GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	[redacted]	SPECIMEN TYPE:	[redacted]	[redacted]
ACC #:	[redacted]	COLLECTION DATE:	[redacted]	
DOB:	[redacted]	RECEIVED DATE:	[redacted]	
SEX:	[redacted]	REPORT DATE:	[redacted]	

Pharmacogenetic Psychiatry Report

Current Patient Medications

Risperdal, Zoloft, Vyvanse, Prozac, Focalin, Adderall, Intuniv

⚠ **Adderall**
Amphetamine

Poor Response to Amphetamine salts (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.

⚠ **Focalin**
Dexmethylphenidate

Poor Response to Dexmethylphenidate (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

⚠ **Vyvanse**
Lisdexamfetamine

Poor Response to Lisdexamfetamine (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

✓ **Intuniv**
Guanfacine

Normal Response to Guanfacine — INFORMATIVE

Pharmacogenetic guidance: Guanfacine is predominantly metabolized by CYP3A4. No genetically guided drug selection or dosing recommendations are available and guanfacine extended-release should be titrated based on the clinical response and tolerability of the individual patient. **Polypharmacy guidance**: The dose of guanfacine extended-release should be reduced to **one half of the standard dose** when co-medicated with a strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, indinavir, ritonavir, nefazodone). When the strong CYP3A4 inhibitor is discontinued, the dose should be increased to the standard recommended dose. Guanfacine dose should be increased up to double the recommended dose when used in combination with a strong CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.). When the CYP3A4 inducer is discontinued, the dose should be reduced to the standard recommended dose within 7-14 days.

✓ **Prozac**
Fluoxetine

Normal Sensitivity to Fluoxetine (CYP2D6: Normal Metabolizer) — INFORMATIVE

Fluoxetine is metabolized to its active metabolite norfluoxetine and to other metabolites by multiple enzymes including CYP2D6, CYP2C19, CYP2C9, and CYP3A4. Fluoxetine can be prescribed at standard label-recommended dosage and administration.

✓ **Risperdal**
Risperidone

Normal Sensitivity to Risperidone (CYP2D6: Normal Metabolizer) — ACTIONABLE

Risperidone can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended until a favorable response is achieved.

✓ **Zoloft**
Sertraline

Normal Sensitivity to Sertraline (CYP2C19: Normal Metabolizer) — ACTIONABLE

Sertraline can be prescribed at standard label-recommended dosage and administration.

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A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE**	Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.		
The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE**	There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

Risk Management

Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Anti-ADHD Agents	Atomoxetine (Strattera) Clonidine (Kapvay) Guanfacine (Intuniv)	Amphetamine (Adderall, Evekeo) Dexmethylphenidate (Focalin) Dextroamphetamine (Dexedrine) Lisdexamfetamine (Vyvanse) Methylphenidate (Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER)	
	Anticonvulsants	Brivaracetam (Briviact) Carbamazepine (Tegretol, Carbatrol, Epitol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Fosphenytoin (Cerebyx) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal, Oxtellar XR) Perampanel (Fycompa) Phenobarbital (Luminal) Phenytoin (Dilantin) Pregabalin (Lyrica) Primidone (Mysoline) Rufinamide (Banzel) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril) Zonisamide (Zonegran)		
	Antidementia Agents	Donepezil (Aricept) Galantamine (Razadyne) Memantine (Namenda)		

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Psychotropic	Antidepressants	Amitriptyline (Elavil) Amoxapine (Amoxapine) Clomipramine (Anafranil) Desipramine (Norpramin) Desvenlafaxine (Pristiq) Doxepin (Silenor) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluoxetine (Prozac, Sarafem) Fluvoxamine (Luvox) Imipramine (Tofranil) Levomilnacipran (Fetzima) Maprotiline (Ludiomil) Mirtazapine (Remeron) Nefazodone (Serzone) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Sertraline (Zoloft) Trazodone (Oleptro) Trimipramine (Surmontil) Venlafaxine (Effexor) Vilazodone (Viibryd) Vortioxetine (Trintellix)	Citalopram (Celexa)	
	Antipsychotics	Aripiprazole (Abilify, Aristada) Asenapine (Saphris) Brexpiprazole (Rexulti) Cariprazine (Vraylar) Chlorpromazine (Thorazine) Fluphenazine (Prolixin) Haloperidol (Haldol) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Paliperidone (Invega) Perphenazine (Trilafon) Pimavanserin (Nuplazid) Pimozide (Orap) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Clozapine (Clozaril) Olanzapine (Zyprexa)	
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin) Diazepam (Valium)		
	Other Neurological Agents	Deutetrabenazine (Austedo) Dextromethorphan / Quinidine (Nuedexta) Flibanserin (Addyi) Valbenazine (Ingrezza)	Tetrabenazine (Xenazine)	

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Dosing Guidance

Amphetamine
Adderall, Evekeo

Poor Response to Amphetamine salts (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.

