



Medication Update 2022

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Conflict of Interest

Dr. Knezevich has no conflicts of interest to report

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Objectives



1. Review the 2022 American Diabetes Association type 2 diabetes guidelines
2. Discuss tirzepatide, a novel GIP / GLP-1 receptor agonist, for the treatment of type 2 diabetes
3. Identify promising novel therapies in phase III clinical trials

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ADA Standards of Medical Care 2022

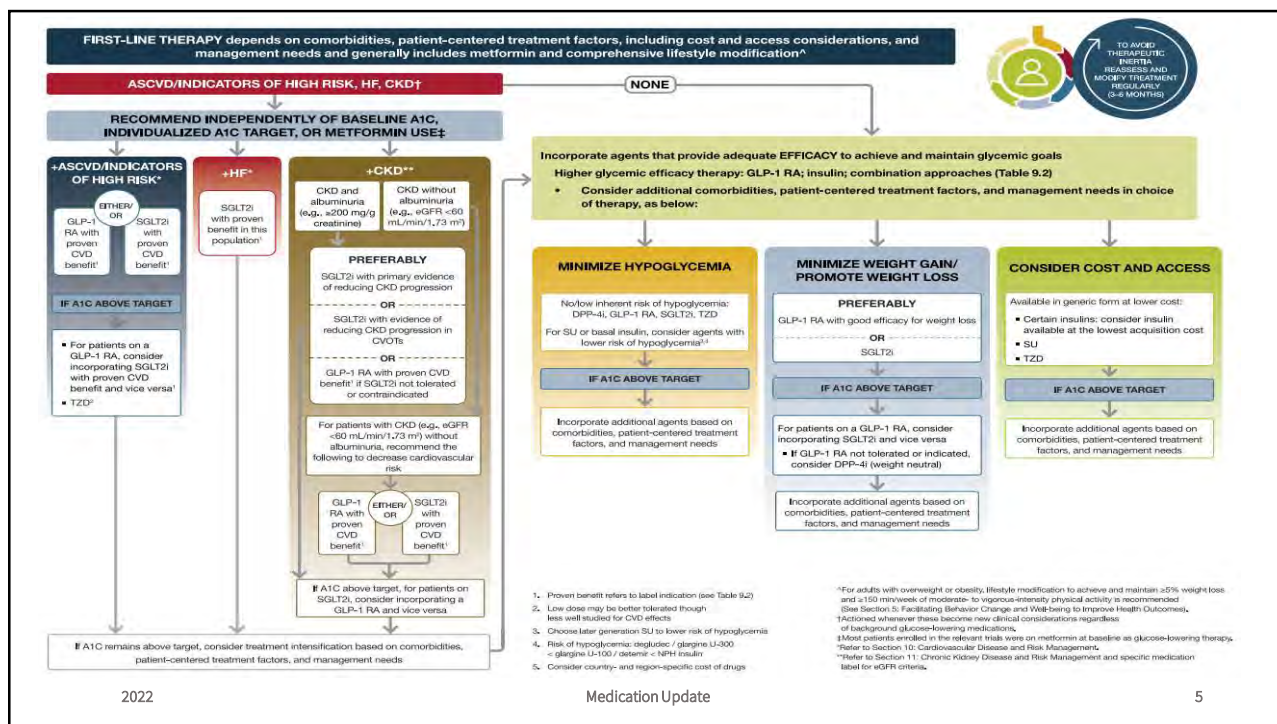


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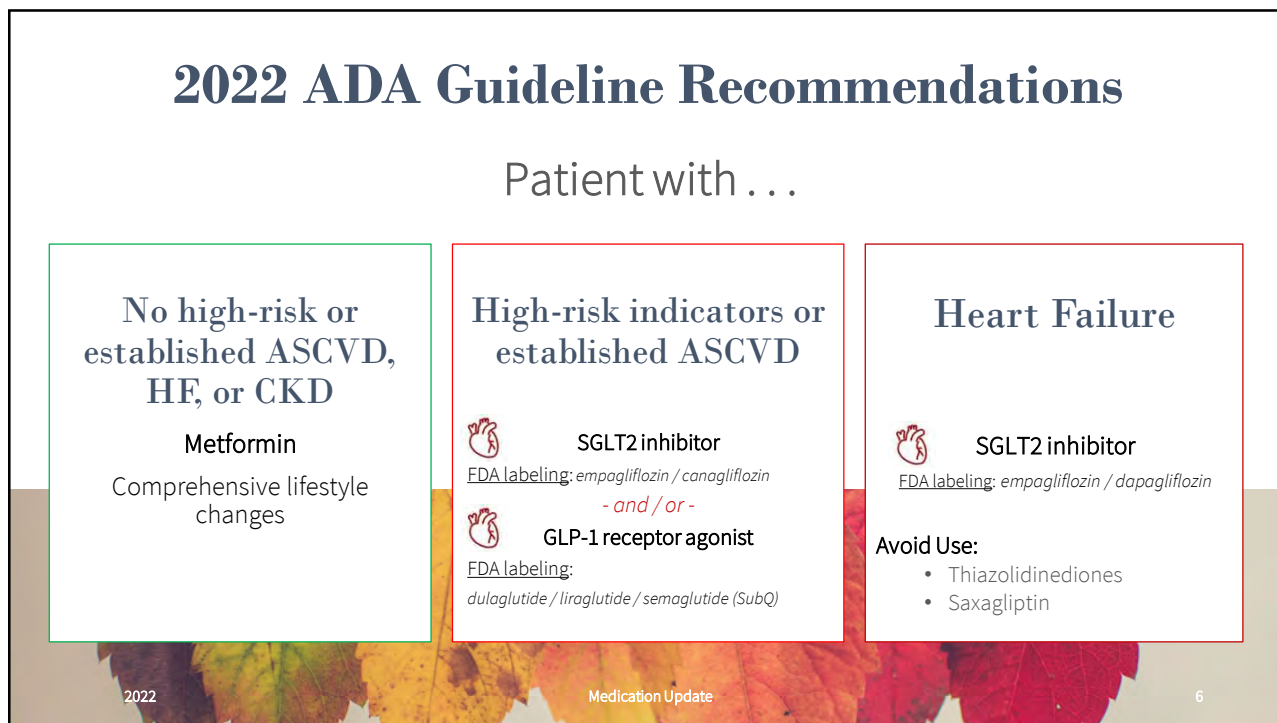
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2022 ADA Guideline Recommendations

Patient with . . .

