

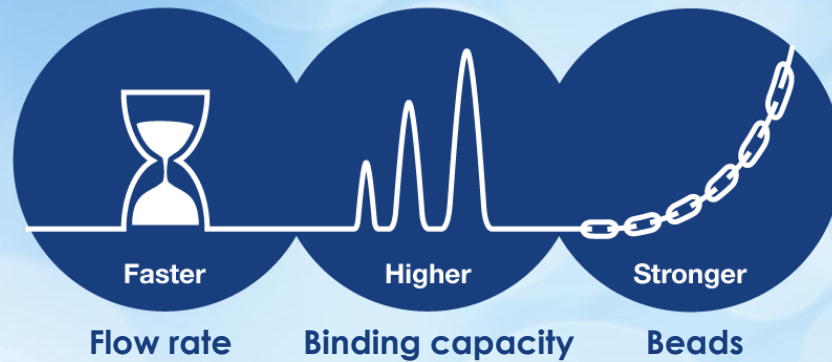
Bio-Works

High performing products that make purification simple

Jonathan Royce, CEO

Pareto

20200902



Investment highlights

Essential product

- › Separation and purification of biomolecules
- › Used in the development and production of pharmaceuticals and diagnostics

Growing customer base

- › Increasing number of customers in scale-up and production phase – 71 by Q2 2020
- › Biosimilar market (esp. Asia) creating opportunities for new suppliers like Bio-Works
- › Enabling a robust order flow over time

Validated technology

- › Best-in-class in independent Takeda test
- › 12 customers currently at production scale with Bio-Works resins

Growth markets

- › Peptides market growing 9.4% annually
- › Oligonucleotides market growing 13.7% annually
- › RNA Therapeutics market growing 8.9% annually

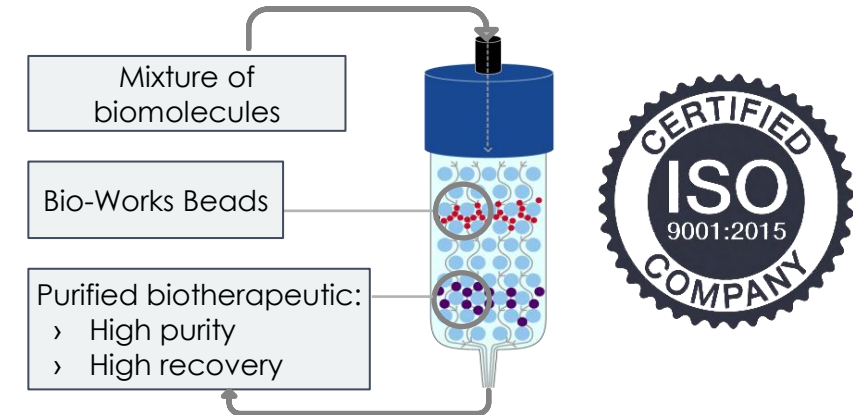
Recurring revenue

- › Serving early stage lab-scale to full-scale commercial producers
- › Products integrated into the customer's development process enables steady long-term growth

Bio-Works overview

Bio-Works at a glance

- › Broad portfolio of high-performing products for purification of biomolecules
- › Market demand fuelled by increased biopharmaceutical and biosimilar production
- › Long term “design-in” effect drives repeat customer sales
- › Experienced management team and board of directors
- › Highly respected Scientific Advisory Board comprised of industry leaders



Products

WorkBeads Q and WorkBeads S

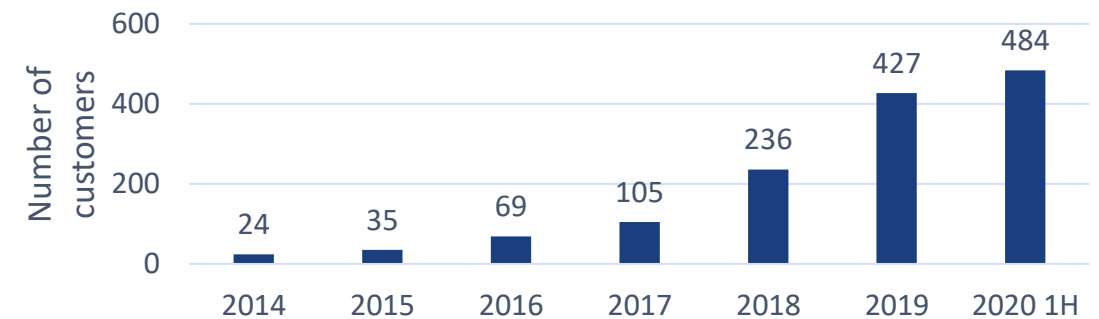
- › Used broadly in the purification of all classes of biomolecules
- › Unique properties for purification of oligos, peptides and mRNA

WorkBeads TREN

- › Novel “multimodal” resin used in antibody purification, viral clearance and endotoxin removal

