INTRODUCTION

varsomeclinical

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Head of Business Development

Saphetor SA

- **Precision medicine & Bioinformatics**
- Creator of VarSome suite
- Founded 2014
- Switzerland, Lausanne
- EPFL Innovation Park
- Several offices around Europe

Challenges in bringing NGS to a clinical practice

1. Annotation data fragmented and spread over many websites

2. New findings and publications generated ‘every day’

3. Little standardization & consistency

→ Assessing pathogenicity for a variant very time consuming

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FREE

Genomics Knowledge Base and Human Genomics Community

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FREE

Challenge #1 – Annotation data fragmented and spread over many websites

→ *Data Integration: 50+ Data Resources, and growing!*

Literature

- PubMed (article title, abstracts & authors)
- VarSome community contributions
- Links from other data sources such as ClinVar, PMKB, UniProt, many databases contain PubMed references.

Clinical

- ClinVar
- UniProt - protein domains & functions
- Cosmic (currently disabled due to licensing)
- GDC (Genomic Data Commons)

Cancer

- ICGC
- PMKB
- CIViC

Population Studies

- GWAS

Transcripts

- RefSeq
- Ensembl

CNVs

- ExAC
- DGV
- Decifer
- ClinVar

Expression

- GTEX (coming soon)
- dbNSFP genes

Pharmaceutical

- DrugBank
- AACT
- FDA approved drugs

In-Silico Tools

- DANN
- Mutation Taster
- Mutation Assessor
- FATHMM
- FATHMM-MKL
- FATHMM-XL
- LRT
- DEOGEN
- EIGEN
- SIFT
- Provean
- Revel
- PrimateAI
- Polyphen (only in VarSome clinical)
- scSNV (splice-site prediction)

Conservation

- GERP
- Phylo P17, P30, P100
- Phast Cons 30 & 100
- FitCons
- MPC
- bStatistic

Frequencies

- GnomAD exomes, genomes, coverage
- Kaviar

Genes

- dbNSFP
- GHR (Genetics Home Reference)
- HPO (Human Phenotype Ontology)
- ClinVar Structural Variants
- PanelApp (Genomics England)
- CGD (Clinical Genomics Database)
- Domino (predicts mode of inheritance)
- PubMed (article title, abstracts & authors)

Challenge #2 – New findings coming every day

→ ***On VarSome we keep the annotation data always up to date!***

Challenge #3 – Little standardization & consistency

→ *Guidelines for standardization*

- **ACMG**
  - Robust (35+ data resources + contributions)
  - Transparent (review each rule)
  - Flexible (adjust the verdict)

- **Coming in Q1 2020**
  - AMP
  - NCCN
  - ASCO

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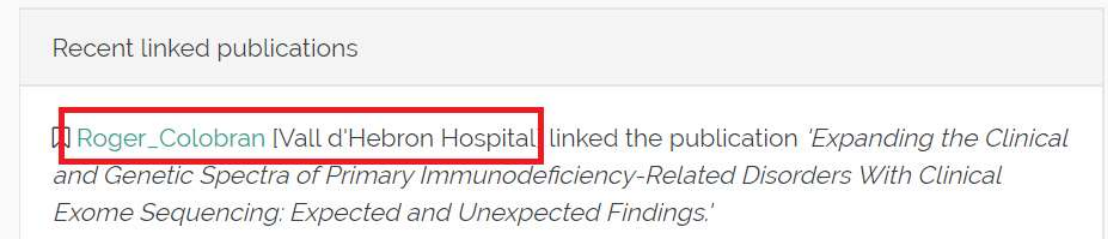
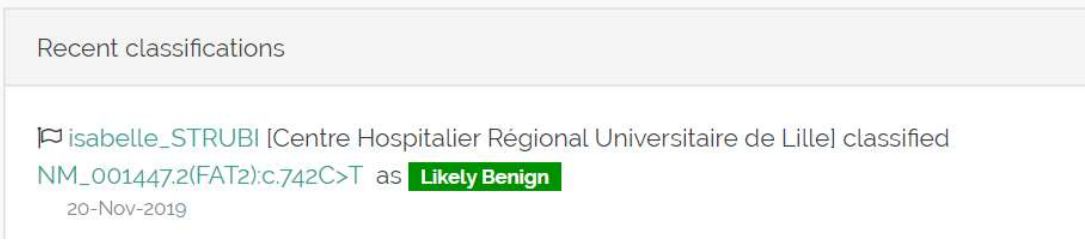
200.000 users globally! Sharing the knowledge with each other.

