

From: [Richard Chen](#)
To: [John West](#); [Christian Haudenschild](#); [Carol Tillis](#)
Subject: final board slides, ready for print
Date: Wednesday, October 31, 2012 1:40:06 PM
Attachments: [board.11.01.12.v6.roc.ppt](#)

Hi Carol,

These are ready for print. I didn't use the personalis template, do you want me to?

R&D Update

Personalis, Inc.

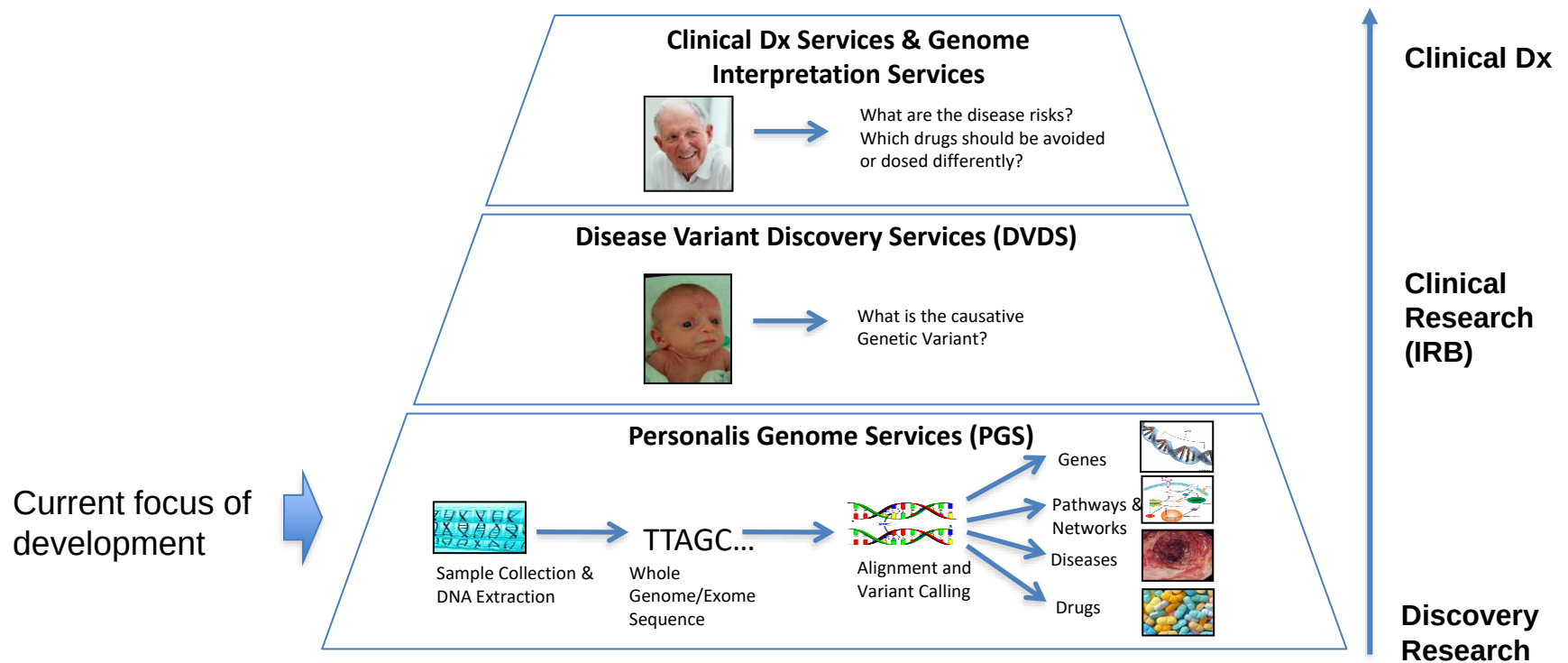
11.01.2012

Richard Chen, CSO

R&D Overview

- Product Development
- Content Development
- Computing Infrastructure
- Hiring

Product Roadmap



Personalis Genome Services for Research

- Currently focused on PGS v1 development
 - In total ~80 features/enhancements, ~370 tasks
 - PRD updated, Continuing Agile development process
 - Winning the VA project has required reprioritizing and resourcing expanded set of features for v1
 - Key differentiating features include: Exome+, accuracy, SV detection, analytics leveraging proprietary content, unique visualization and enhanced reporting
 - Improving overall system performance optimization to better achieve throughput requirements of VA project and other large projects
 - 4 new hires have allowed us to catch up to our staffing requirements
- Engaging early customers/collaborators including Moyamoya for early revenue, feedback and testing of our prototype service
- PGS v1 service on track to launch at AGBT conference Feb 2012, First VA genomes will be processed around the same time
- Submitted 6 talks to AGBT to support the PGS launch
 - Topics focus on key differentiators including accuracy, SV detection, proprietary content, and “success stories” applying our technology