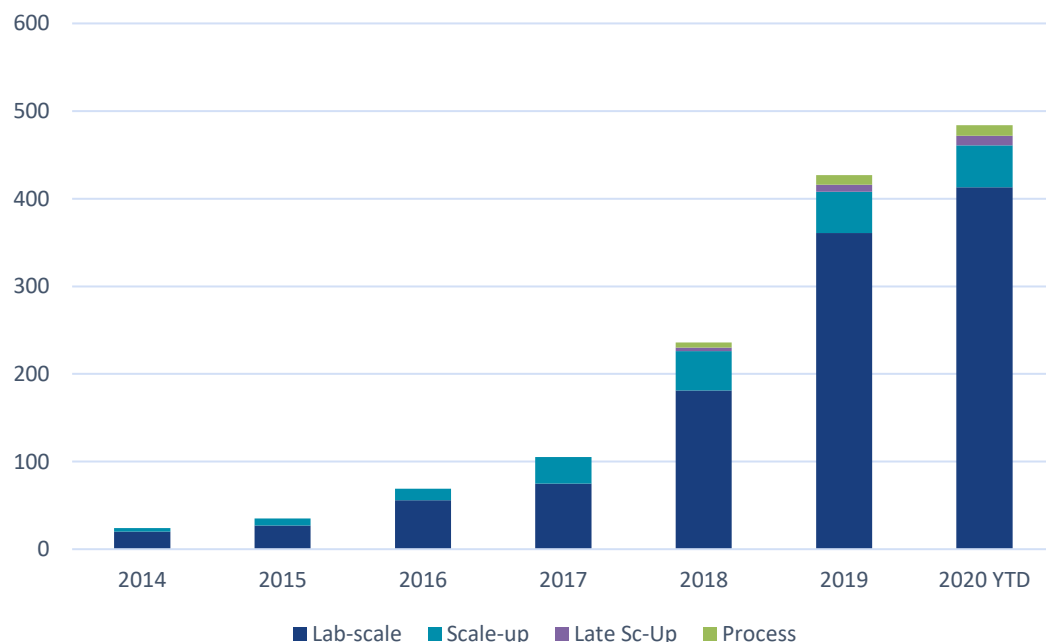
Strong traction with global customer base

Combination of direct sales and local distributors developing customer base



Consecutive customer growth and sales funnel progress

Accumulated - Number of Customers by Type



- › Strong consecutive YoY growth
- › Continued growth in 2020 despite commercial challenges presented by COVID-19

Sales funnel progressing in all phases

	DISCOVERY PHASE Low volumes, tech validation	SCALE-UP PHASE Larger volumes, process testing	PRODUCTION PHASE Largest volumes, full production
4Q18	181 customers	49	6
4Q19	361 customers	55 (8 late scale-up)	11
2Q20	413 customers	59 (11 late scale-up)	12
	+52 customers	+4 customers	+1 customers

1H20 highlights

KEY STATS 1H2020	1H19	1H20
Net Sales	SEK 2.2m	SEK 3.7m
Order intake	SEK 2.5m	SEK 4.7M
Cash flow from operating activities	SEK -81M	SEK -22M
Bank balance	SEK 35.6M	SEK 54.3M
Earnings per share	SEK -1.12	SEK -0.69

1H20 highlights

- › Strong growth in all sales regions
- › New board members strengthen already experienced team
- › CEO transition completed from Mats Johnson to Jonathan Royce
- › Successful annual ISO 9001:2015 audit
- › COVID-19 campaign resulted in several new collaborations
- › New distributors added in Taiwan, India and US subsidiary established
- › 12 customers in production phase; 11 more in late scale-up

Order growth 1H20 vs TY19



Full focus on driving sales going forward

- › Surpassed target of 400 active customers by year end 2019
- › Continued focus on growing our customer base while nurturing existing customs along the buyer journey
- › Increased focus on core applications:
 1. Peptide purification
 2. Oligonucleotide purification
 3. mRNA purification

Continued strengthening of Board of Directors

2019



Peter Ehrenheim

Chairman of the Board

- › Background from Pharmacia, Amersham and GE Healthcare
- › Chairman in Medcap, Boule Diagnostics, Sophion and Director in Biotage



Thomas Eklund

Board Director

- › Background from Investor Growth Capital, AAC Capital and Handelsbanken Market
- › Lead investor in Swedish Orphan, Vårdapoteket, Memira, Carmel Pharma etc.

2020



Johan Sedih

Board Director

- › Background from Elekta Group
- › Chairman in SyntheticMR AB and Director in Dirac Research AB