- Publication links
- Variant classifications
- Comments and discussions
- Cross-border collaborations - Connecting users & laboratories





Do it Yourself versus Do it Right

- Bioinformatician solves the primary and secondary analysis
- However, he or she usually struggles with the tertiary analysis (i.e. interpretation)
  - To do it right, you need to evaluate as much annotation data as possible

    → Challenge #1 – Fragmentation of annotation data

	DIY	DIR varsome
Bioinformaticians	1+	10%
Software Engineers	0	80%

The challenge lies in the interpretation part of the pipeline, which requires engineering skills rather than bioinformatics ones

→ However, having an *in house* bioinformatics expertise is an advantage.

→ We develop tools, <u>not a replacement for a bioinformatician</u> in your team.

→ Our tools allow your bioinformatician to be more productive and systematic, and thus <u>increase the diagnostic yield for your patients.</u>

Watch VarSome Video!

https://www.youtube.com/watch?v=5FB0PogqgCU

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VarSome Clinical is a clinically-certified platform allowing fast and accurate variant discovery, annotation, and interpretation of NGS data for whole genomes, exomes, and gene panels.

CE IVD

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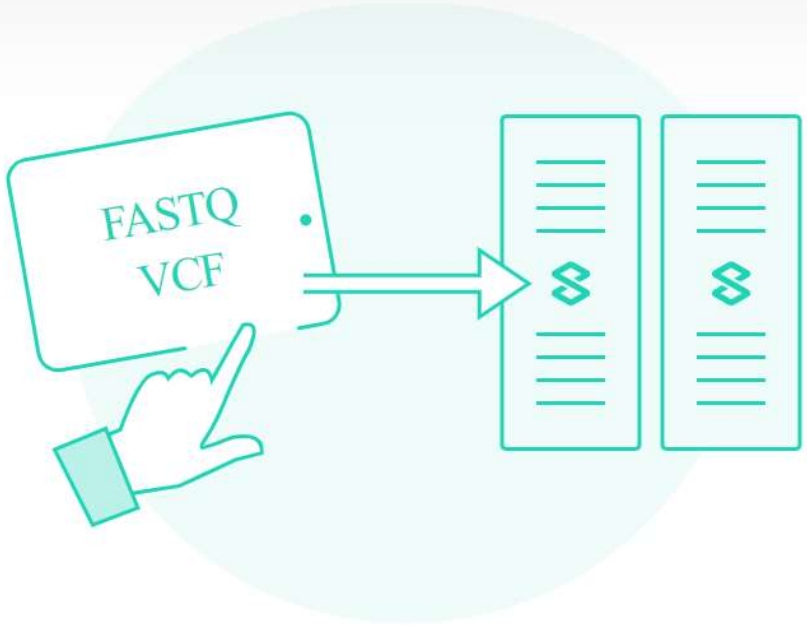

1 Upload FASTQ or VCF

VarSome Clinical accepts FASTQ and VCF files. You can upload the data easily and securely through its web interface or you can harness *VarSome*'s powerful API for an automated and secure data transfer. Once the data are uploaded, you can start the analysis!