Chronic Kidney Disease
(eGFR < 60 mL/min)

Albuminuria (≥ 300 mg/g creatinine): SGLT2 inhibitor
 FDA labeling: dapagliflozin / canagliflozin

Albuminuria NOT present:
 SGLT2 inhibitor
 - and/or -
 GLP-1 receptor agonist with CVD benefit
 (dulaglutide / liraglutide / semaglutide (SubQ))

Promote Weight Loss

GLP-1 receptor agonist
 (semaglutide > dulaglutide –
 liraglutide > exenatide > lixisenatide)
 - and/or -
SGLT2 inhibitor

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2022 ADA Guideline Recommendations

No high-risk or established ASCVD, HF, or CKD

Metformin

Comprehensive lifestyle changes

High-risk indicators or established ASCVD

SGLT2 inhibitor
 FDA labeling: empagliflozin / canagliflozin
 - and/or -
GLP-1 receptor agonist
 FDA labeling: dulaglutide / liraglutide / semaglutide (SubQ)

Heart Failure

SGLT2 inhibitor
 FDA labeling: empagliflozin / dapagliflozin

Avoid Use:

- Thiazolidinediones
- Saxagliptin

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2022 ADA Guideline Recommendations

Chronic Kidney Disease

(eGFR < 60 mL/min)

Albuminuria (≥ 300 mg/g creatinine): **SGLT2 inhibitor**
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Heart Failure

SGLT2 inhibitor

Avoid:

- Thiazolidinediones
- Saxagliptin

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Guideline Recommendations

Chronic Kidney Disease

(eGFR < 60 mL/min)

Albuminuria

(≥ 300 mg/g creatinine): SGLT2i (with proven benefit)

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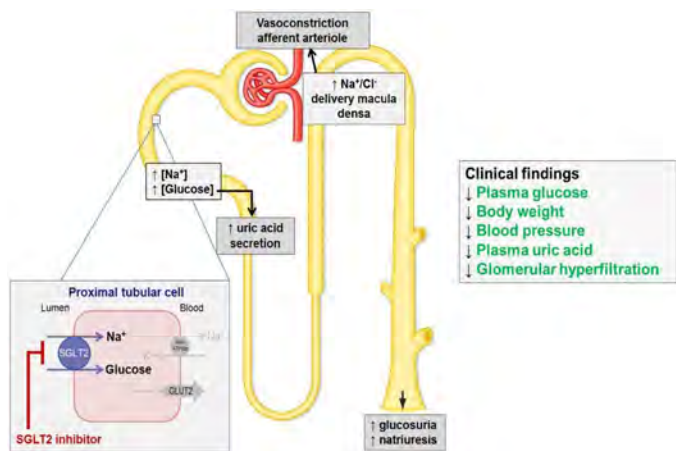
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Mechanism of Action

SGLT-2 inhibitors



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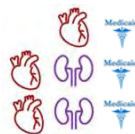
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C/JASN ePress. Published on March 2, 2017 as doi: 10.2215/CJIN.06080616

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SGLT2 Inhibitors



Commercially available oral agents:

Empagliflozin (*JARDIANCE*) - 10 / 25 mg strengths

Dapagliflozin (*FARXIGA*) - 5 / 10 mg strengths

Canagliflozin (*INVOKANA*) - 100 / 300 mg strengths

Ertugliflozin (*STEGLATRO*) - 5 / 15 mg strengths

Combination Formulations

Metformin + SGLT-2 inhibitor

DPP-4 inhibitor + SGLT-2 inhibitor

Metformin + DPP-4 inhibitor + SGLT-2 inhibitor

Effectiveness

Blood glucose lowering affect decreases with diminishing renal function

Cardioprotective affects are

Contraindications

Loss of productivity costing consumers thousands of dollars

Costs

Loss of productivity costing consumers thousands of dollars

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SGLT2 Inhibitors

Orally available agents:

-  Empagliflozin (*JARDIANCE*) - 10 / 25 mg strengths
-  Dapagliflozin (*FARXIGA*) - 5 / 10 mg strengths
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Combination Formulations

- Metformin + SGLT-2 inhibitor
- DPP-4 inhibitor + SGLT-2 inhibitor
- Metformin + DPP-4 inhibitor + SGLT-2 inhibitor

Effectiveness

Millennials account for about a quarter of the \$48 billion spent on other products in 2018

Contraindications

Loss of productivity costing consumers thousands of dollars

Costs

Loss of productivity costing consumers thousands of dollars

Counseling

Sick Day Guidance

SGLT2 Inhibitors

<p>Empagliflozin (JARDIANCE) 10 mg / 25 mg</p> <p>Canagliflozin (INVOKANA) First beautifully designed product that's both stylish and functional</p>	<p>Dapagliflozin (FARXIGA) GLP-1 RA</p> <p>SGLT2-inhibitor</p> <p>Ertugliflozin (STEGLATRO) Designed with the help and input of experts in the field</p>
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2022 Guideline Recommendations Summary

<p>No high-risk indicators or established ASCVD, HF, or CKD Metformin w/ Comprehensive lifestyle changes</p> <p>Heart Failure First beautifully designed product that's both stylish and functional</p>	<p>High-risk indicators or established ASCVD GLP-1 RA</p> <p>SGLT2-inhibitor</p> <p>Chronic Kidney Disease (eGFR < 60 mL/min) Designed with the help and input of experts in the field</p>
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Mechanism of Action

GLP-1 Receptor Agonist

GLP-1

- Caloric intake ↓ ↓
- Energy expenditure =
- Heart rate ↑
- Insulin secretion ↑ ↑
- Glucagon secretion ↓ ↓
- Gastric emptying ↓ ↓
- Chylomicron production ↓ ↓
- No prominent direct effect
- Na excretion ↓ (transient)
- Meal-associated bone remodelling ↑
- Included effects: (Insulin ↑ and glucagon ↓)
- Glucose uptake, glycogen ↑
- Hepatic glucose production ↓
- Intrahepatic fat ↓

Human endogenous GLP-1
T_{1/2}: ~2 mins

Exendin-based GLP-1	Human GLP-1 analogues	
Exenatide (4.19 kDa) 53% homologous	Semaglutide (4.11 kDa) C-16 fatty acid (palmitoyl) 94% homologous	Dulaglutide (59.67 kDa) 90% homologous
Lixisenatide (4.86 kDa) 50% homologous	Liraglutide (3.75 kDa) C-16 fatty acid (palmitoyl) 97% homologous	

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Loveshin JA. Can J Diabetes. 2017; 41: 524-535.