Peter Nählstedt

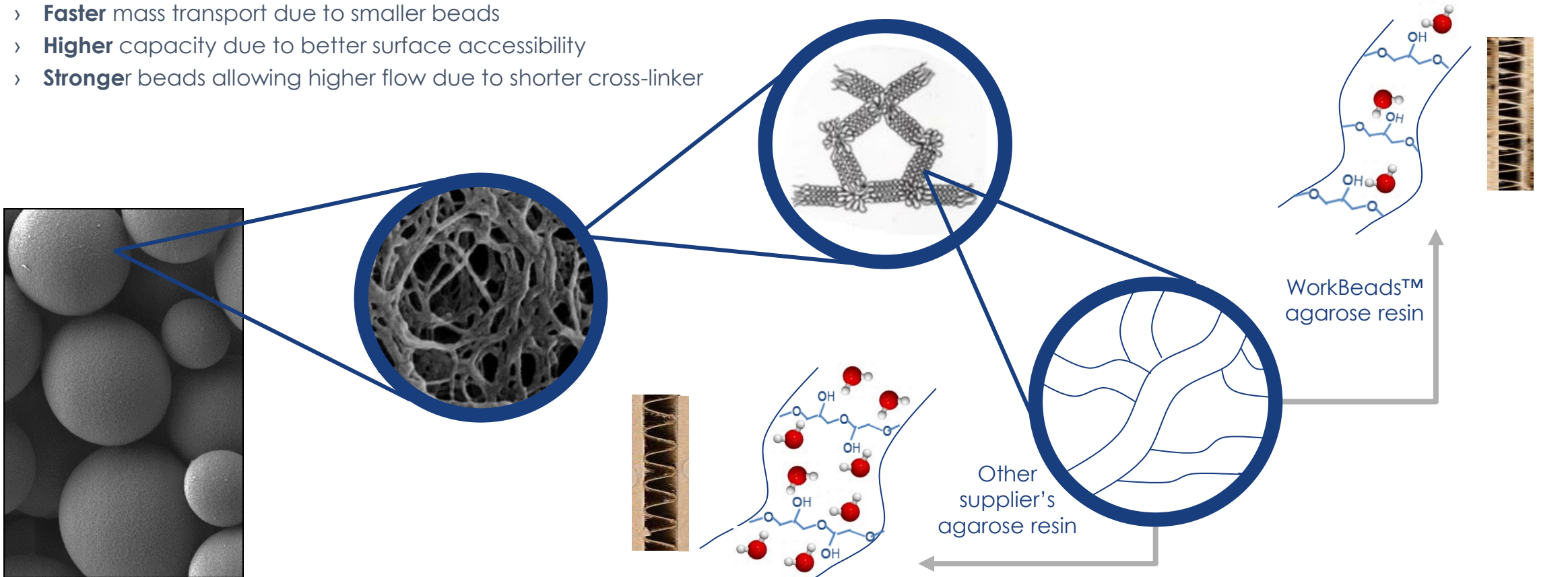
Board Director

- › Background from GE Healthcare and Probi
- › Chairman in Double Good AB and Supersynbiotics AB and Director in SenzaGen AB

WorkBeads characteristics

Characteristics result in:

- › **Faster** mass transport due to smaller beads
- › **Higher** capacity due to better surface accessibility
- › **Stronger** beads allowing higher flow due to shorter cross-linker



WorkBeads best-in-class in independent Takeda test

Takeda poster

Challenging antibody purification process development: solving CEX peak splitting phenomenon

Anna Senczuk¹, Zijian Ma¹, Junfen Ma¹

¹ Takeda Downstream Process Development, Pharmaceutical Sciences, 200 Shire Way, Lexington, MA, 02421, USA



Better Health. Brighter Future

Introduction

Peak splitting during CEX chromatography has been well documented in literature (1-4). The factors that were found to contribute are resin hydrophobicity, loading factor and molecule propensity to aggregation. We encountered similar problem with mAb X and approached it by testing its stability as Protein A elute and experimenting with multiple conditions and resins to understand this phenomenon and find suitable processing options. Although the conditions were identified to avoid peak splitting, the significant impurity burden and low Protein A yield were still an issue. We found that harvest filtration for impurity removal was very effective and yielded simpler process.

Materials and Methods

All chromatography experiments were performed using Akta Avant 150. Monoclonal antibody A as recovered from cell culture by depth filtration with depth and 0.2um filter train. In some experiments the depth filter harvest was pH adjusted to 6.5 with 1M acetic acid and filtered through Emphaze hybrid purifier. mAb X (pI 7.1) was then Protein A purified and the eluate was subjected to purification stability screen using DynaPro Plate Reader II.

Background

Protein A Step eluate had pH ~4.3 and no significant turbidity. After low pH treatment, the neutralization step proved very challenging: pool neutralized to pH 5.0 gave high turbidity and ~50% product loss while pool neutralized to pH 7.5 gave >70% loss. Those findings prompted stability testing in wide range of pH and salt. CEX condition screen and resin screen and finally harvest pre-treatment with Emphaze hybrid purifier. Experimental schematic is shown below.



Stability testing

Using mAb X Protein A eluate, the impact of NaCl, pH and Arginine was investigated by DLS. We examined monomer, dimer and aggregate content in response to pH and salt conditions. The screen showed that pH is the predominant factor impacting monomer content.

- 50 mM Arg was added to Protein A elution buffer, neutralization pH was set at 4.2
- ≥50 mM Arg was also added to CEX acetate buffers, pH kept at 4.2

pH and NaCl

Only pH had statistically significant impact on monomer ($p < 0.001$). Monomer at >70% level is seen when $pH < 4.0$ dimerization is >10% when $pH > 4.2$

pH and Arginine

Arg-pH interaction was statistically significant ($p < 0.001$) for monomer content. Monomer is maintained when $pH < 3.75$ and Arg <25 mM but dimer is minimized when Arg 50-150 mM

CEX load factor, pH and Arginine screen

Poros XS with 50 mM acetate: 75 mM Arg pH 4.2. Peak splitting is observed at all loading levels, but is most pronounced at ≤17 mg/mL-r loading

Poros XS with 50 mM acetate 75 mM Arg, 17 mg/mL-r load. At pH 4.8 and 5.1 peak splitting is much less pronounced than at pH 4.2

Poros XS with 50 mM acetate 17 mg/mL-r load. At low loading, peak splitting is seen at all Arg levels, but is minimized at higher Arg conc.