Exome Plus

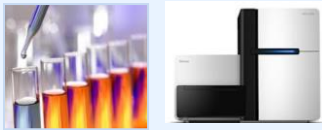
Review of Key Goals & Milestones

- Problems with standard exome sequencing
 - Typical exome sequencing misses a lot of exome (not fully targeted, low coverage on high GC regions, other problematic regions)
 - Lots of biomedically interpretable content missed on standard exomes (regulatory regions, disease relevant variants in intergenic regions, intronic var)
 - The Personalis Exome Plus aims to solve these issues by augmenting standard exomes with custom pullout data
 - Milestones
 - Defined and prioritized High-value (Interpretable) Content
 - Defined and prioritized Top Exome Problematic regions
 - Designed and Received Enrichment Probes/Kits from Agilent
 - Next Steps
 - Evaluate first kits, refine spec and reorder
 - Refine cost model
 - Anticipate that this will be launched in 2 phases:
 - Targeting the first release as part of the PGS v1 launch in Feb 2013.
 - More research intensive parts of Exome Plus will be part of a 2nd release in 2013.
- Personalis EX2100

Personalis Genome Services for Research

Key Differentiated features in v1

Sequencing



Sample Prep Sequencing

- Exome and WGS with optimized sample prep
- Exome Plus capability extending standard exome coverage to biomedically important non-coding regions
- Exome Plus capability improves accuracy of standard exomes
- CLIA sequencing capability

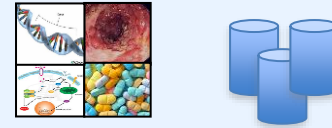
Pipeline



Alignment Variant
Discovery

- State of the art pipeline resulting in better alignments, tested and optimized for accuracy and performance
- Personalis enhanced reference genome for improved alignment and accuracy
- Improved variant (SNP/Indel/SV) calling through integration of orthogonal methods to improve accuracy

Annotation



Proprietary DB
Annotation Public DB
Annotation

- Three high-quality, detailed, manually curated proprietary databases that enable genome annotation and analysis of complex disease, Mendelian disease, pharmacogenomics, and regulatory regions
- Comprehensive genome annotation integrating and managing data from over 30 public databases

Analytics



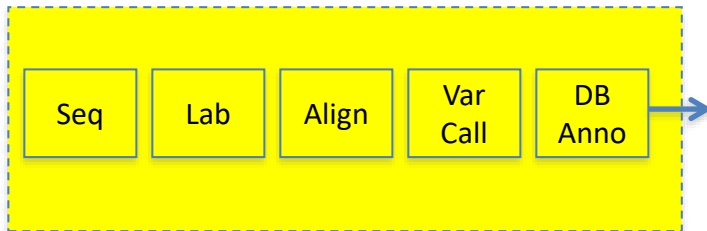
QC Reports Analysis &
Interpretation

- Cutting edge analytics engine for case control analysis reveals statistically significant enrichment of genes, pathways, and diseases
- Analytics powered by proprietary databases
- Proprietary family/pedigree analysis and filtering methods
- Comprehensive QC reporting for better accuracy assessment