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Daily GLP-1 receptor agonists

<p>Exenatide (BYETTA) 10 mg / 25 mg</p>	<p>Liraglutide (VICTOZA) Multi-dose pen: 0.6, 1.2, 1.8 mg</p>
<p>Lixisenatide (ADLYXIN) First beautifully designed product that's both stylish and functional</p>	<p>Semaglutide (Rybelsus) Tablet: 3, 7 and 14 mg Do NOT crush, split or chew Must be taken ALONE on an empty stomach with only a sip of water</p>

Weekly GLP-1 receptor agonists

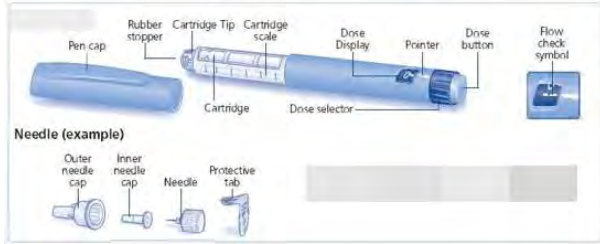
<p>Exenatide ER (BYDUREON BCise)</p>	<p>Dulaglutide (TRULICITY)</p>
<p>Semaglutide (OZEMPIC)</p>	
<p>Injection: 0.25, 0.5, 1, and 2 mg Multidose pen device Must be taken ALONE on an empty stomach with only a sip of water</p>	

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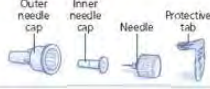
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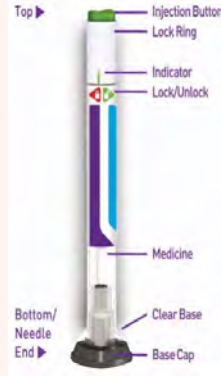
Pen Technology



Needle (example)



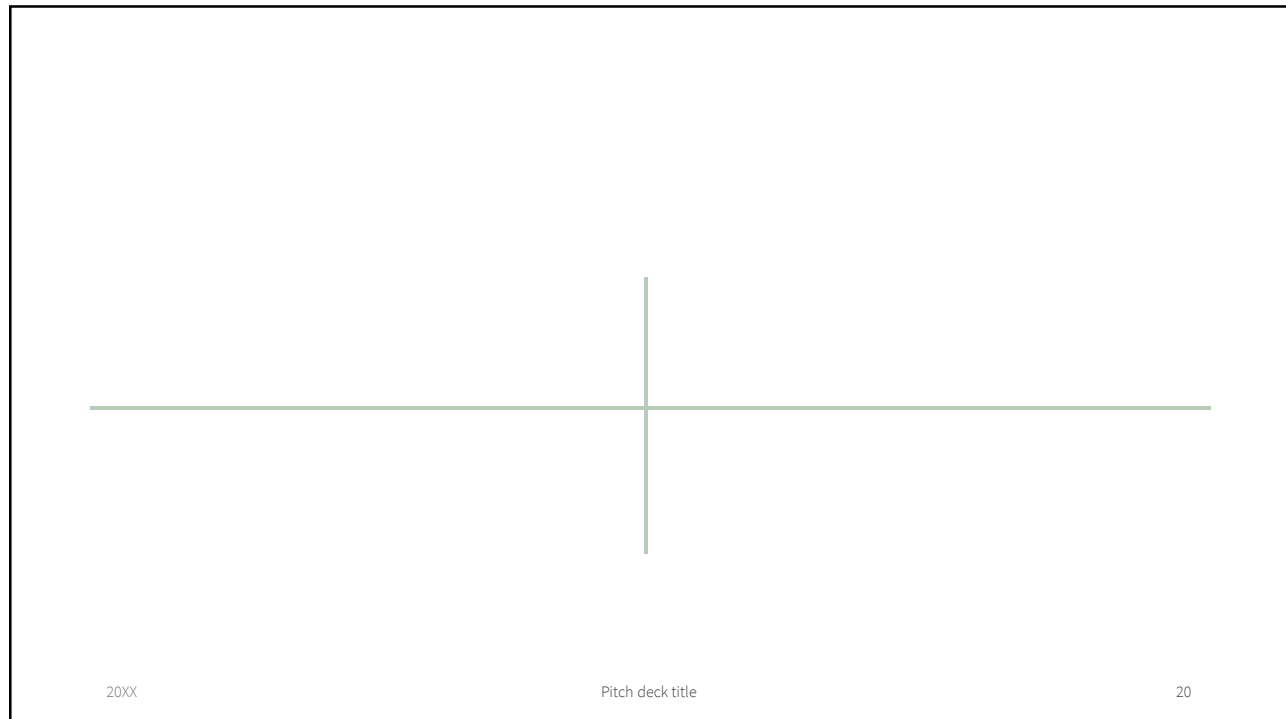
Pen needles required



Exenatide / Liraglutide / Lixisenatide / Semaglutide (SQ)

Dulaglutide

Exenatide ER



Converting Between Agents

Agent	Frequency	Equivalent Dose†			
		0.75 mg	1.5 mg	3.4.5 mg	
Exenatide	QW		2 mg		
Dulaglutide	QW	0.25 mg	0.5 mg	1 mg	2 mg
Semaglutide	QW				
Liraglutide	QD	0.6 mg	1.2 mg	1.8 mg	
Lixisenatide	QD	10 µg	20 µg		
Oral semaglutide	QD	3 mg	7 mg	14 mg	
Exenatide	BID	5 µg	10 µg		

- Is this a formulary issue or a GI side effect?

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Aid to GLP-1


IMPORTANT

- Typically resolves after several weeks of therapy
- Start at a low dose and titrate slowly . . .