Key Analytical Data

Elution pool	NaCl	% Monomer (DLS)	DNA (mg/L)
Protein A	50 mM Arg in elution	2.9	148,142
Poros XS pH 4.2		3.0	151
Poros XS pH 4.5		2.6	102
Poros XS pH 4.8	50 mM Arg in load	2.2	73
Poros XS pH 5.1		1.4	3,840
Poros XS 50 mM Arg		2.4-4.0	148
Poros XS 75 mM Arg		3.1	39,438
Poros XS 100 mM Arg	pH 4.2	1.9	22,096
Poros XS 125 mM Arg		1.8	26,565

Low pH provides DNA removal but causes on-resin aggregation. Arg-100 mM allows for aggregate removal but negates DNA removal.

Impurity Removal prior to Protein A

Protein A load was filtered with Emphaze hybrid purifier at 350L/m² throughput and subjected to purification through ProA and Poros XS. Product quality and yield were much improved.

Sample	ACP (mg/mL)	DNA (mg/mL)	Peak (mg/mL)	SEC main %	Step Yield (%)
Control Protein A pool (50 mM Arg)	2900	150,480	42	94.7	74
Emphaze Protein A pool	287	42	36	96.5	93
Control Neutralization post viral inactivation pH 5.0					~50
Emphaze Protein A/Neutralization post viral inactivation pH 5.0					97
Control CEX pool (50 mM Arg, pH 4.2)	9	150	34	94.4	89
Emphaze ProA/CEX pool	LOQ	1.7	4.2	97.7	94

Do other CEX resins contribute to peak splitting?

Poros XS has the most hydrophobic bead and hydrophobic grafted polymer that seem to induce peak splitting the most. In contrast, BabyBioS—an agarose resin without grafted polymer delivered symmetrical peaks in all conditions tested: load factor <20 mg/mL-r, pH 4.2-5.1, Arg. 0-125 mM.

Resin	Ligand	Bead size (ave um)	Charge density (meq/mL)	Relative resin hydrophobicity (bead and grafted polymer)	Observed peak splitting
Poros XS	SO ₃ ⁻	50	135	+++ Divinylbenzene	+++
Capto SP	SO ₃ ⁻	40	140	++ Agarose + polymer	+/-
SP Sepharose	SO ₃ ⁻	90	180-250	++ Agarose + polymer	+/-
Nuvia	SO ₃ ⁻	85	90-150	+ Polyacrylate + polymer	+/-
BabyBio S	SO ₃ ⁻	45	180-250	- Agarose, no polymer	-

Conclusion

- Peak splitting observed on Poros XS seems to be related to on resin aggregation. The degree of splitting depends on bead hydrophobicity and is exacerbated by load factor <20 mg/mL-r
- Having tested mAb X purification stability by DLS, conditions were found that minimized peak splitting, but resulted in poor DNA removal (pH 4.2 and 100 mM Arg)
- Application of Emphaze hybrid purifier filtration to Protein A load appeared to solve the problem by removing DNA and improving yield at every step tested
- The exact nature Emphaze filter benefit is under investigation

References

1. Cation exchange surface mediated denaturation of an aggregated monoclonal antibody (mAb). Chong et al., J. Chromatogr. B (2012) 100-110.
2. Loading and aggregation of monoclonal antibodies on cation exchange columns: effects of resin type, load buffer and protein stability. Guo, L. and Combs, G. L. Chromatogr. A (2012) 184-194.
3. Surface induced two-step elution behavior of a monoclonal antibody during cation exchange chromatography. Guo et al., J. Chromatogr. A (2012) 85-94.
4. Insights into understanding aggregation formation and dissociation in cation exchange chromatography for a structurally unstable Fc-fusion protein. Chong et al., J. Chromatogr. B (2012) 110-122.