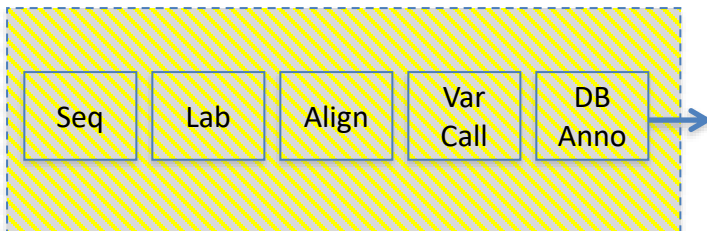
Personalis Genome Services for Research

Key customer use cases addressed in PGS v1 Release

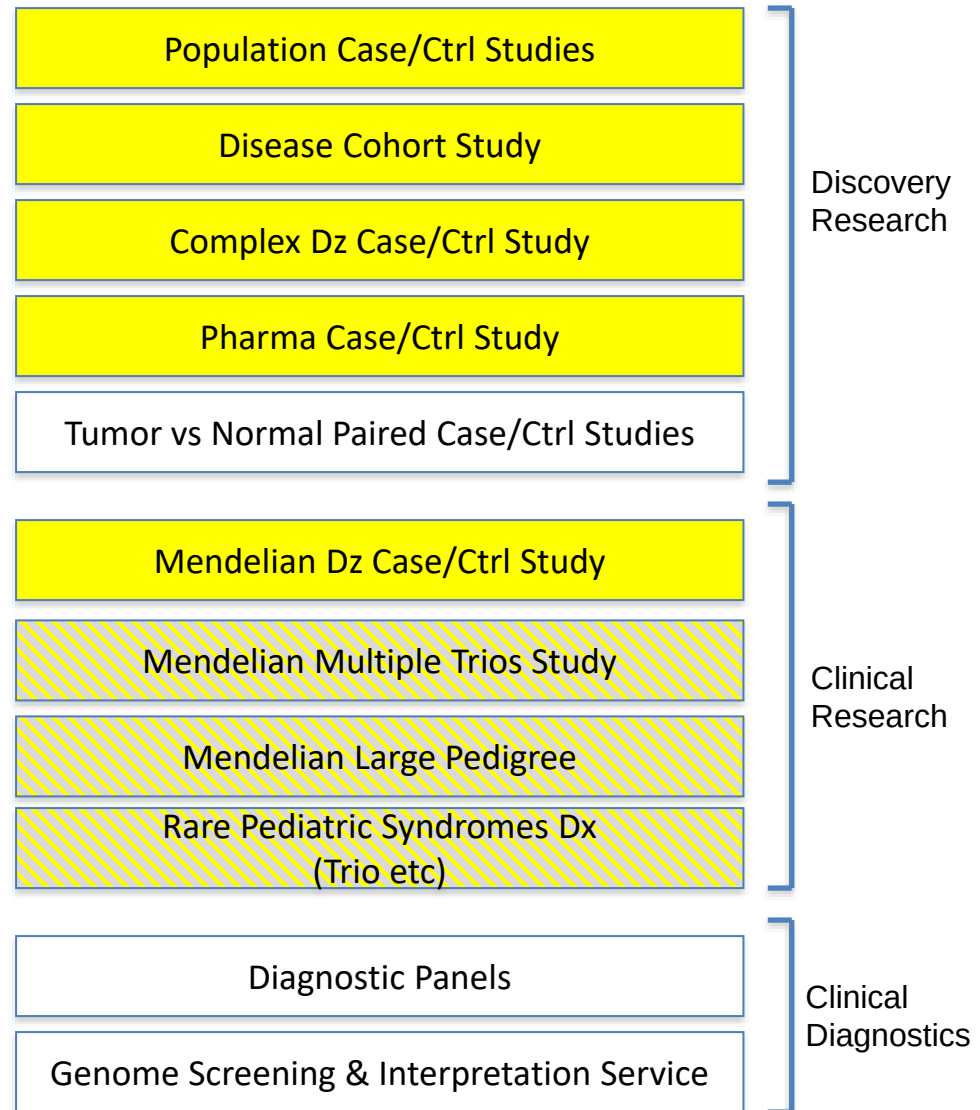
Standard Seq & Pipeline



CLIA Seq and Pipeline

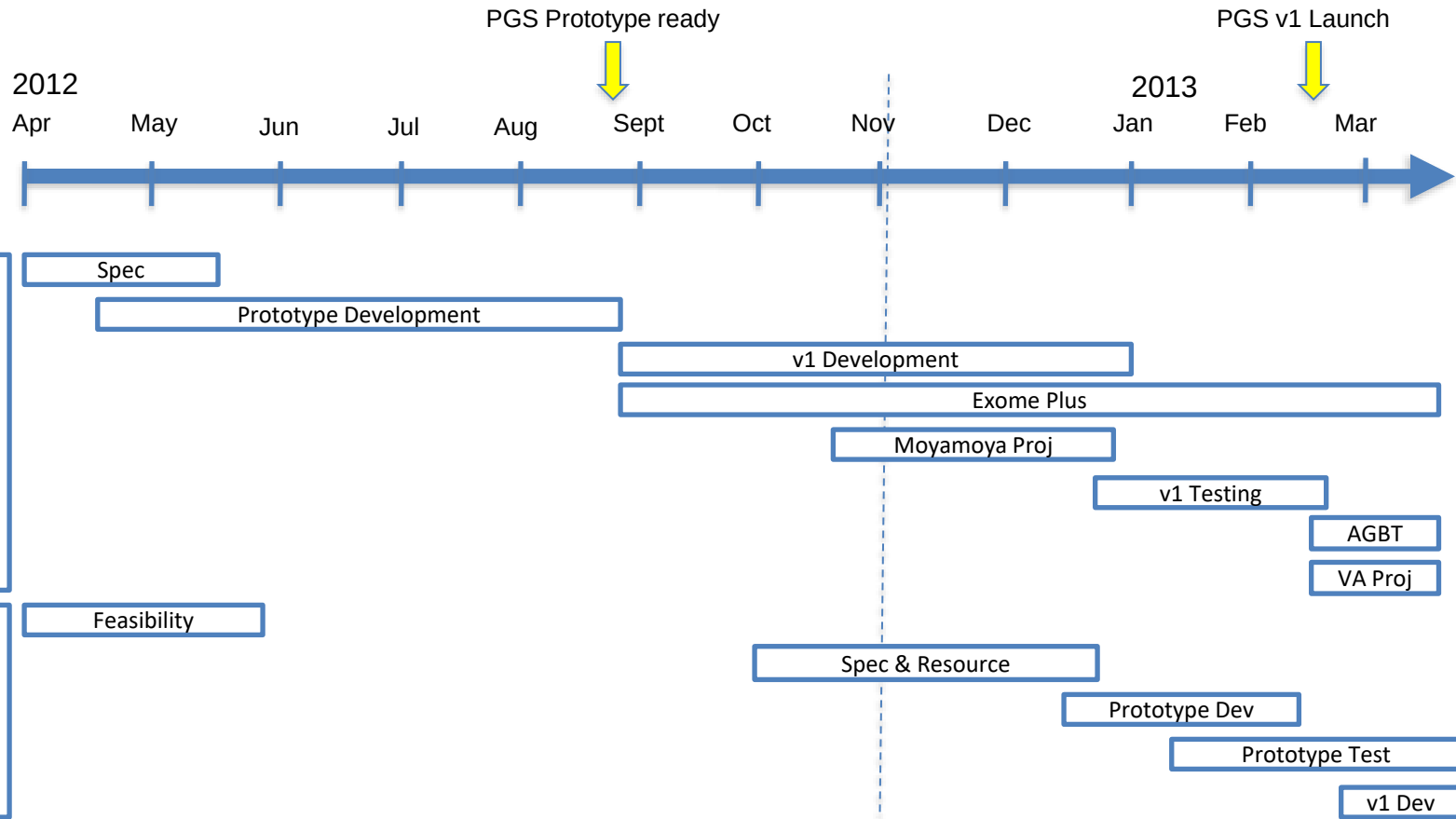


-  PGS v1 Release
-  Prototype Features at v1



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Summary of High-Level Timelines

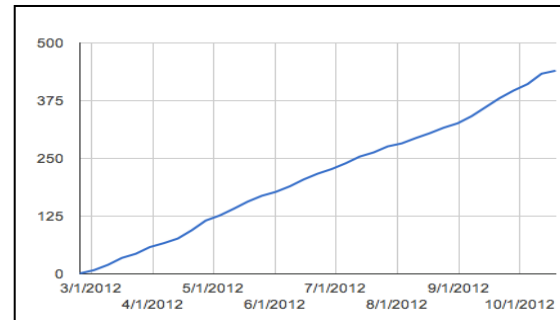


Content Development Updates

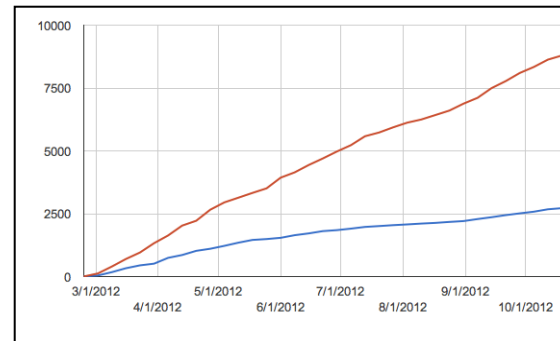
- Newly granted access to large public sequencing projects including
 - UK10K : 4000 genomes, 6000 exomes
 - > \$16 M investment from Wellcome Trust 2010
 - > 4,000 whole genomes in healthy individuals
 - > 6,000 exomes in disease areas such as neurodevelopment, obesity, rare diseases
 - NHLBI GO Exome Sequencing Project: ~500 exomes: Heart, Lung, Blood Dz
 - 1000 Genomes (exomes)
 - Personal Genomes Project (whole genomes)
 - dbGAP data – Kabuki syndrome, Miller syndrome exomes
 - Represents > 2.5 PB of data in total and > \$20M in research grants to date
- May be a cost-effective way to build our library of genomes that enable us to
 - Establish population allele frequencies to enable filtering of disease causing var
 - Provide potential control sets when customers don't have controls for comparison
 - Establish normal ranges for genomes for quality control purposes
 - Validate our pipeline and algorithms