Decrease in GI motility 


 Nausea


 Promotion of weight loss


 Increase in satiety (transient)

Tips for patients:

- Eat more frequent small meals
- Avoid spicy foods
- Avoid high-fat foods
- Slow down when eating

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Injection Therapy:

GLP-1 receptor agonists

No high-risk indicators or established ASCVD, HF, or CKD

Metformin with Comprehensive lifestyle changes

First to market

First beautifully designed product that's both stylish and functional

Tested

Conducted testing with college students in the area

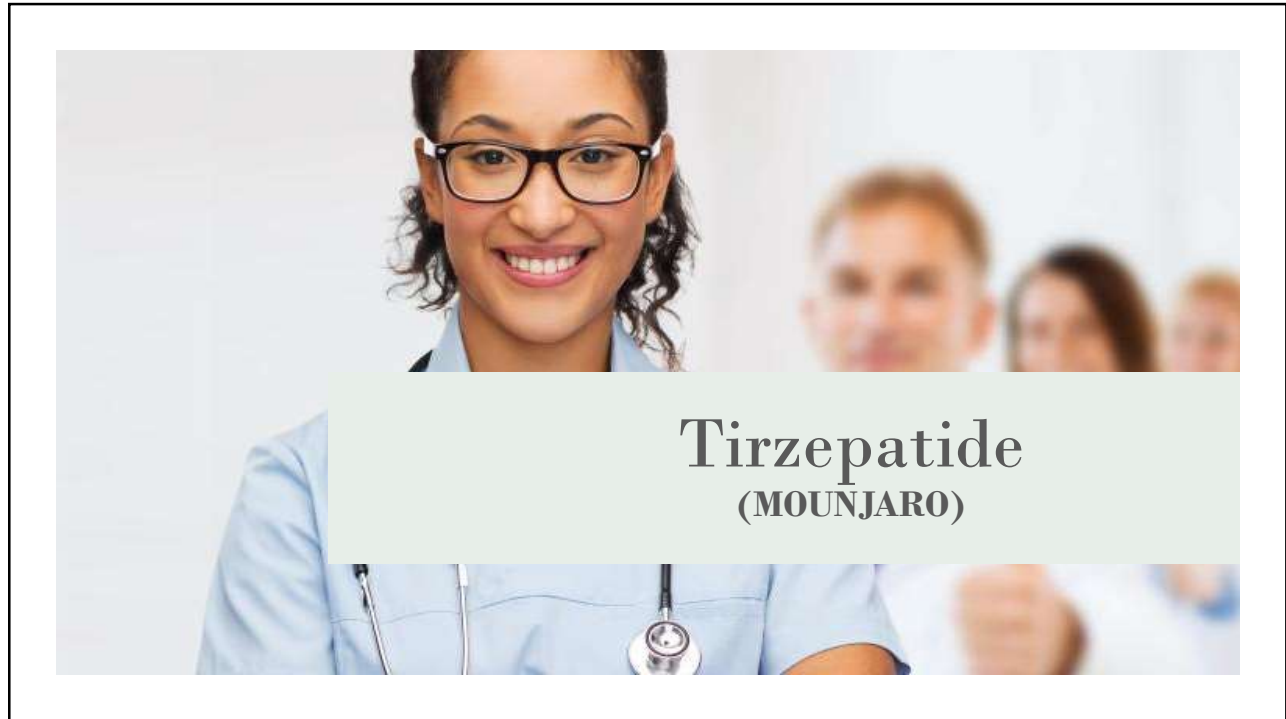
Authentic

Designed with the help and input of experts in the field

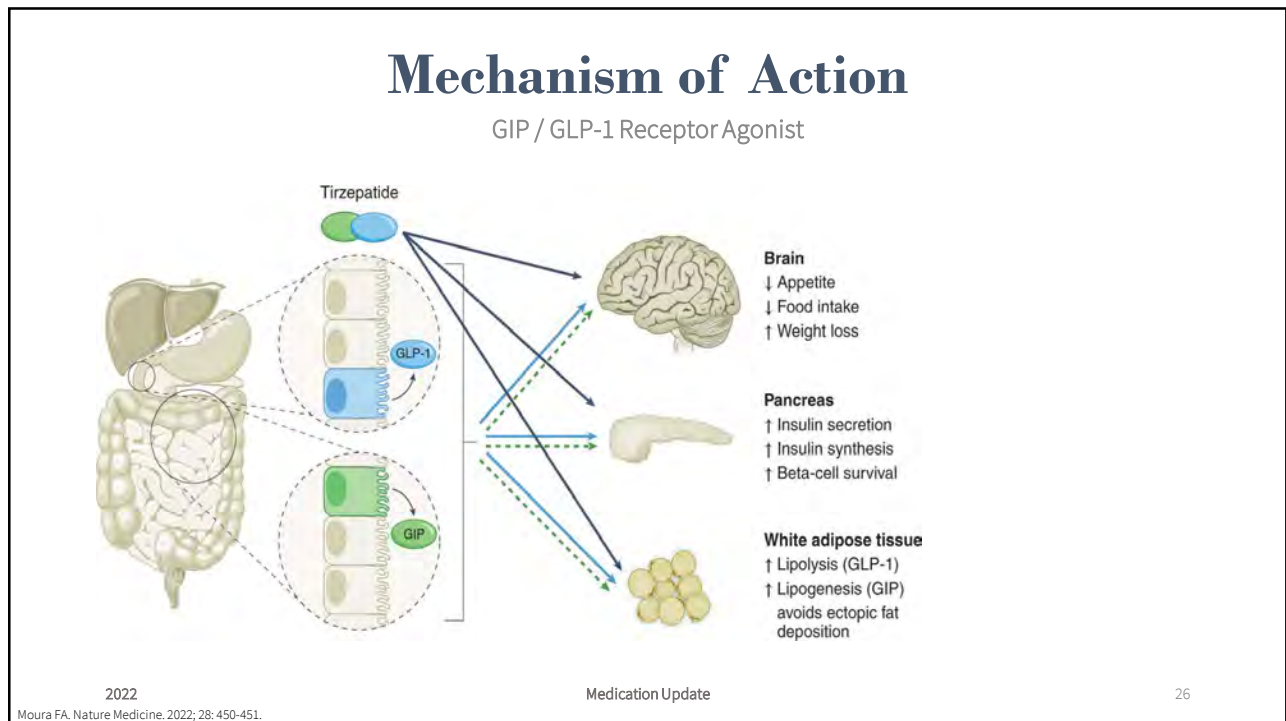


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Tirzepatide (MOUNJARO)

