



Society of Actuaries in Ireland

Prospects for Covid-19 Medicines (Revisited)

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Disclaimer

The views expressed in this presentation are those of the presenter and not necessarily those of the Society of Actuaries in Ireland.



Introductory Summary

- Pfizer/BioNTech vaccine data a great success – but need broader innovation

Medicine Type	Progress & Prospects (ranked out of 5)				
Vaccines	✓	✓	✓	✓	✓
Antivirals	✓	✓	✓	✓	✓
Immunomodulators	✓	✓	✓	✓	✓
Engineered Antibodies	✓	✓	✓	✓	✓

- Pandemic will be over by end 2021 with the following protections in place

Covid-19 Protection	Required Medicinal Innovation
Minimal risk of exposure to virus	Vaccines (herd effect)
Low risk of symptomatic virus infection IF exposed	Vaccines & Engineered Antibodies & Antivirals
Minimal risk of death IF symptomatically infected	Engineered Antibodies & Antivirals & Immunomodulators



Agenda

1. Progress & prospects for vaccines
2. Progress & prospects for antivirals
3. Progress & prospects for immunomodulators
4. Progress & prospects for engineered antibodies
5. End 2021 Scenario & Concluding Thoughts



1. Progress & Prospects for Vaccines



Vaccines – Progress To Date

- Gamble on novel mRNA & viral vector vaccines paying off handsomely
 - Sensational Pfizer/BioNTech 90%+ mRNA vaccine effectiveness (VE)
 - No serious safety issues
 - AstraZeneca/Oxford aiming for 3bn doses a year (vs. 1.5bn worldwide flu capacity)
- Historical 5-10 years for vaccine R&D slashed
 - Novel vaccines allow speedy prototype development
 - Switched from sequential to parallel activities
 - Very generous US “Warp Speed” R&D support (especially smaller biotechs)
- Not everything has gone well
 - Most vaccines need 2 shots (vs. desired 1 shot)
 - Manufacturing sluggish to ramp up



Vaccines – Pfizer/BioNTech Result Considerations

- Trial will continue & ‘final look’ VE will be based on 164 infection events
 - 90%+ VE was an ‘interim look’ based on 94 events (see Appendix A)
- For trial logistical reasons, 90%+ VE was in terms of symptomatic Covid-19
 - A separate VE will be compiled in terms of total Covid-19 infections
 - This separate VE (relevant for herd immunity) could be somewhat lower
- Likely near 100% take-up of 2nd dose by motivated trial volunteers
 - Shingrix shingles vaccine : trial 2nd dose = 95% take-up vs. real-world = c.75% take-up
- No children <12 years included in trial
 - An additional trial will be needed for regulatory approval



Vaccines – Pfizer/BioNTech Result Considerations

- Pregnant women excluded from trial
 - Clinical trials for teratogenicity risk (e.g. thalidomide) not yet completed
 - Initial regulatory approvals may exclude pregnant women
- Trial included ages up to 85
 - Age cohort analyses may indicate waning VE for older lives
- Reduction in % admitted to hospital important to watch
 - Measure captures whether vaccine reduces both incidence & severity of infection
 - Reasonable proxy for reduction in mortality
 - Finite hospital capacity a core contributor to lockdowns & restrictions



Vaccines – Pfizer/BioNTech Result Considerations

- Result PR said ‘up to 50m doses’ available by end 2020
 - But as recently as 5 October the target was ‘up to 100m doses’ by end 2020
- mRNA vaccines require extreme cold storage
 - Pfizer/BioNTech < -70°C & Moderna < -20°C
 - Not suited for many developing countries or rural areas in developed countries
- Next Steps
 - ‘Final’ VE data (based on 164 infection events)
 - Multiple secondary analyses disclosed (including safety)
 - Trial published in leading peer-reviewed academic journal
 - Disclosures from regulatory approval processes (esp. transparent US ‘AdCom’ expert panel)