Highlights

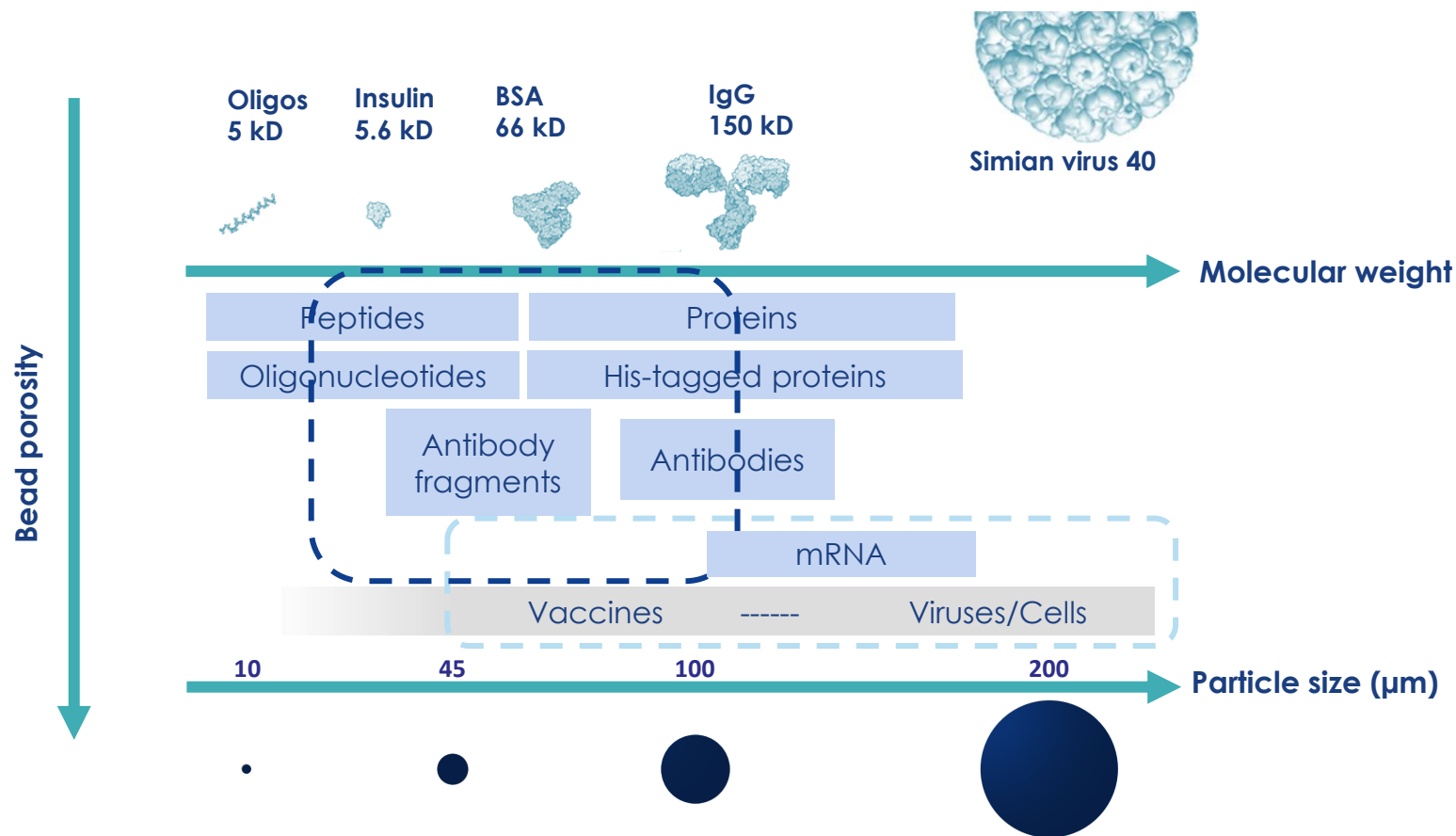
- › Purest result
- › Symmetrical peaks in all conditions

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WorkBeads: Differentiated products for many applications



Key differentiator:

- › Dynamic capacity
- › Purity

Key differentiator:

- › Flow dynamics
- › Purity

Two recent product launches

WorkBeads Dsalt

Quick and easy separation of high- and low molecular weight substances for efficient desalting and/or buffer exchange of proteins, large peptides or nucleic acids.



WorkBeads NiMAC

Quick and easy purification of His-tagged proteins and other proteins with an affinity for nickel ions

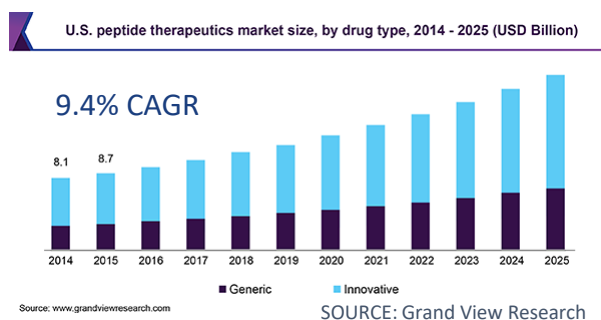
Very high resistance to reducing agents such as DTT and chelating substances such as EDTA, enabling purification of proteins from sources such as eukaryotic cell



Bio-Works application focus

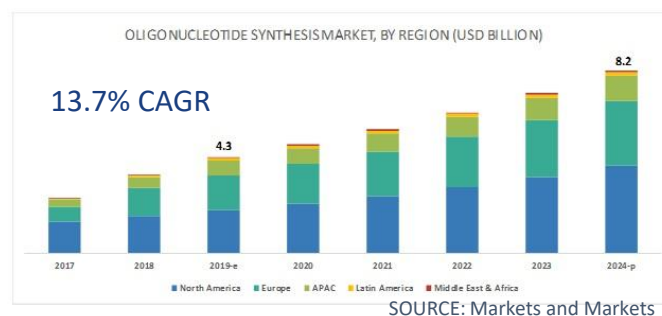
Peptides

- Bio-Works has high performing products for purification of peptides
- Proven track record in large scale manufacturing
- Technical depth via internal resources and Scientific Advisory Board