- ✓ ANNOTATE FASTQ
- ✓ ANNOTATE VCF
- ✓ JOINT CALLING
- ✓ MULTI-SAMPLE ANALYSIS

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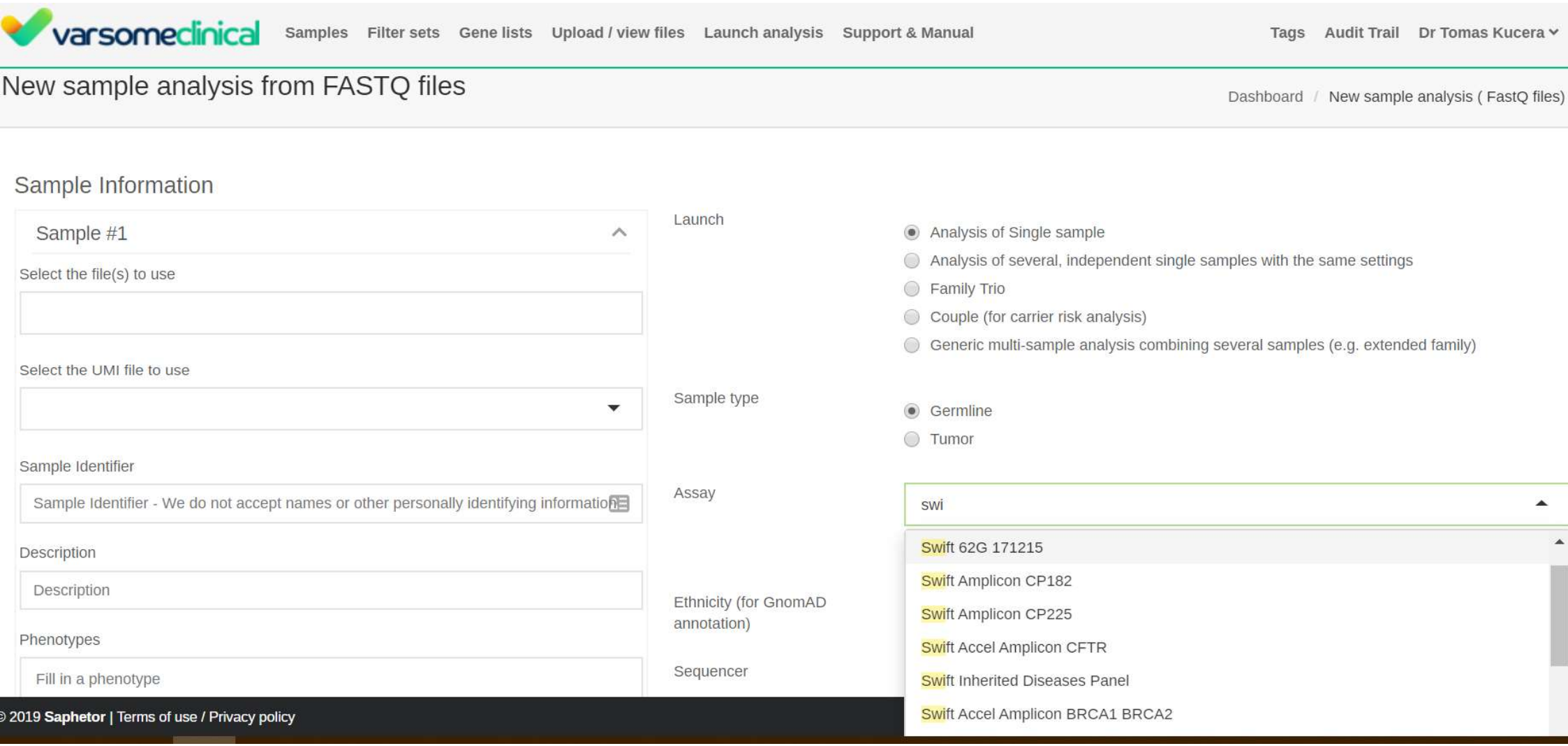
2 Annotation & Classification

VarSome Clinical's robust pipeline is capable of analyzing whole genomes, exomes, and gene panels, for individual samples, trios, families, and cohorts in minutes. *VarSome Clinical* leverages the massive cross-referenced knowledge base of the free *VarSome* and offers also access to licensed databases.

- ✓ OVER 30 DATA RESOURCES
- ✓ ACMG CLASSIFICATION
- ✓ PROPRIETARY DATA RESOURCES
- ✓ QUALITY CONTROL REPORTS

Launching an analysis



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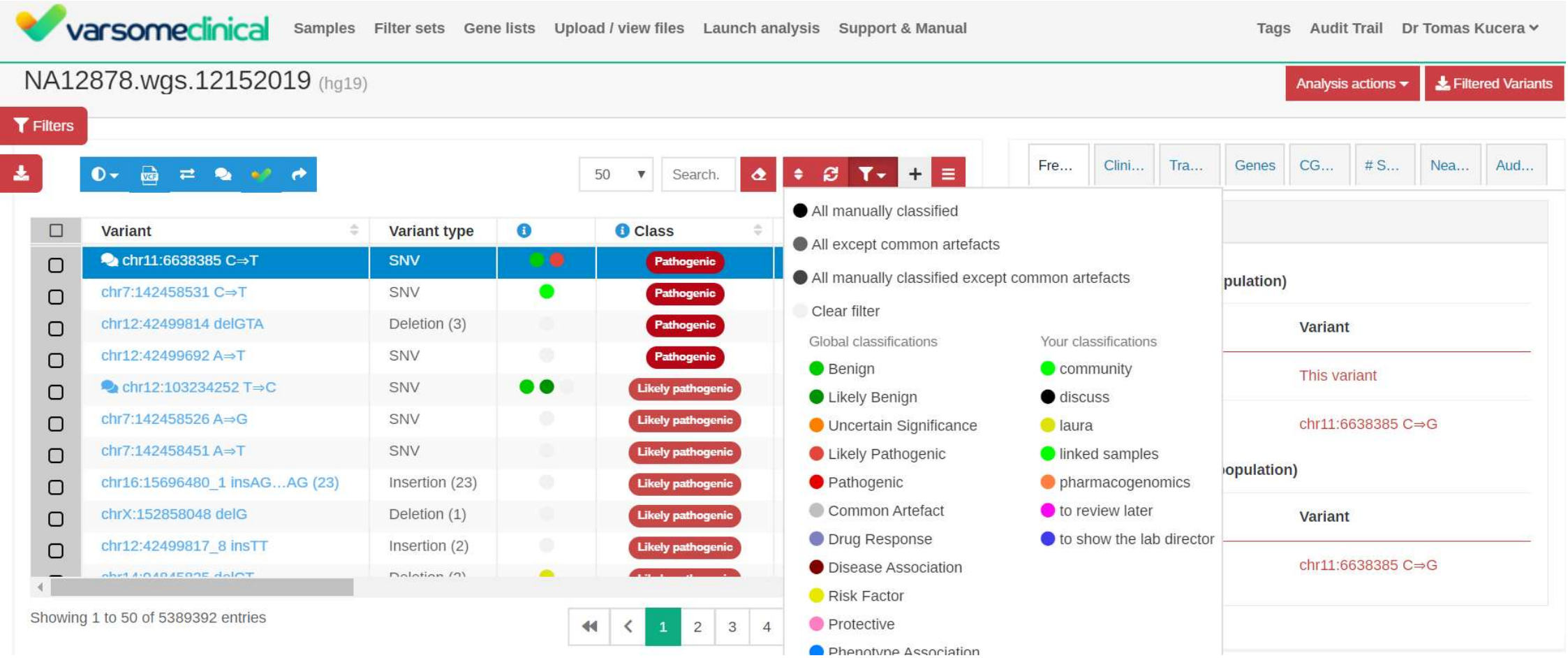
3 Intuitive Web Portal