FDA Indication

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Tirzepatide Trials

SURPASS-2

Tirzepatide compared to Semaglutide 1 mg

Open-label

SURPASS-3

Tirzepatide compared to insulin degludec

Open-label

SURPASS-4

Tirzepatide compared to insulin glargine

Open-label

SURPASS-5

Tirzepatide add on to insulin glargine

Double-blind

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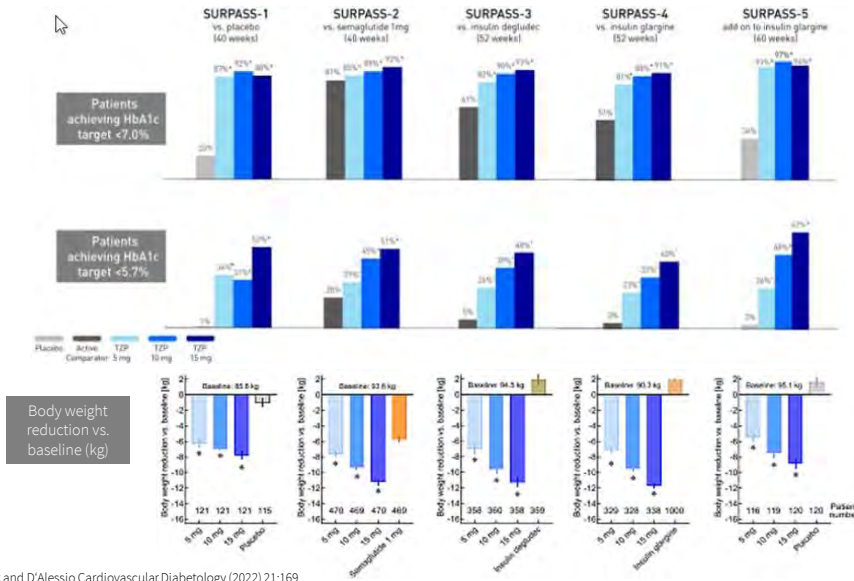
Nauck and D'Alessio Cardiovascular Diabetology (2022) 21:169

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Tirzepatide Trial Results

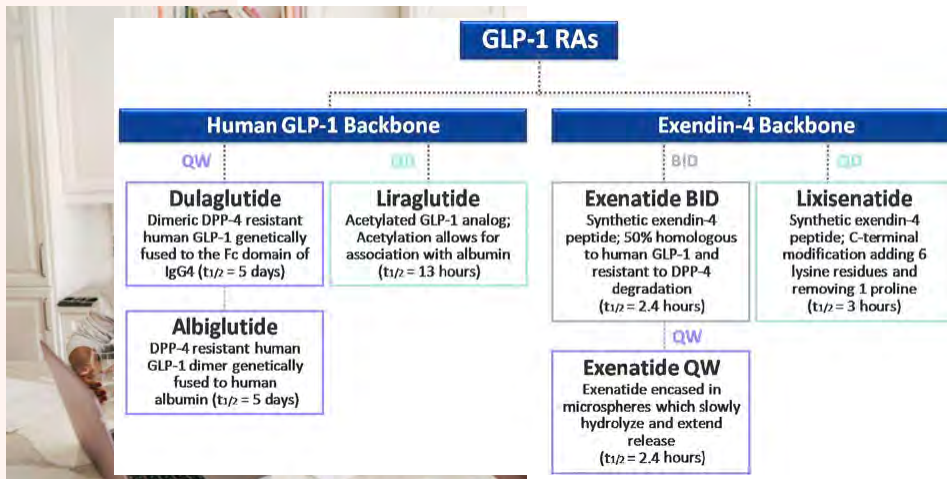


Key Takeaways

- 1 All doses of tirzepatide were superior to placebo, long-acting GLP-1 receptor agonist and basal insulin in reducing HbA1c and body weight
- 2 Tirzepatide does NOT increase the odds of hypoglycemia
- 3 Incidence of GI ADEs experienced with tirzepatide similar to GLP-1 receptor agonists

Nauck and D'Alessio Cardiovascular Diabetology (2022) 21:169

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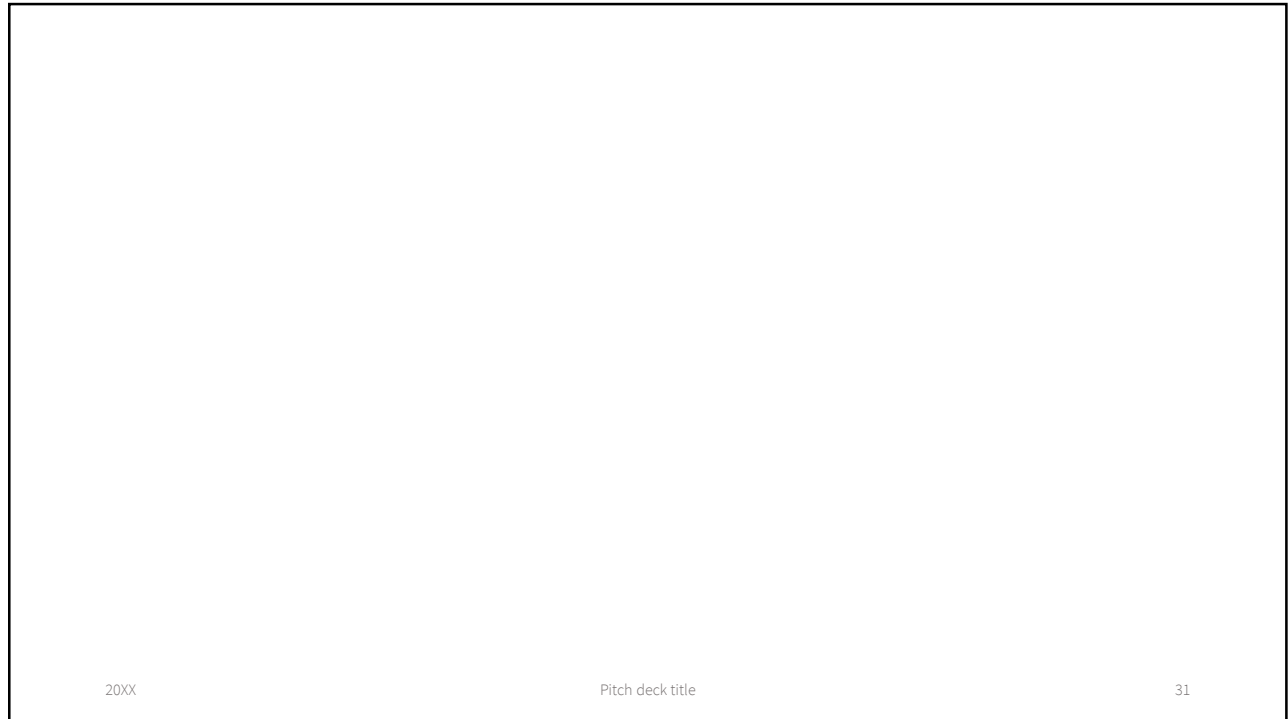