Citalopram
Celexa

Reduced Response to Citalopram (HTR2A: Homozygous for G allele (rs7997012)) — INFORMATIVE

The patient is homozygous for G allele in HTR2A variant rs7997012. Preliminary studies report that this genotype may be associated with an unfavorable response to citalopram.

Clozapine
Clozaril

Possible Non-Response to Clozapine (CYP1A2: Normal Metabolizer- Possible Inducibility) — INFORMATIVE

Smokers may be at risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Dexmethylphenidate
Focalin

Poor Response to Dexmethylphenidate (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Dextroamphetamine
Dexedrine

Poor Response to Dextroamphetamine (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, dextroamphetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Lisdexamfetamine
Vyvanse

Poor Response to Lisdexamfetamine (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to amphetamine stimulants. If prescribed, lisdexamfetamine should be administered at the lowest effective dose, and dosage should be individually adjusted.

Methylphenidate
Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER

Poor Response to Methylphenidate (COMT: Low COMT Activity) — INFORMATIVE

The patient's genotype result predicts a reduced therapeutic response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Olanzapine
Zyprexa

Possible Non-Response to Olanzapine (CYP1A2: Normal Metabolizer- Possible Inducibility) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Tetrabenazine

Xenazine

Normal Sensitivity to Tetrabenazine (CYP2D6: Normal Metabolizer) ACTIONABLE

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 normal metabolizers is 100 mg, with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

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Test Details

Gene	Genotype	Phenotype	Clinical Consequences
ADRA2A	5749G>A G/A	Heterozygous for rs1800545	
COMT	Val158Met A/A	Low COMT Activity	Consistent with a significantly reduced catechol O-methyltransferase (COMT) function.
CYP1A2	*1F/*1L	Normal Metabolizer- Possible Inducibility	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid metabolism may occur in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
CYP2C19	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C19 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C9	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2D6	*1/*29	Normal Metabolizer	Consistent with a typical CYP2D6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP3A4	*1/*1B	Normal Metabolizer	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3/*3	Poor Metabolizer	Consistent with a poor CYP3A5 activity. This phenotype is the most common in the general population. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
HTR2A	-1438G>A A/G	Heterozygous for the A allele (rs6311)	The patient carries one copy of the variant allele at rs6311 which may be associated with greater serotonin 2A receptor gene expression.
HTR2A	rs7997012 G/G	Homozygous for G allele (rs7997012)	Reduced response to citalopram and escitalopram

Alleles Tested: ADRA2A 5749G>A, C-1291G; **COMT** Val158Met; **CYP1A2** *1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W, *3, *5, *6, *7, *8, *11, *15, *16; **CYP2C19** *2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *13, *17; **CYP2C9** *2, *3, *4, *5, *6, *8, *11; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *11, *12, *15, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *1B, *3, *6, *8, *11, *12, *13, *15, *16A, *16B, *17, *18A, *18B, *22; **CYP3A5** *1D, *2, *3, *3B, *3C, *6, *7, *8, *9; **HTR2A** -1438G>A, rs7997012

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Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities and lifestyle habits. Technical limitations include the possibility of laboratory error and inaccuracy of the test due to unknown rare variants.

Methodology: Bead array and e-sensor based assays detect listed alleles and most rare variants with known clinical significance and analytical sensitivity and specificity >99%.

Lab Disclaimer: Genesys Diagnostics Inc. has validated the Genotype Test. The performance characteristics of this test were determined by Genesys Diagnostics Inc. This test is an FDA modified and Lab Developed Test.

Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Report was signed out electronically by [redacted]

PATIENT INFORMATION

NAME: [redacted]
ACC #:
DOB:
SEX:

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS

Name: [redacted]
DOB:
ACC #:

Pharmacogenetic Test Summary

ADRA2A	5749G>A G/A	Heterozygous for rs1800545
COMT	Val158Met A/A	Low COMT Activity
CYP1A2	*1F/*1L	Normal Metabolizer- Possible Inducibility
CYP2C19	*1/*1	Normal Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*1/*29	Normal Metabolizer
CYP3A4	*1/*1B	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
HTR2A	-1438G>A A/G	Heterozygous for the A allele (rs6311)
HTR2A	rs7997012 G/G	Homozygous for G allele (rs7997012)