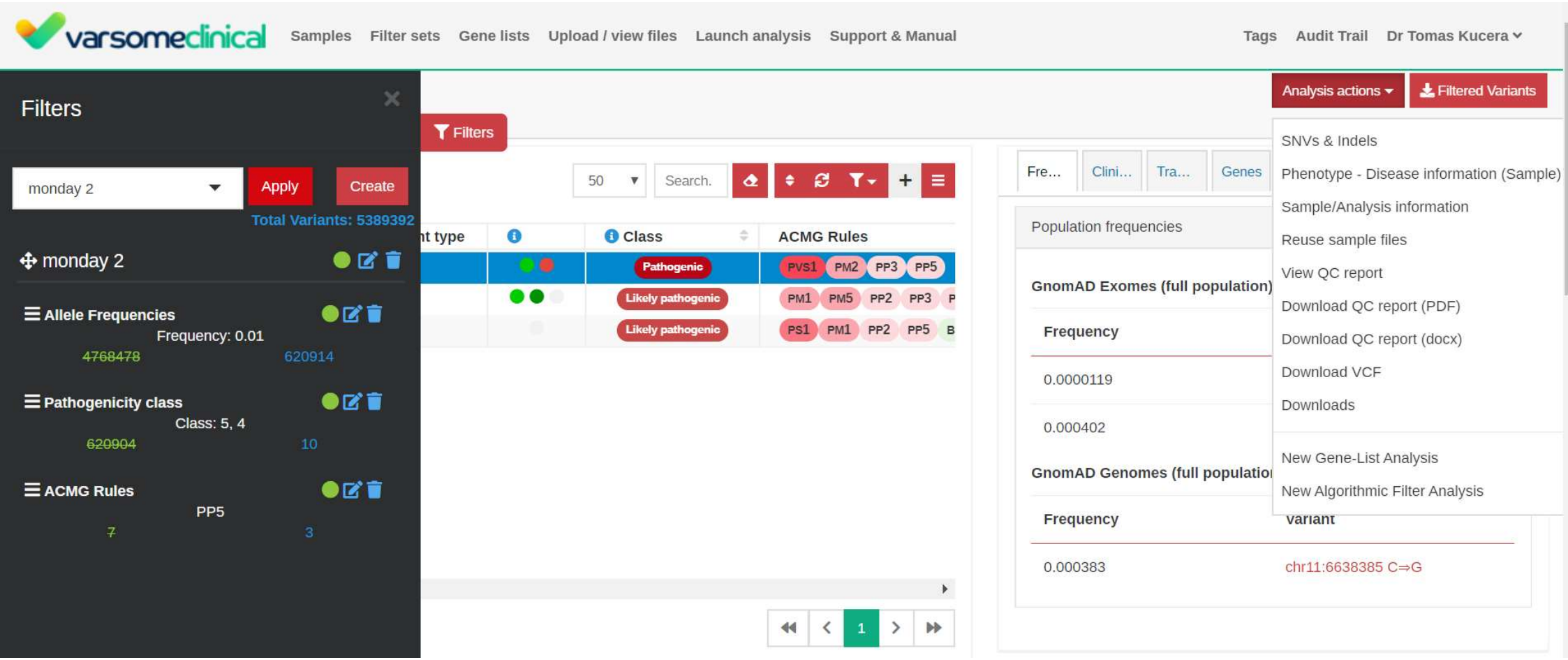
VarSome Clinical's feature-rich and intuitive web interface allows filtering variants according to pathogenicity, ACMG classification, allele frequency, gene list or phenotype, to name a few! Dynamic and algorithmic filters allow you to perform simple or advanced filtering, like segregation analysis, identification of *de novo* variants or variants in imprinted genes, and much more!