MendelDB Dashboard

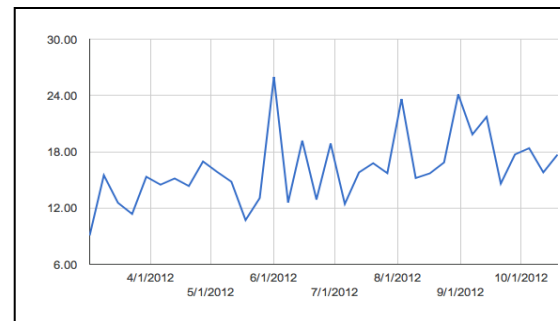
- High quality curated DB of Mendelian phenotypes and their variants
 - Managed by Sarah Garcia and Gemma Chandratillake, both Genetics Ph.D. & Genetic Counselors
- Critical content to support Disease Variant Discovery Service and Genome Interpretation Service
- Finished (~560) GeneReviews > 600 common Mendelian disease phenotypes
- Will then continue phenotype curation and variant curation from other sources
- Flexible workforce for other curation tasks in the future



phenotypes



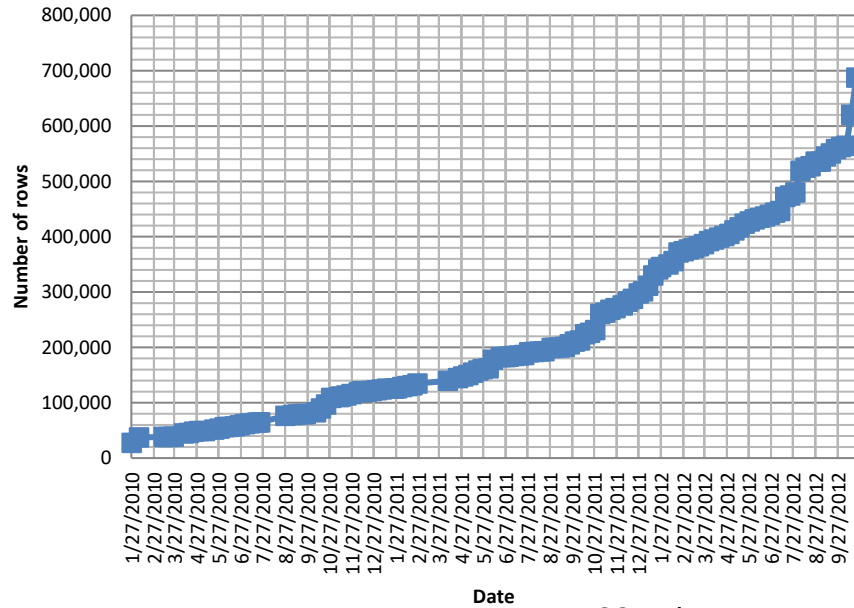
genes (blue)
variants (red)



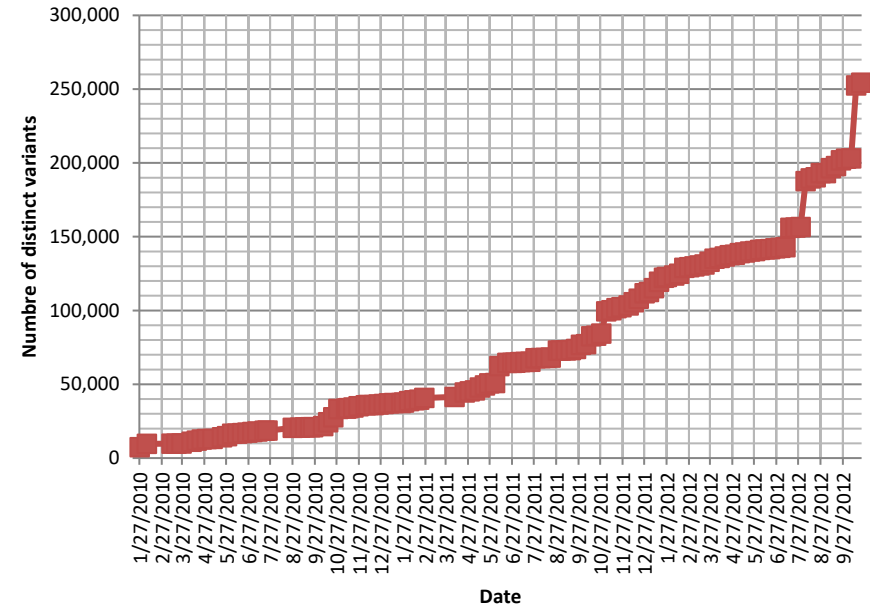
productivity
(rows/hr)