For a complete report contact Genesys Diagnostics
www.gdilabs.com

Risperdal & Prozac	Patients receiving concurrent therapy with duloxetine, fluoxetine or paroxetine with risperidone should be observed for increases in risperidone side effects, including extrapyramidal and Parkinsonian symptoms.The US manufacturer of risperidone (Risperdal) recommends that when fluoxetine or paroxetine is co-administered with risperidone that the dose should be reduced. The risperidone dose should not exceed 8 mg per day when co-administered with fluoxetine or paroxetine. When initiating therapy with risperidone, the dose of risperidone should be titrated slowly. It may be necessary to increase the risperidone dose, when fluoxetine or paroxetine is discontinued.The US manufacturer of extended release risperidone microspheres for injection (Risperdal Consta) recommends that patients maintained on this product continue to receive the recommended 25 mg dose when fluoxetine or paroxetine is initiated, unless clinical judgment necessitates lowering the dose or interrupting therapy. If a decision is made to lower the dose, the dose may be lowered to 12.5 mg 2 to 4 weeks before the initiation of fluoxetine or paroxetine. When initiating the product in patients maintained on fluoxetine or paroxetine, a starting dose of 12.5 mg can be considered. The efficacy of this dose has not been confirmed in clinical trials.One set of authors recommended a low initial dose of paroxetine of 10 mg/day to 20 mg/day in patients receiving risperidone.	MODERATE
Adderall & Zoloft	The concurrent use of amphetamines with SSRIs or SNRIs should be approached with appropriate monitoring.Instruct patients receiving concurrent therapy to report any signs or symptoms of serotonin syndrome immediately.Monitor blood pressure during concurrent therapy and adjust dosage or change medication for persistent increases in blood pressure.	MODERATE
Adderall & Prozac	The concurrent use of amphetamines with SSRIs or SNRIs should be approached with appropriate monitoring.Instruct patients receiving concurrent therapy to report any signs or symptoms of serotonin syndrome immediately.Monitor blood pressure during concurrent therapy and adjust dosage or change medication for persistent increases in blood pressure.	MODERATE
Vyvanse & Zoloft	The concurrent use of amphetamines with SSRIs or SNRIs should be approached with appropriate monitoring.Instruct patients receiving concurrent therapy to report any signs or symptoms of serotonin syndrome immediately.Monitor blood pressure during concurrent therapy and adjust dosage or change medication for persistent increases in blood pressure.	MODERATE
Vyvanse & Prozac	The concurrent use of amphetamines with SSRIs or SNRIs should be approached with appropriate monitoring.Instruct patients receiving concurrent therapy to report any signs or symptoms of serotonin syndrome immediately.Monitor blood pressure during concurrent therapy and adjust dosage or change medication for persistent increases in blood pressure.	MODERATE

Unrecognized Medications: *None*

Highly elevated risk for indicated condition or adverse drug reaction. Medication can be prescribed with monitoring; alternative therapy may be needed.

Moderately elevated risk for indicated condition or adverse drug reaction. Medication can be prescribed with monitoring; therapy adjustment may be needed.

Typical risk for indicated condition or adverse drug reaction. Medication can be prescribed according to standard dosing guidelines.

PHARMACOGENETIC RESULTS

DRUG-DRUG INTERACTIONS

ACTIONABLE	Recommendations are suitable for implementation in a clinical setting. Recommendations extracted from evidence based guidelines issued by international pharmacogenetic consortia, professional societies or regulatory bodies (CPIC, DPWG, FDA, EMA, CPNDA, ACMG).
INFORMATIVE	Recommendations are informative and implementation in a clinical setting is optional. The evidence documenting these drug-gene associations may be limited or insufficient and may require further investigation. There are no established evidence based guidelines issued by international pharmacogenetic consortia, professional societies or regulatory bodies.
MODERATE	Drug interactions of moderate severity. The clinician should assess the patient's characteristics and take action as needed.
SERIOUS	Severe drug interaction or contraindicated drug combination which may produces serious consequences in most patients. This drug combination generally should not be dispensed or administered to the same patient. Action is required to reduce risk of severe adverse interaction.

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CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Anti-ADHD Agents	**Amphetamine (Adderall, Evekeo)**		●		⚠ Zoloft ⚠ Prozac
	Atomoxetine (Strattera)	●			⊗ Prozac ⚠ Risperdal
	Clonidine (Kapvay)	●			
	Dexmethylphenidate (Focalin)		●		
	Dextroamphetamine (Dexedrine)		●		⚠ Prozac ⚠ Zoloft
	Guanfacine (Intuniv)	●			
	Lisdexamfetamine (Vyvanse)		●		⚠ Prozac ⚠ Zoloft
	Methylphenidate (Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER)		●		
Antianginal Agents	Ranolazine (Ranexa)	●			⚠ Risperdal
Antiarrhythmics	Flecainide (Tambocor)	●			⚠ Prozac ⚠ Risperdal ⚠ Zoloft
	Mexiletine (Mexitil)	●			
	Propafenone (Rythmol)	●			⚠ Prozac ⚠ Risperdal