Vaccines – Timelines (Available in 2021)*

No.	Manufacturer / Sponsor	Vaccine Type	Doses	Capacity p.a. (bn People)	Stage	Trial Size	Trial Result (Expected)	Available in EU
1	Pfizer / BioNTech	mRNA	2	<=0.65	Approval	43,538 (US)	9/11/20	Q1 21
2	Moderna	mRNA	2	0.25 - 0.5	Phase III	30,000 (US)	16/11/20? **	Q1 21
3	AstraZeneca / Oxford University	Viral Vector	2	1.5	Phase III	10,560 (UK) 10,000 (Brazil) 40,051 (US)	Dec. 20 Dec. 20 Q1 21	Q1 21
4	Novavax	Subunit	2	1.0	Phase III	15,000 (UK) 30,000 (US)	Jan. 21 Q2 21	Q2 21
5	Johnson&Johnson	Viral Vector	1-2	0.5 - 1.0	Phase III	60,000 (US-1D) 30,000 (UK-2D)	Q1/Q2 21 Q2 21	Q2 21
6	Medicago / GSK	Subunit	2	0.5	Phase III	30,000 (US/Can.)	Q2 21	Q3 21
7	Sanofi / GSK	Subunit	2	0.5	Phase II	440 (US)	Q4 20	Q3 21
8	CureVac	mRNA	2	0.5	Phase II	691 (S. America)	Q4 20	Q4 21
9	Arcturus	mRNA	1	0.3	Phase II	456 (Singapore)	Q4 20	Q4 21

* Excluded Chinese & Russian candidates

** Has exceeded 53 infectious events needed for “1st look” analysis – will require VE of c.70%+ to pass (see Appendix A)



Vaccines – Orders & Roll-Out (EU & UK)

No.	Manufacturer / Sponsor	By	Order Finalised	Doses Ordered	Doses Optioned	Doses Ordered - % Population Vaccinated	Available to Dose
1	Pfizer / BioNTech	EU	11 November	200m	100m	22%	Q1 21
		UK	20 July	40m	-	30%	
2	Moderna	EU	Not Yet	80m	80m	9%	Q1 21
3	AstraZeneca / Oxford University	EU	14 August	300m	100m	33%	Q1 21
		UK	17 May	100m	-	75%	
4	Novavax	UK	14 August	60m	-	45%	Q2 21
5	Johnson & Johnson	EU	8 October	200m	200m	22% - 44%	Q2 21
		UK	14 August	30m	22m	22% - 45%	
6	Sanofi / GSK	EU	18 September	300m	-	33%	Q3 21
		UK	29 July	60m	-	45%	
7	CureVac	EU	Not Yet	225m	180m	25%	Q3 21

- Total current orders (% population) : EU = 144% - 166% & UK = 217% - 240%
- Population-wide vaccination : EU = c.Q4 21 & UK = c.Q3 21
- Moderna = smallest EU order & not selected by UK



2. Progress & Prospects for Antivirals



Antivirals – Summary Points

- Antiviral = any drug that attacks or inhibits an invasive virus
- Plausible for 3 new antivirals to be launched by end 2021
- Quick to make with no capacity constraints (unlike antibodies & vaccines)
- For outpatients, reducing hospitalisation rates is key target
- Antiviral combos could materially reduce mortality



Antivirals – Progress To Date

- Veklury (Remdesivir) is the only approved Covid-19 antiviral
 - Hospital Length of Stay : 15 to 10 days (p-value* <0.1%)
 - Faster bed turnover boost hospital capacity
 - Mortality : 15.2% to 11.4% (p-value 7% so didn't prove)
 - But WHO Solidarity trial indicates only minor benefits
- Hydroxychloroquine (HCL) discredited
 - In UK Recovery & WHO Solidarity trials, mortality worsened
- Lopinavir & Ritonavir (proven HIV antivirals) failed in Recovery & Solidarity trials
- Figuring out what doesn't work is worthwhile progress

* P-value = probability the difference between placebo trial arm & drug trial arm is due to chance (generally <5% needed for regulatory approval)



Antivirals – Prospects

- #1 – Azithromycin (Tablet Delivery)
 - Old antibiotic with some broad antiviral properties
 - Included in the very large UK Recovery trial so modest benefits provable
- #2 – Veklury (Inhaler Delivery)
 - Currently restricted to inpatients by IV delivery
 - Trialling inhaler delivery for outpatients or if exposed to virus
 - Antiviral rule of thumb : earlier use = better outcomes
- #3 – Molnupiravir (Capsule Delivery)
 - Similar “Trojan Horse” mechanism as Veklury
 - Capsule delivery so usable in outpatients



