting from failure to generate the active form of the drug, as is the case with pro-drugs.

CYP2C19 *2/*2 Poor Metabolizer (PM):
This patient's genotype is consistent with significantly reduced CYP2C19 enzymatic activity. PMs are at increased risk of drug-induced side effects due to diminished drug elimination of active drugs. Patients with no CYP2C19 function (PMs) taking clopidogrel lack adequate antiplatelet response and remain at risk for cardiovascular events, including thrombosis, myocardial infarction, stroke, and death.

CYP2C9 *1/*3 Intermediate Metabolizer (IM):
This patient's genotype is consistent with reduced CYP2C9 enzymatic activity. Reduced CYP2C9 activity leads to lower dose requirement (e.g., warfarin) due to decreased clearance, increased elimination half-life, and increased time to reach steady-state blood concentrations.

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4. Finally, at the back of the report there are tables of genes and the commonly prescribed drugs they influence.

CYP2C19 common medications

Amitriptyline	Elavil, Levate	Lansoprazole	Prevacid
Carisoprodol**	Soma	Methadone (active portion)	Various Brands
Citalopram	Celexa	Nelfinavir	Viracept
Clopidogrel**	Plavix	Omeprazole	Prilosec
Dexlansoprazole	Dexilant	Pantoprazole	Protonix
Diazepam	Valium	Rabeprazole	Aciphex
Escitalopram	Lexapro	Sertraline	Zoloft
Esomeprazole	Nexium	Voriconazole	Vfend
Imipramine	Tofranil		

(**indicates prodrug)

CYP2C9 common medications

Celecoxib	Celebrex	Losartan	Cozaar
Diclofenac	Cataflam, Voltaren XR	Meloxicam	Mobic
Fluvastatin	Lescol	Naproxen	Aleve
Glimepiride	Amaryl	Phenytoin	Dilantin
Glipizide	Glucotrol	Rosuvastatin	Crestor
Glyburide	Diabeta	Tolbutamide	Orinase
Ibuprofen	Advil, Motrin	Warfarin	Coumadin

CYP3A4/CYP3A5 common medications

PSYCHIATRY		***PAIN MANAGEMENT***	
Benzodiazepines		Alfentanil	Alfenta
Alprazolam	Xanax	Buprenorphine	Subutex, Suboxone
Midazolam	Versed	Cyclobenzaprine	Flexeril
Triazolam	Halcion	Fentanyl	Actiq, Duragesic
Antipsychotics		***UROLOGY***	
Buspirone	Buspar	Alfuzosin	Uroxatral
Carbamazepine	Tegretol	Avanafil	Stendra
Lurasidone	Latuda	Darifenacin	Enablex
Quetiapine	Seroquel	Doxazosin	Cardura
Ziprasidone	Geodon	Dutasteride	Avodart
		Finasteride	Proscar
Antidepressants		Oxybutynin	Ditropan

Together, these report elements give you the information necessary to guide medication decisions for your patient – to recognize potential risks and opportunities that might otherwise have gone unnoticed.

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