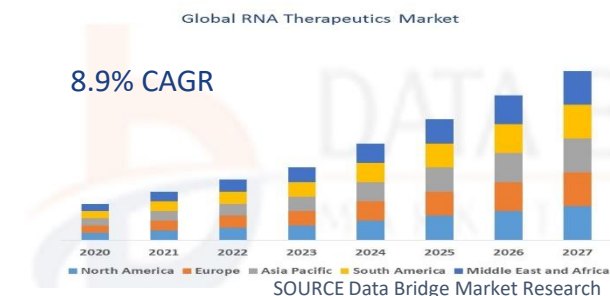
Oligonucleotides*

- Relatively new field
- Bio-Works' products reduce cost of purification and consumption of hazardous solvents
- Track record in R&D purifications
- Technical depth in our Applications team

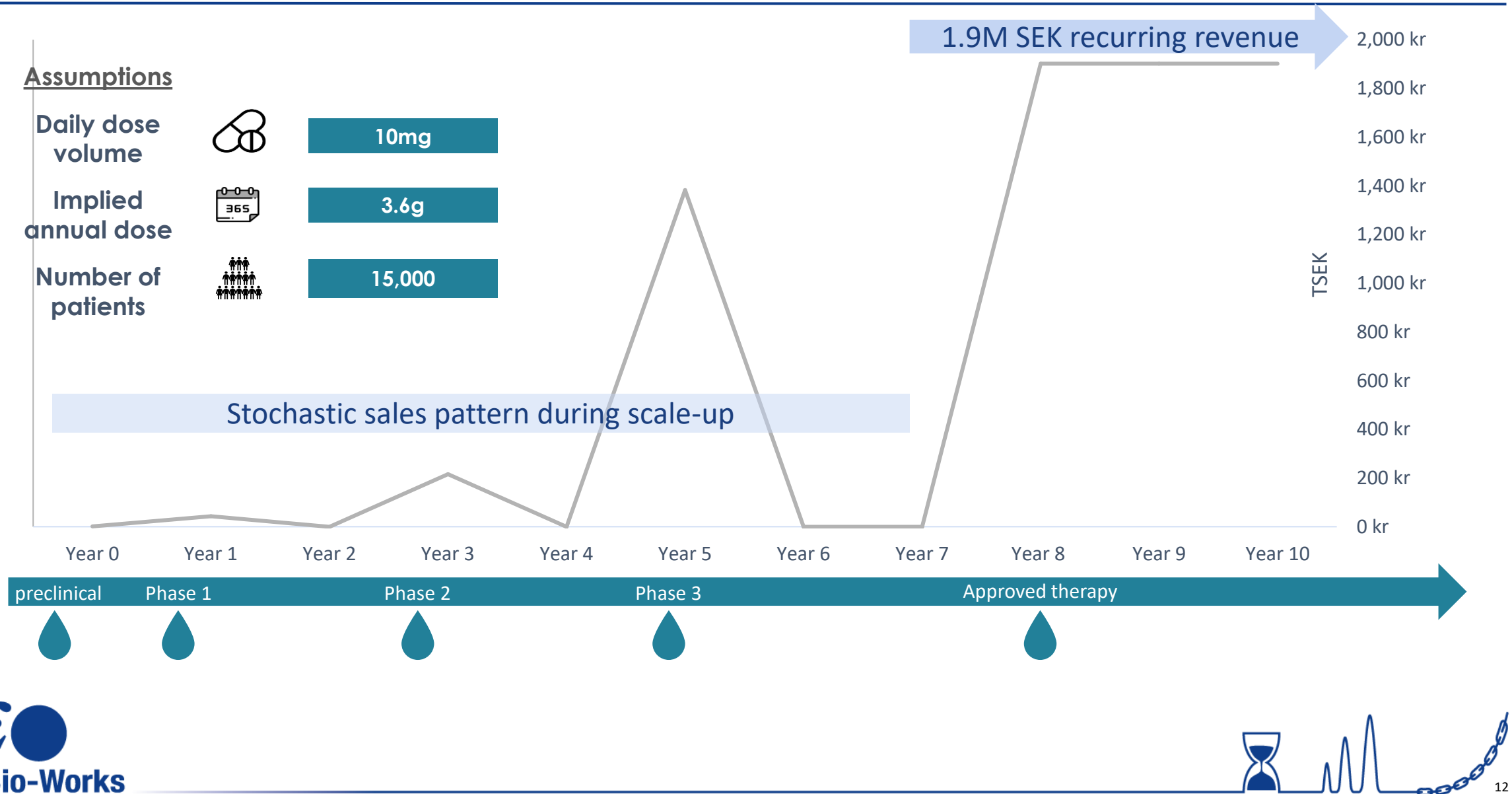


Therapeutic RNA

- New therapeutic area—no “gold standard” resin in this relatively new field
- 2 major groups:
 - **asRNA (antisense RNAs/ +siRNA)** are optimal targets for Bio-Works' existing products
 - **mRNA (therapeutic mRNA/ vaccines):** prototypes have been developed



Case study – revenue development for peptide project



71 customers in scale-up and production

Five customer categories

Small/Mid-size Biotech

- › Close to research and often early stage
- › **Relatively low resin volume needs**
- › Projects or company can be acquired by Pharma

Diagnostics/Special

- › Target molecule usually high value component
- › **Low to mid resin volume needs**
- › Products often directed to 'mass' market