Antivirals – Prospects II

- #4 – PF-07304814 (IV Delivery)
 - Targets critical part of Covid-19 virus (3CL protease)
 - Targeted approach similar to successful HIV & Hepatitis C (HCV) antivirals
- #5 – AT-527 (Tablet Delivery)
 - Also targets critical part of Covid-19 virus (RNA polymerase)
 - Roche paid \$350m initial signing fee for ex-US rights
- #6 – Avigan (Tablet Delivery)
 - Influenza antiviral only approved in Japan (teratogenic!)
 - In Japanese hospital trial, Length of Stay = 15 to 12 days (p-value 1.4%)
 - Larger trials underway in US & UK



Antivirals - Timelines

No.	Antiviral Name	Manufacturer / Sponsor	Treatment Setting	Trial Stage	Trial Size (Patients)	Trial Result Expected	Drug Available
1	Azithromycin	Oxford University (UK)	Inpatient	Phase III	5,000+	Q1 21	Q1 21
2	Veklury (Inhaled)	Gilead (US)	Outpatient	Phase II	281	Q4 20	Q3 21
3a	Molnupiravir	Merck (US)	Outpatient	Phase III	1,450	Q2 21	Q3 21
3b	Molnupiravir	Merck (US)	Inpatient	Phase III	1,300	Q2 21	Q3 21
4	PF-07304814	Pfizer (US)	Inpatient	Phase I	56	Q4 20	Q4 21
5a	AT-527	Atea (US) / Roche (Swiss)	Outpatient	<Phase III	???	???	???
5b	AT-527	Atea (US) / Roche (Swiss)	Inpatient	Phase II	190	Q1 21	Q4 21
6a	Avigan	Appili (Canada)	Outpatient	<Phase III	826	Q3 21	Q4 21
6b	Avigan	Fujifilm (Japan)	Inpatient	Phase III	450	Q2 21	Q4 21



3. Progress & Prospects for Immunomodulators



Immunomodulators – Introduction & Summary Points

- Hyperinflammation = underlying cause of many severe Covid-19 cases
- Immunomodulator = any drug that calms inflammation and/or immune system
- Hope is an existing immunomodulator will benefit patients
- Dexamethasone was a solid – but isolated – success
- A lot of trials in progress but many are too small & are running late



Immunomodulators – Progress To Date

- Covid-19 hyperinflammation is unique but, worryingly, still not understood
 - Abnormal blood clotting is a good example
- Sharp contrast with clarity on Covid-19 antiviral targets
- Focus is on repurposing existing immunomodulators
 - Steroids (e.g. dexamethasone)
 - Autoimmune disease drugs (treating arthritis, MS, asthma, psoriasis, lupus, Crohn's etc.)
 - Leukaemia/lymphoma/myeloma drugs (treating cancerous immune system)



Immunomodulators – Dexamethasone Triumph

UK Recovery Trial Category	Number of Inpatients	Number of Deaths	Dexamethasone Change in Mortality	P-Value
All	6,425	1,519	-13%	<0.1%
Ventilation Support	1,007	372	-35%	<0.1%
Oxygen Only Support	3,883	925	-20%	0.2%
No Oxygen Support	1,535	222	+22%	14%

- Only trial to date to convincingly show mortality benefit
- Sheer size of trial allowed credible secondary analyses
- ‘No Oxygen Support’ category did worse on Dexamethasone
 - Weakening immune system to Covid-19 outweighs suppressing hyperinflammation?
 - Insight of excluding this category boosted mortality benefit from 13% to 20%-35%
- Note that 222 deaths & 22% adverse trend not enough to hit 5% p-value threshold



Immunomodulators – Other Progress

- Olumiant – Arthritis (JAK Mechanism) - Hospitalised Covid-19 Patients
 - Length of Stay = 8 to 7 days (p-value 4% - so a success)
 - Mortality = 7.8% to 5.1% (p-value 9% - so not proven)
 - Only seeking approval in US
- Actemra & Kevzara – Arthritis (IL-6 Mechanism) – Hospitalised Covid-19 Patients
 - 3 out of 4 completed trials failed (all moderately sized)
 - UK Recovery running likely definitive large trial with high doses
- Ilaris – Fever Syndromes (IL-1 Beta Mechanism) – Hospitalised Covid-19 Patients
 - Mortality = 7.2% to 4.9% (p-value = 33%)
 - Frustrating a 32% fall in mortality insufficient for success – 454 lives trial too small