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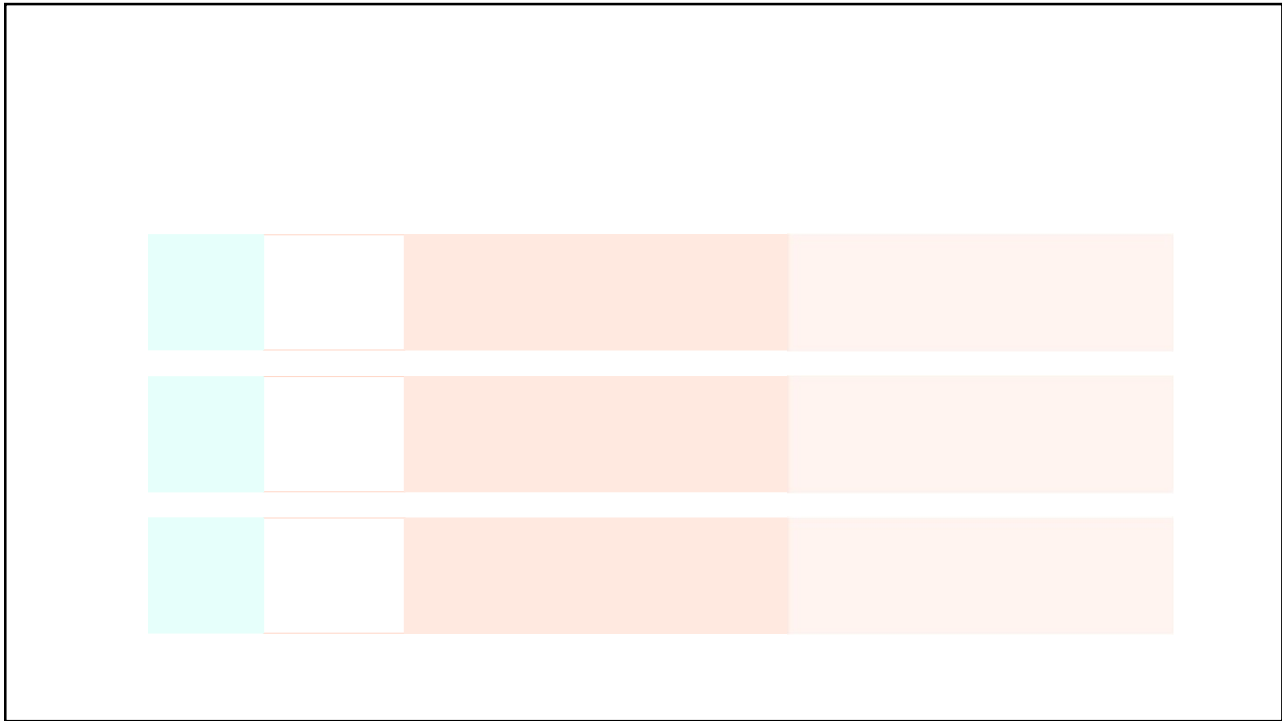
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Insulin Icodec



Weekly basal insulin



Teplizumab

Monoclonal antibody to delay

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Teplizumab



Teplizumab

Monoclonal antibody to delay

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Market comparison

	\$3B	icodec	Addressable market
		Teplizumab	Serviceable market
	\$1B	Few competitors	Obtainable market

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Insulin Icodec



Insulin Icodec

Weekly basal insulin



Teplizumab

Monoclonal antibody to delay

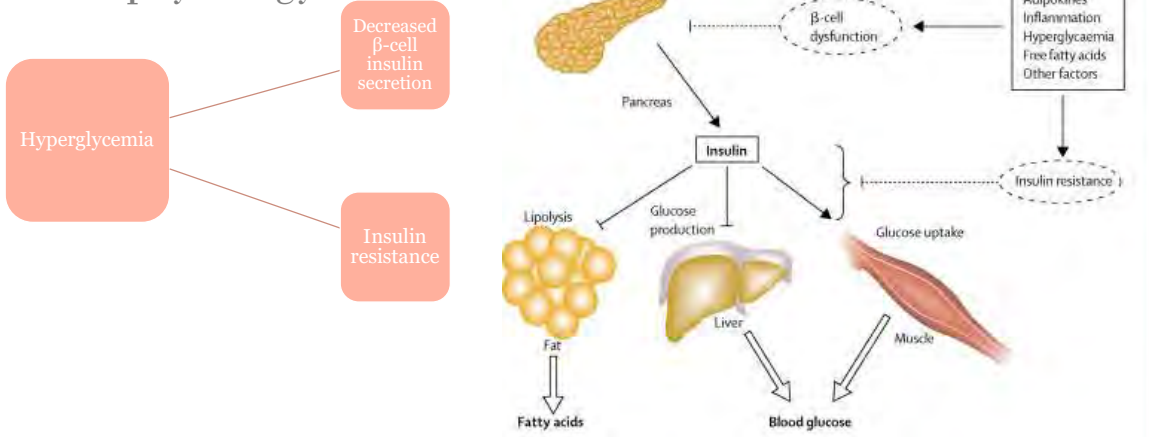
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Etiology | Pathophysiology