VarimedDB Dashboard

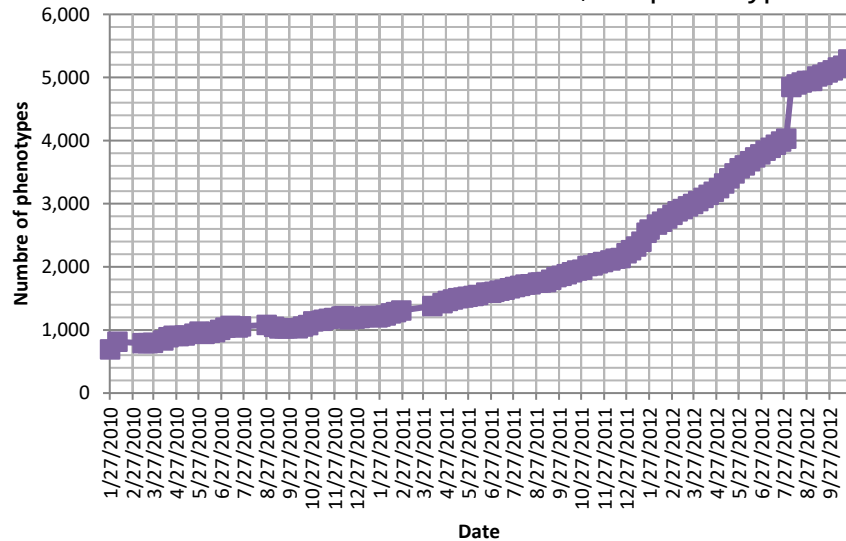
687,432 relationships



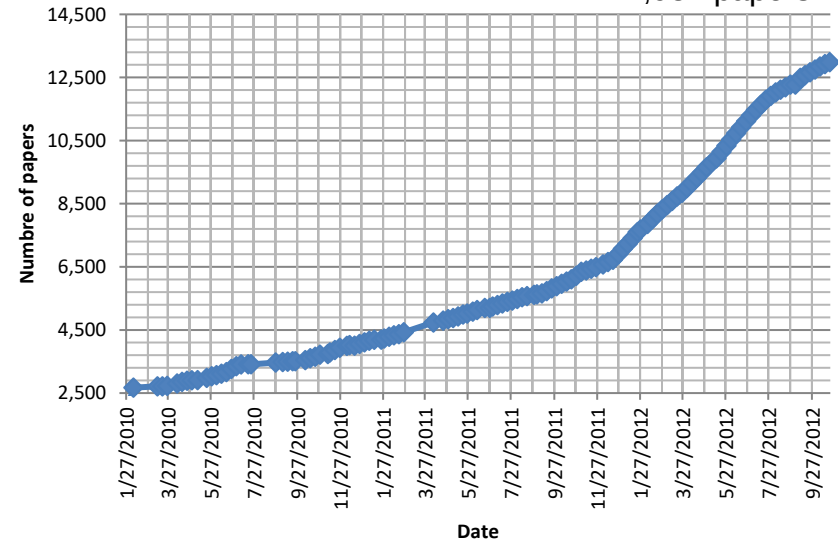
254,306 variants



5,284 phenotypes



12,981 papers



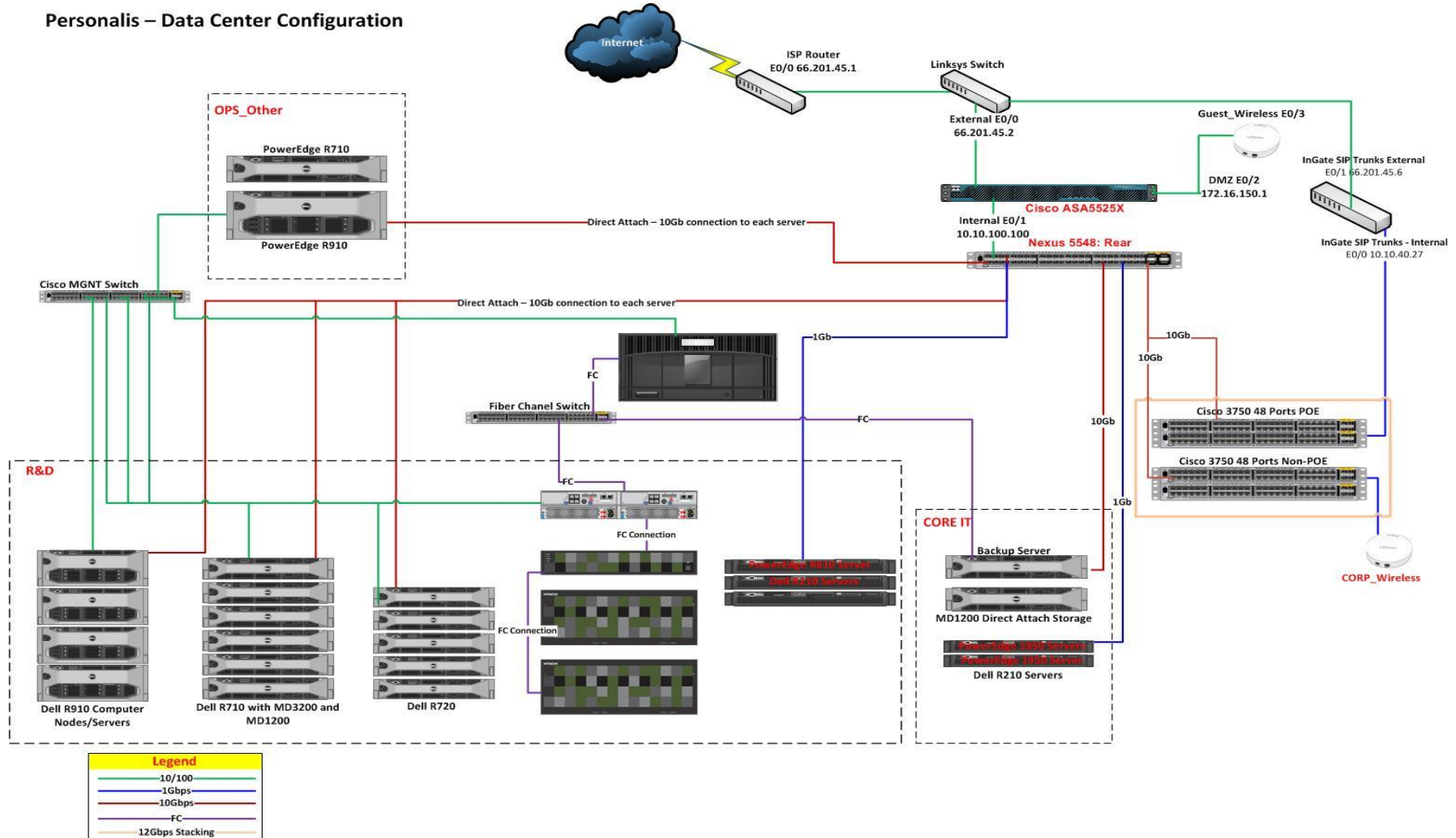
Personalis EX2100

Scientific Computing Infrastructure

- Hiring is a key challenge:
 - Director of High Performance Computing and Architecture
 - Linux Systems Admin
- Doing a reassessment of scientific computing needs (storage, CPUs) for next 6 months because of recent (good) developments:
 - **Ops: VA project** (processing >300 genomes every 2 months)
 - Ops: Moyamoya and customer projects
 - R&D: Access to very large public genome/exome databases (as discussed earlier)
 - R&D: General R&D needs
- Near Term Needs
 - Additional 107 TB of storage for Hitachi HNAS
 - Backup solution ordered (disk to disk, and disk to tape)