CMO/CDMO companies

- › Service provider, usually to small- and big Pharma
- › **Mid to mid-high resin volume needs**
- › Projects usually transferred to Biotech or Pharma

Small Pharma

- › Often new or special drugs that may take off
- › **Mid to mid-high resin volume needs**
- › Company may grow fast or be acquired by big Pharma

Big Pharma

- › Usually block-buster drugs
- › **High to very high resin volume needs**
- › Scale-up projects will almost certainly transfer to manufacturing

Global sales

Current sales in 32 countries, covering all global regions

North America

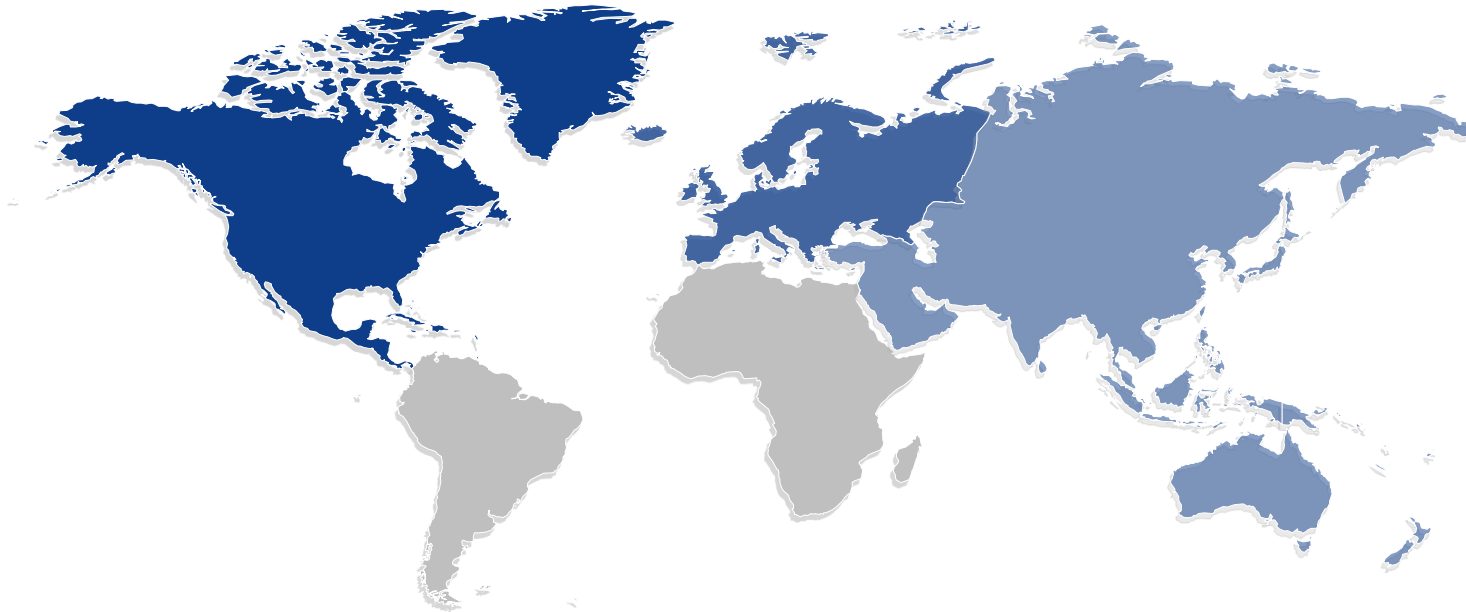
- › Direct sales and distribution
- › Bio-Works Inc established Q1 2020

Europe

- › New Regional Sales Managers
- › Focus on Germany and UK
- › Distributors in Eastern Europe and Southern Europe

Asia & Australia

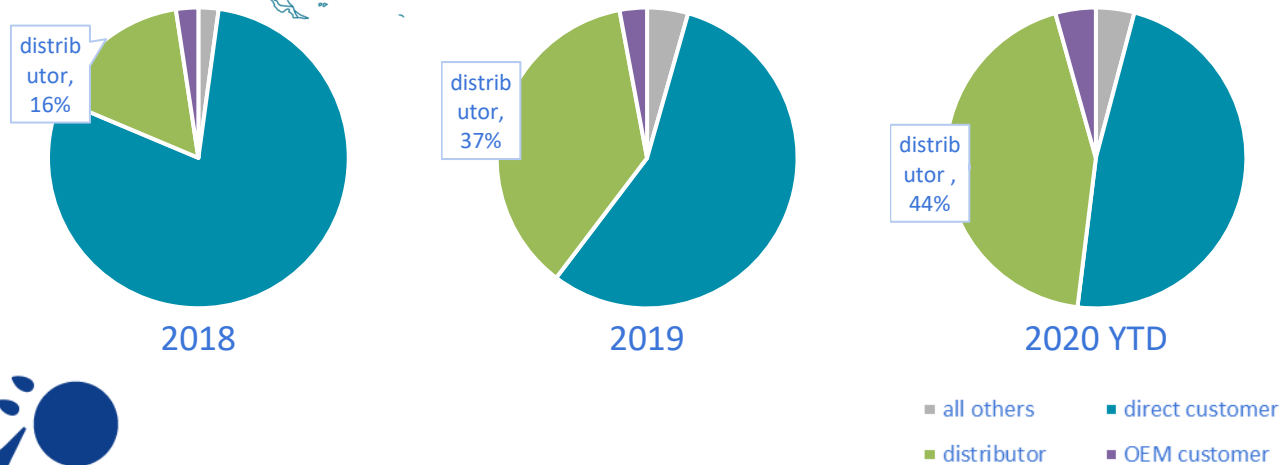
- › Distribution channel strategy
- › Two distributors added in India
- › Increased support presence