Immunomodulators - Timelines

No.	Immunomodulator Name	Manufacturer / Sponsor	Drug Mechanism	Trial Stage	Trial Size	Trial Result Expected	Drug Available
1	Actemra	Oxford University	IL-6	Phase III	c.2,500+	Q1 21	Q1 21
2	CD24Fc	OncolImmune	Siglec 10	Phase III	241	Q4 20	Q2 21
3	Aviptadil	Relief	VIP	Phase III	165	Q1 21	Q2 21
4	Lenzilumab	Humanigen	GM-CSF	Phase III	515	Q1 21	Q3 21
5	Tavalisse	Rigel/Imperial College	SYK	Phase III	456	Q3 21	Q3 21
6	Ultimoris	Alexion	C5	Phase III	270	Q3 21	Q3 21
7	Otilimab	GSK	GM-CSF	Phase III	800	Q2 21	Q4 21
8	Mavrimumab	Kiniksa	GM-CSF	Phase III	573	Q2 21	Q4 21
9	EB05	Edesa	TLR4	<Phase III	865	Q2 21	Q4 21
10	Vilobelimab	InflaRx	C5a	Phase III	360	Q3 21	Q4 21

- Bar Actemra, trials likely too small to prove mortality reductions
- Most trial timelines have slipped from original targets



4. Progress & Prospects for Engineered Antibodies



Engineered Antibodies – Summary Points

- Engineered antibodies = enhanced forms of immune system antibodies
- Initial results in outpatients are excellent
- Setbacks in inpatient trials - not suited for the sickest people?
- Alternative for c.1% population not suitable for vaccination
- Manufacturing at required scale is the big obstacle



Engineered Antibodies - Background

- Antibodies a core immune defence - but quantity & quality may be insufficient
- Concept : enhance the best 'natural' antibodies & then mass produce
 - Successful with RSV and Ebola viruses
- Double (cocktail) antibody design practically eliminates virus mutation risk
- 'Natural' antibodies have a c.1-2 month lifespan
 - Some engineered antibodies designed for 6-12 months & are an alternative to vaccines
- Drawback is bypassing immune system's antibody-making factories
 - Engineered antibody course (c. 7g weight) vs vaccine shots (c. 200µg) = 35,000:1 ratio!



Engineered Antibodies – Progress To Date

- 4 distinct patient settings
 - Inpatients, outpatients, exposed to virus & vaccine alternative
- Excellent interim data in outpatient setting

Antibody Name	Number of Trial Participants	Lowered Viral Count?	Hospitalisation Reduction	Treatment Algorithm?
REGN-COV2	799	Yes	-57%	Yes
Bamlanivimab & Etesevimab	452	Yes	-75%	Yes

- Trial data in the inpatient setting has been poor
 - Bamlanivimab trial stopped early for futility
 - REGN-COV2 trial partially stopped early for futility (if requiring high flow oxygen)
 - Suggests antibodies ineffective when hyperinflammation the key issue



Engineered Antibodies - Timelines

Antibody Name	Manufacturer / Sponsor	Lifespan (months)	Approval Inpatient	Approval Outpatient	Approval Exposed	Approval Vaccine
REGN-COV2	Regeneron (US)	1-2	Q2 21	Q2 21	Q4 21	N/A
REGN-COV2	Oxford University (UK)	1-2	Q3 21	N/A	N/A	N/A
VIR-7831	Vir (US) / GSK (UK)	3-6	Q3 21	Q2 21	Q1 22	N/A
CT-P59	Celltrion (S. Korea)	1-2	Q4 21	Q3 21	Q3 21	N/A
Bamlanivimab (&Etesevimab)	Eli Lilly (US)	1-2	Failed	Q4 21	Q4 21	N/A
AZD7442	AstraZeneca (UK)	6-12	Q4 21	Q4 21	Q4 21	Q4 21
MP0420	Novartis (Swiss)	6-12	H1 22	H1 22	H1 22	H2 22

- Wide EU availability could lag approval due to constrained production
- Regeneron, AstraZeneca & Novartis initial production bought by national govts.