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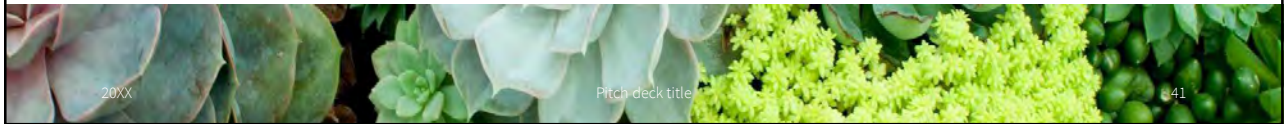
Our competition

Contoso

- Our product is priced below that of other companies on the market
- Design is simple and easy to use, compared to the complex designs of the competitors
- Affordability is the main draw for our consumers to our product

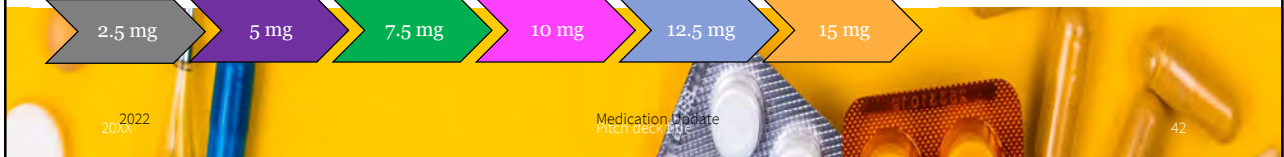
Competitors

- Company A Product is more expensive
- Companies B & C Product is expensive and inconvenient to use
- Companies D & E Product is affordable but inconvenient to use

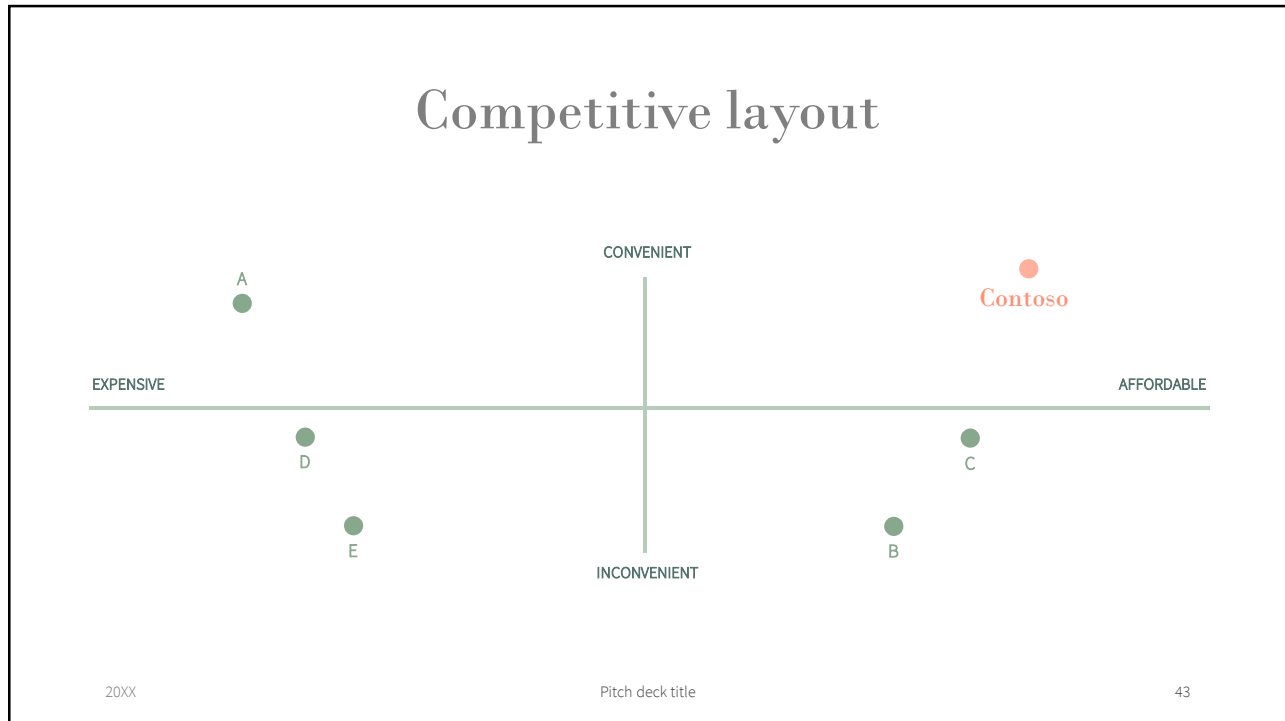


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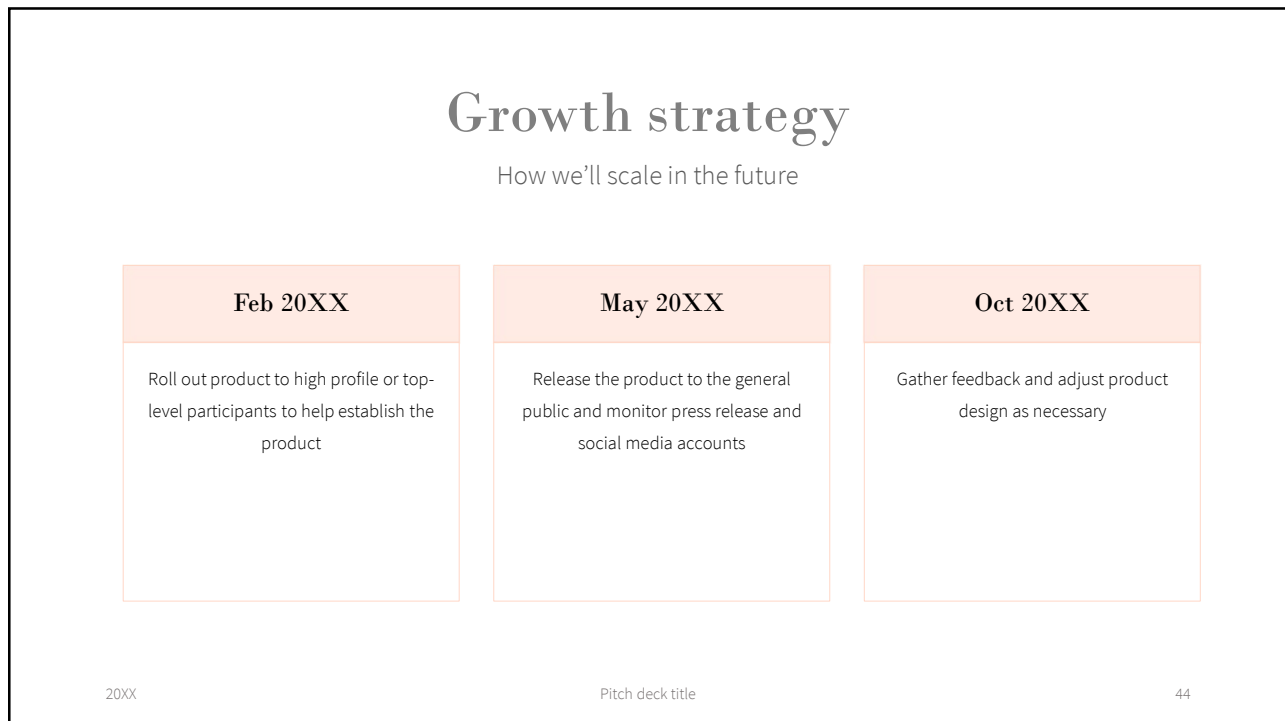
Dosing / Titration / Cost