Distributor strategy in growth markets delivering results



- Close relationships with distributors
 - Dedicated Business Development Managers working with each region
 - Training, joint sales calls and annual distributor meetings
- Careful selection of distributors working with related or similar products



Important milestones reached 2019 and 2020 YTD

	Broad testing of WorkBeads affimAb globally
	Orders increased by 88%
	US sales rapidly growing
	Annual ISO recertification completed
	Launched WorkBeads Dsalt and WorkBeads NiMAC
	Key additions of experienced Board representation
	Distributors delivering revenue in growth markets

Focus next coming months



Lead generation and scale-up development: Continued search for new customers and nurturing of those already using Bio-Works products



Digitalization of marketing tools and sales tactics. Adapt to the “new normal” of COVID-19.



Customer target: **>500** by year end 2020



Acceleration of sales efforts including active collaborations with KOL customers and academics

Path to growth ahead

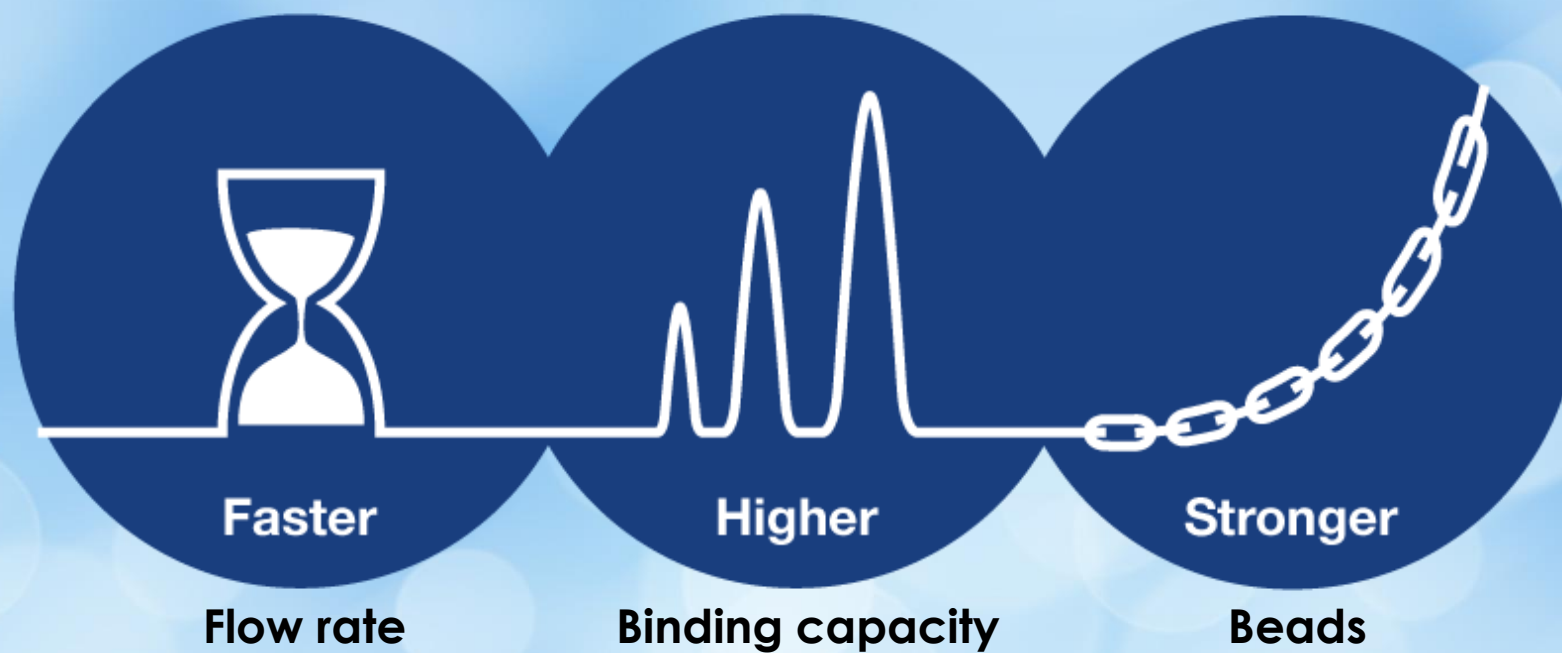
Competitive, essential products are the foundation for accelerated sales.

Sales pipeline is being filled with more customers with scale-up potential

More customers validating products, strengthening the Bio-Works brand.

Focus on growth markets where Bio-Works products have a proven track record of performance.

The “stickiness” effect enables revenue growth and cash flows as customers reach production stage



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Bio-Works

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