6. End 2021 Scenario



Current Medicinal Protection

WHO Patient State*	WHO Score*	WHO Descriptor*	Approved Medicinal Treatments
Uninfected	0	No evidence of infection	Pfizer/BioNTech vaccine (max. 22%-33% population)
Ambulatory	1	No limitation of activities	None
	2	Limitation of activities	None
Hospitalised Mild Disease	3	No oxygen therapy	Veklury (IV) (5 days)
	4	Low flow oxygen	Dexamethasone Veklury (IV) (5 days)
Hospitalised Severe Disease	5	High flow oxygen or non-invasive ventilation	
	6	Intubation & ventilation	Dexamethasone Veklury (IV) (10 days)
	7	Ventilation & organ support	
Dead	8	Death	N/A

* WHO Ordinal Scale is the worldwide standard for Covid-19 infection states



Hypothetical Medicinal Protection (End 2021)

WHO Patient State	WHO Score	WHO Descriptor	Hypothetical Medicinal Treatments
Uninfected	0	No evidence of infection	Vaccine (mRNA / viral vector / subunit with adjuvant) Vaccine alternative (long-acting engineered antibodies) Engineered antibodies (exposed to Covid-19 & high-risk)
Ambulatory	1	No limitation of activities	Engineered antibodies (high-risk) Oral/Inhaled antiviral cocktail (high-risk)
	2	Limitation of activities	Engineered antibodies (high-risk) Oral/Inhaled antiviral cocktail (all)
Hospitalised Mild Disease	3	No oxygen therapy	Engineered antibodies (all) IV antiviral cocktail (all) Dexamethasone (high-risk)
	4	Low flow oxygen	Engineered antibodies (all) IV antiviral cocktail (all) Dexamethasone (all)
Hospitalised Severe Disease	5	High flow oxygen or non-invasive ventilation	Dexamethasone (all) IV antiviral cocktail (all)? Immunomodulator (all)?
	6	Intubation & ventilation	
	7	Ventilation & organ support	



Is End 2021 Hypothetical Medicinal Protection Realistic?

Date	Drug Name	Drug Type	Setting	Outcome
29/04/20	Veklury (IV)	Antiviral	Inpatient	✓✓
05/06/20	Hydroxychloroquine	Antiviral	Inpatient	✗
16/06/20	Dexamethasone	Immuno	Inpatient	✓✓✓
17/06/20	Hydroxychloroquine	Antiviral	Inpatient	✗
29/06/20	Lopinavir & Ritonavir	Antiviral	Inpatient	✗
02/07/20	Kevzara	Immuno	Inpatient	✗
29/07/20	Actemra	Immuno	Inpatient	✗
01/09/20	Kevzara	Immuno	Inpatient	✗
14/09/20	Olumiant	Immuno	Inpatient	✓
18/09/20	Actemra	Immuno	Inpatient	✓
29/09/20	Favipiravir	Antiviral	Inpatient	✓
15/10/20	Interferon	Antiviral	Inpatient	✗
15/10/20	Lopinavir & Ritonavir	Antiviral	Inpatient	✗
15/10/20	Veklury (IV)	Antiviral	Inpatient	✗
26/10/20	Bamlanivimab	Antibody	Inpatient	✗
06/11/20	Ilaris	Immuno	Inpatient	✗
09/11/20	BNT162b	Vaccine	Vaccination	✓✓✓

Date	Drug Name	Drug Type	Setting	Outcome
Q4 20	Convalescent Plasma	Antibody	Inpatient	
	CD24Fc	Immuno	Inpatient	
	Jakafi	Immuno	Inpatient	
	AZD1222 (Brazil)	Vaccine	Vaccination	
	AZD1222 (UK)	Vaccine	Vaccination	
	mRNA-1273	Vaccine	Vaccination	

Date	Drug Name	Drug Type	Setting	Outcome
Q1 21	CT-P59	Antibody	Exposed	
	CT-P59	Antibody	Outpatient	
	REGN-COV2	Antibody	Inpatient	
	REGN-COV2	Antibody	Outpatient	
	VIR-7831	Antibody	Outpatient	
	ABX464	Antiviral	Inpatient	
	APN01	Antiviral	Inpatient	
	Azithromycin	Antiviral	Inpatient	
	Actemra	Immuno	Inpatient	
	Actemra & Veklury	Immuno	Inpatient	
	Aviptadil	Immuno	Inpatient	
	Betaseron	Immuno	Inpatient	
	Jakafi	Immuno	Inpatient	
	Lenzilumab	Immuno	Inpatient	
	Olumiant	Immuno	Inpatient	
Farxiga	Other	Inpatient		
	NVX-CoV2373 (UK)	Vaccine	Vaccination	