- ✓ DYNAMIC FILTERS
- ✓ ALGORITHMIC FILTERS
- ✓ SAMPLE CROSS-REFERENCING
- ✓ VARIANT SHARING

Browsing the results



Filtering the variants



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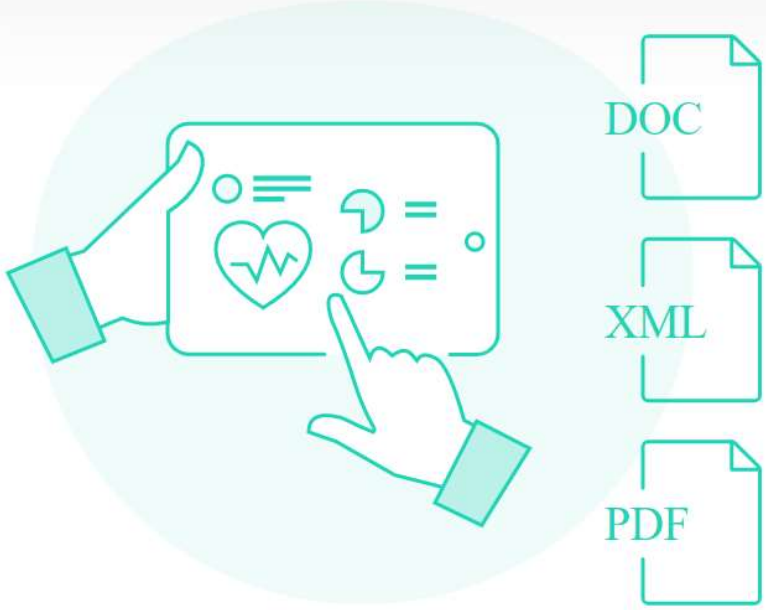
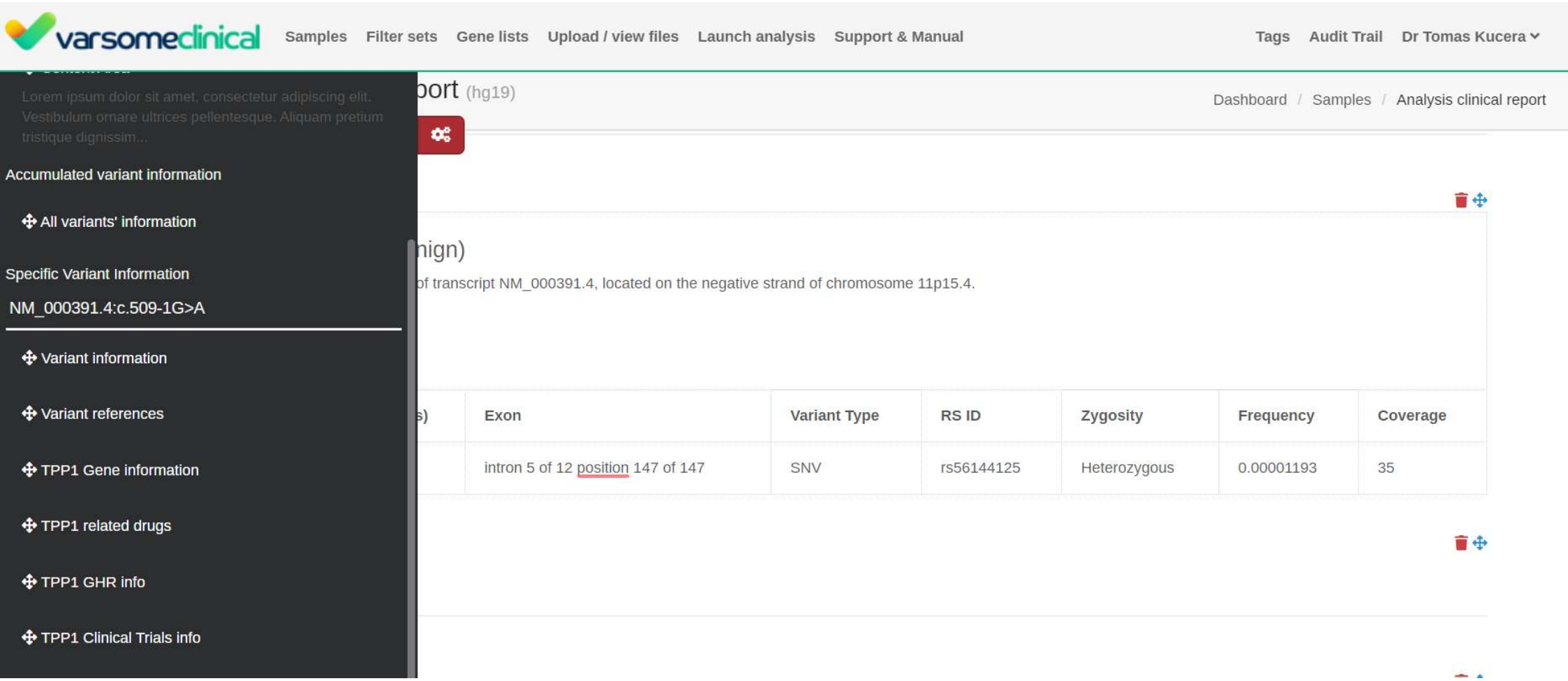