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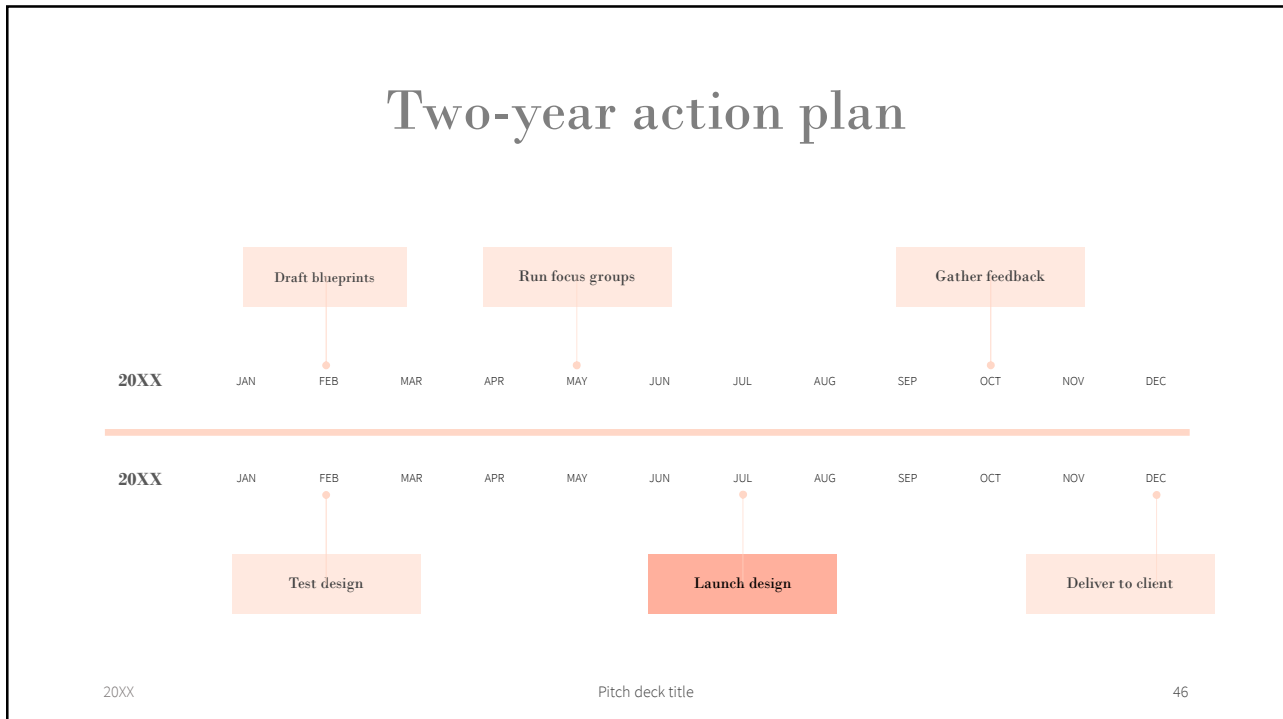
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Financials

	Year 1	Year 2	Year 3	
Income				
Users	50,000	400,000	1,600,000	
Sales	500,000	4,000,000	16,000,000	
Average price per sale	75	80	90	
Revenue @ 15%	5,625,000	48,000,000	216,000,000	
Gross profit	5,625,000	48,000,000	216,000,000	
Expenses				
Sales & marketing	5,062,500	38,400,000	151,200,000	70%
Customer service	1,687,500	9,600,000	21,600,000	10%
Product development	562,500	2,400,000	10,800,000	5%
Research	281,250	2,400,000	4,320,000	2%
Total expenses	7,593,750	52,800,000	187,920,000	

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Meet the team



Takuma Hayashi
President



Mirjam Nilsson
Chief Executive Officer



Flora Berggren
Chief Operations Officer



Rajesh Santoshi
VP Marketing

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Meet the team



Takuma Hayashi
President



Mirjam Nilsson
Chief Executive Officer



Flora Berggren
Chief Operations Officer



Rajesh Santoshi
VP Marketing



Graham Barnes
VP Product



Rowan Murphy
SEO Strategist



Elizabeth Moore
Product Designer



Robin Kline
Content Developer

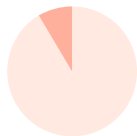
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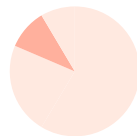
Funding



Properties

\$12,000

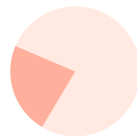
Revenue obtained from property rentals



Angel investments

\$14,000

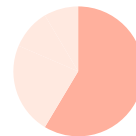
Amount obtained through other investors



Cash

\$32,000

Liquid cash we have on hand



Shares

\$82,000

Number of shares converted into USD

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Summary

At Contoso, we believe in giving 110%. By using our next-generation data architecture, we help organizations virtually manage agile workflows. We thrive because of our market knowledge and great team behind our product. As our CEO says, "Efficiencies will come from proactively transforming how we do business."



Thank you

Jon T. Knezevich, Pharm.D., BCPS, DPLA
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