Date	Drug Name	Drug Type	Setting	Outcome
Q2 21	Bamlanivimab	Antibody	Exposed	
	Bamlanivimab & Etesevimab	Antibody	Outpatient	
	CT-P59	Antibody	Inpatient	
	Favipiravir	Antiviral	Inpatient	

Date	Drug Name	Drug Type	Setting	Outcome
Q2 21 Cont.	Molnupiravir	Antiviral	Inpatient	
	Molnupiravir	Antiviral	Outpatient	
	Cenicriviroc	Immuno	Inpatient	
	Firazyr	Immuno	Inpatient	
	Mavrilimumab	Immuno	Inpatient	
	Otezla	Immuno	Inpatient	
	Otilimab	Immuno	Inpatient	
	Razuprotafib	Immuno	Inpatient	
	Aspirin	Other	Inpatient	
	Xarelto & Aspirin	Other	Inpatient	
	AZD1222 (US)	Vaccine	Vaccination	
	CVnCoV	Vaccine	Vaccination	
	NVX-CoV2373 (US)	Vaccine	Vaccination	
	Sanofi/GSK Vaccine	Vaccine	Vaccination	

Date	Drug Name	Drug Type	Setting	Outcome
Q3 21	AZD7442	Antibody	Exposed	
	AZD7442	Antibody	Inpatient	
	AZD7442	Antibody	Outpatient	
	AZD7442	Antibody	Vaccination	
	hVIG	Antibody	Inpatient	
	REGN-COV2	Antibody	Exposed	
	VIR-7831	Antibody	Exposed	
	VIR-7831	Antibody	Inpatient	
	AT-527	Antiviral	Outpatient	
	Favipiravir	Antiviral	Outpatient	
	PF-07304814	Antiviral	Inpatient	
	Veklury (Inhaled)	Antiviral	Outpatient	
	EB05	Immuno	Inpatient	
	Meplazumab	Immuno	Inpatient	
	Tavalisse	Immuno	Inpatient	
	Ultomiris	Immuno	Inpatient	
	Vilobelimab	Immuno	Inpatient	
	Aspirin	Other	Inpatient	
ARCT-021	Vaccine	Vaccination		
CoVLP	Vaccine	Vaccination		
	UQ-CSL V451	Vaccine	Vaccination	

Date	Drug Name	Drug Type	Setting	Outcome
Q4 21	MP0420	Antibody	Exposed	
	MP0420	Antibody	Inpatient	
	MP0420	Antibody	Outpatient	
	Aplidin	Antiviral	Inpatient	
	AT-527	Antiviral	Inpatient	
	IMU-838	Antiviral	Inpatient	
	SNG001	Antiviral	Inpatient	
	SNG001	Antiviral	Outpatient	
	AZD7442	Antibody	Vaccination	

70+ shots on target between now and end 2021!



Concluding Thoughts

Time Period	Peak Restrictive Measures (consistent with <u>predicted</u> medicinal innovation)
Q1 2021	Level 5
Q2 2021	Level 3-4
Q3 2021	Level 2
Q4 2021	Level 1

Christmas 2021 will be a return to full normality in Ireland



Appendix A – Vaccine Trials - Result Timelines In Detail

	Pfizer / BioNTech (US Trial)		Moderna (US Trial)		AstraZeneca / Oxford University (UK Trial)		AstraZeneca / Oxford University (US Trial)	
Trial Size	43,538		30,000		10,560		40,051	
Trial Started	27 July		27 July		22 May		31 August	
	N*	VE*	N	VE	N	VE	N	VE
1st Look	32	77%	53	74%	???	???	75	c.65%
2nd Look	62	68%	106	57%	???	???	N/A	N/A
3rd Look	92	63%	N/A	N/A	N/A	N/A	N/A	N/A
4th Look	120	59%	N/A	N/A	N/A	N/A	N/A	N/A
Final Look	164	52%	151	50%	???	c.50%	150	c.50%
Mgt. Guidance	“Nov. 2020”		“Nov. 2020”		“Dec. 2020”		“H1 2021”	

* N = number of infection events needed to trigger a look & VE = minimum required vaccine effectiveness for success

- It’s clear trial designs didn’t envisage 90%+ VE was plausible!
- US regulator requested Pfizer/BioNTech cancel its 1st look (32 events clinically insufficient)
- By the time debate over 1st look was resolved, number of events had shot up to 94
- Personal view : Pfizer/BioNTech 1st look out of line with its peers & correct decision to drop it



Q&A