4 Clinical Report Generation

Once you have narrowed down the list of variants of interest, you can proceed with the generation of the clinical report, which includes all the details of your variants, including literature references and your custom comments. The layout of the report can be fully customized according to your unique branding policy.

- ✓ CUSTOMIZABLE REPORTS
- ✓ CE-IVD CERTIFICATION
- ✓ AUDIT TRAIL

Interactive reporting



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Watch VarSome Clinical Video!

https://www.youtube.com/watch?v=5EWB74kxMaM

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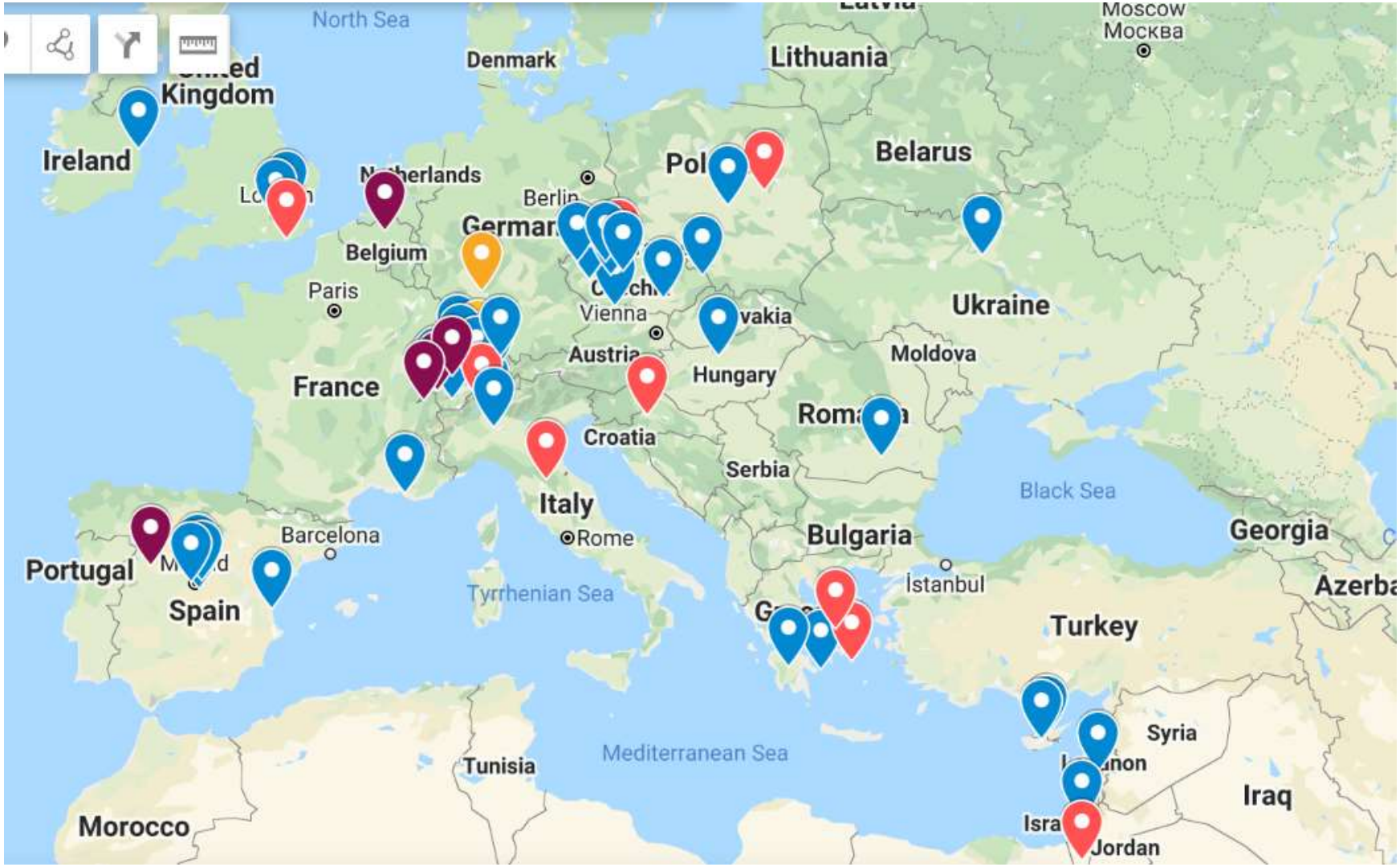