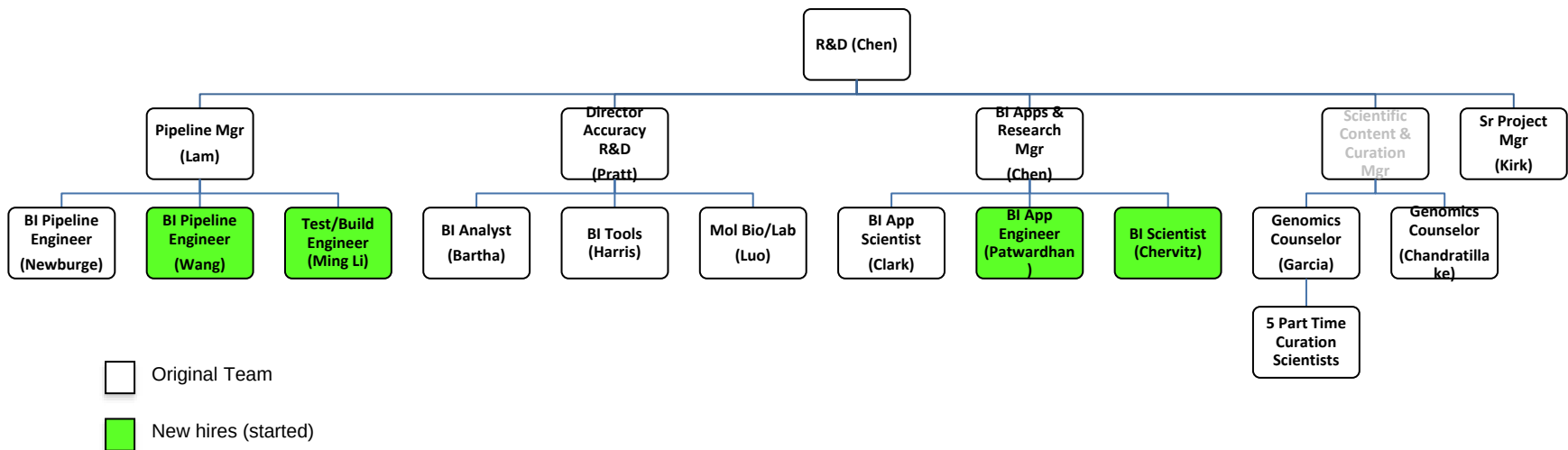
Scientific Computing Infrastructure

Personalis – Data Center Configuration



Hiring Update

- A member our R&D team has been on medical leave for nearly 2 months
- New Hires have enabled us to reach our target staffing in the pipeline & apps groups
 - Anil Patwardhan, Ph.D.: Sr Bioinformatics Scientist
 - Steve Chervitz, Ph.D.: Sr Bioinformatics Scientist
 - Ming Li, Ph.D.: Sr Software Lead (Test and Build Engineer)
 - Jing Wang, Ph.D: BI Engineer
- Open Positions
 - Director of High Performance Computing and Architecture
 - Linux systems admin



Summary of Resource Allocation

	Accuracy R&D Mark Pratt Gabor Barth Jason Harris Shujun Luo	Pipeline R&D Hugo Lam Daniel Newburger Ming Li Jing Wang	Apps R&D Rong Chen Michael Clark Anil Padawardhan Steve Chervitz	Content R&D Sarah Garcia Gemma Chandratillake PT Curators
Personalis Genome Services				
Disease Variant Discovery Service				
Customer Projects				
Research Projects				
Ethics Board				

AMP Conference

Takeaways Regarding Reimbursement of Clinical Dx

- Annual conference attended by molecular pathologists
- CPT coding changes to reduce code stacking for genetic tests
- Key Private payer reimbursement criteria
 - Lee N. Newcomer, MD, MHA, SVP, UnitedHealthcare
 - Analytic validity
 - Clinical validity
 - Clinical utility
- Medicare reimbursement excludes
 - Screening if no signs/symptoms
 - Risk assessment for patient or family member if no signs/symptoms
 - Diagnoses that are not actionable
- Implications for our clinical dx strategy
 - Focus on clinical dx asso with specific diseases/disease categories that are actionable (e.g. cardiomyopathy panels, heritable cancer, etc) and/or currently reimbursed will maximize chances of reimbursement. Focused interpretation on disease panels reflexing to whole exome or genome may be a way to do this.
 - Healthy people genetic screening (GIS) will have a harder time getting reimbursement in the short to medium term

Risks and Mitigation

Risk	Mitigation
• Aggressive timeline	• Minimized “research” features that could result in product delay, focused on achievable, differentiated features for v1
• Pipeline performance risk	• Approximately 2 days to run 1 whole genome currently on a 40 core machine • Prioritizing performance optimization, goal to reduce by 50% • Assess how we can address with more hardware, cloud
• Product Differentiation	• Prioritized differentiation in three key product areas: Exome+ , SV’s, accuracy/quality, content, visualization • Giving conference talks at AGBT to discuss differentiation
• Exome plus costs, may limit margins on product	• Actively working on cost model and ways to reduce cost
• New sequencing platforms antique our accuracy gains	• Obtain data from orthogonal seq platforms and integrate as appropriate
• Hiring of Unix sys admin and director of high performance computing.	• Redoubled efforts with in-house recruiter to identify more leads
• Long lead time content curation and content quality items for GIS and DVDS	• Started dev on those items with long lead times to develop concurrently with Pipeline (MendelDB, etc)
• Licensing of applications and content for analysis	• Systematically reviewing and applying for licenses for key content and algorithms
• Ethical use of Genomes for R&D	• Ethics board approval for all Genomes used for R&D • Part of orientation training

Next Steps & Priorities

- Continue development on PGS v1 priorities with goal of Feb 2013 launch at AGBT
- Execute on product features required for VA project, enable success
- Start implementing DVDS workflow and exploring early collaborations
- Continue Hiring for open scientific computing positions
- Continue to execute on content priorities, develop longer term content strategy
- Continue to work with OPS team to deliver successes with early customers and collaborators