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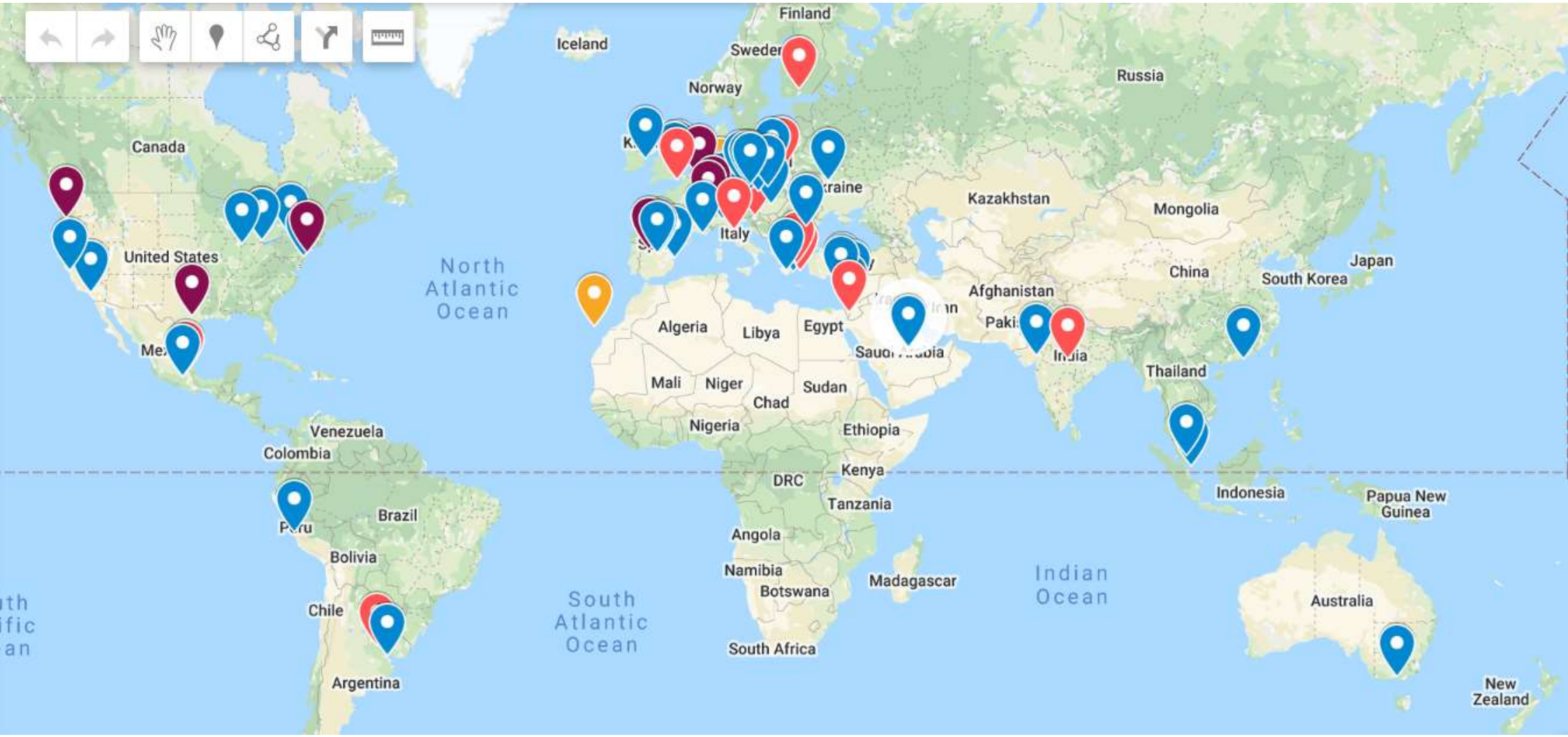

General Pricing Guidelines

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1. **NO License Fee**

2. **Sample Fee**
   - FASTQ – Number of megabases in reads
   - VCF – Number of variants

3. **Volume Discounts**

4. **Small User Fee**

Price by megabases in reads per sample (1 megabase = 1 million bases)	Per sample
Up to 250 megabases	
250 to 500 megabases	
500 to 1,000 megabases	
1,000 to 2,000 megabases	
2,000 to 4,000 megabases	
4,000 to 8,000 megabases	
8,000 to 20,000 megabases	
20,000 to 40,000 megabases	
40,000 to 80,000 megabases	
80,000 to 150,000 megabases	

Price by number of variants per sample	Per sample
1 to 100	
101 to 400	
401 to 1,000	
1,001 to 2,000	
2,001 to 4,000	
4,001 to 10,000	
10,001 to 20,000	
20,001 to 40,000	
40,001 to 80,000	

Modes of use

1. Stand-alone Solution – Pay as you go

- VarSome Clinical open for any kind of NGS sample
- Be it gene panel, exome, genome
- Invoicing on a monthly basis depending on the platform use
- No License Fee
- Just Sample Fee
- Plus Small User Fee + Small Storage Fee

- **Credit:** You may prepay a credit and then use it towards the use of the platform, as opposed to monthly invoicing

Modes of use

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<u>2. Bundled Solution</u> – Pre-payment

- Assay bundled with VarSome Clinical for data analysis and reporting
- Pre-payment of a certain number of analysis
- An analysis token – price depends on the number and type of samples

4bases

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PARAGON GENOMICS

Partners in the pipeline:

NONACUS
Advancing Non-Invasive Healthcare

parseq lab

TWIST BIOSCIENCE

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RESULTS FOR LIFE

VIENNA LAB

Slide 25

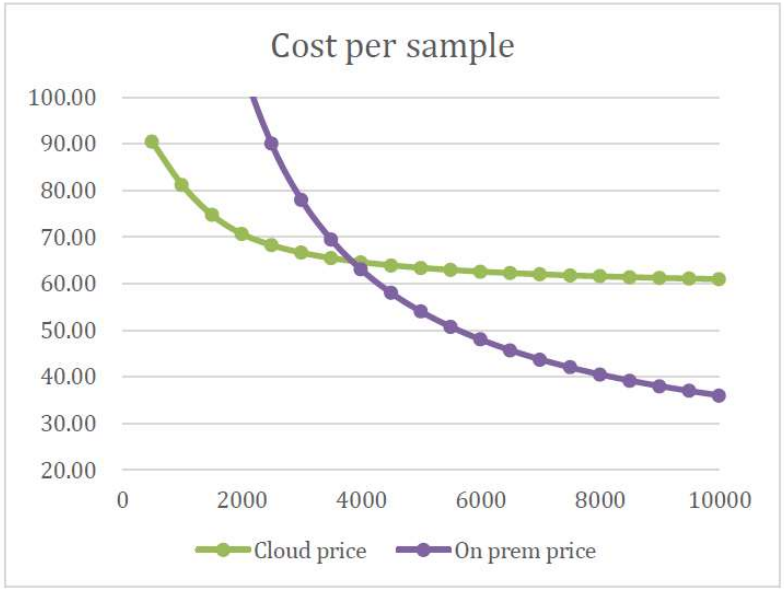
TK1 add agillent logo
Tomas Kucera, 27-Jan-20

Modes of use

3. **On Prem Installation**
   - For partners, labs and hospitals with large volume (aggregated) of samples
   - Fixed Yearly/Monthly License Fee
   - Plus 80% discounted sample fee
   - Becomes economical since a certain number of samples (4000 exomes, for example)

Model situation

- In line with Part 1, assuming the sample fee: list price 90 € per single sample (average exome, starting from FASTQ)



Working together with distributors

- **Distributor may provide you with a better quotation then us directly**
- **Distributor to be your primary point of contact**
- **Distributor to provide 1st level of support**
- **VarSome to provide:**
    - Customizations – We like to work very closely with our clients.
    - Trainings
    - Documentation
    - 2nd level of support – We back you up!

Contact

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